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Efeitos do Treino Neuromuscular na Paralisia Facial Periférica Idiopática em Fase Aguda, Subaguda e Crónica

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PALAVRAS-CHAVE: PARALISIA BELL; EXERCÍCIO FACIAL; REABILITAÇÃO FACIAL; SIMETRIA E FUNÇÃO FACIAL; SINCINESIAS.

Não há factos eternos, como não há verdades absolutas

Friedrich Nietzsche

Esta longa viagem científica finalizou na paragem dos “agradecimentos”, a simplicidade desta palavra, abraçada a um gesto de bondade, de generosidade e de humanidade, tinha o encanto de uma sustentável leveza de nomes e de contributos. Inesperadamente, a espontaneidade da catalogação desvaneceu e por longos e infindáveis minutos o pensamento voou e a actividade motora paralisou…o tempo de esboçar e personificar as faces, delineando individualidades ou quiçá traçando a essência do realismo artístico na tela cerebral, que paulatinamente sofreu metamorfoses pelas sucessivas interrupções sinápticas e convergiu no surrealismo. Neste mapa mental, as reminiscências do *“The Empire of Lights”* desofuscaram e entoaram harmoniosamente melodias líricas de um poema luso “Não sei por onde vou… Só sei que não vou por aí!”

Nesta página, os preceitos académicos são naturalmente desnudados de dogmas, de ciência, de exactidão, de perfeição… assomando o sentimento de liberdade, emoção, afecto, humildade e respeito. O trilho científico da autora foi edificado sobre alicerces de perseverança, esperança, inocência, dedicação, amizade, amor, vida…resultantes de percursos sem saída, sentido único, proibido…e de visibilidade turva ou cristalina. Na intemporalidade do passado, presente e futuro e de delongas mutações camaleónicas, a personalidade da autora foi continuamente impulsionada por uma palete de cores reflectidas de saberes reais e fictícias. Imortalizar nesta página as memórias destas vivências e descrever a erudição cultural e científica absorvida sofregamente, parece uma proeza divina ou uma narrativa humanamente prosaica e redutora. Assim, a bifurcação deste “fim” poderia culminar com um toque em *delete* e proporcionaria ao leitor a neutralidade desta página, presenteando-o com a volúpia das suas fantasias, a primazia das suas especulações…ou neste subtil esquisso pensamento, que ousadamente a autora o submete ao espectro óptico do leitor… e com esta reflexão e respectiva vénia, a autora agradece a TODAS as pessoas que engrandeceram o seu conhecimento, nutriram os seus sonhos e persistem no percurso da sua vida.

OBRIGADA pela inspiração!

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Resumo

A paralisia facial periférica idiopática (PFPI) é uma disfunção súbita do nervo facial de etiologia desconhecida, desencadeando a paralisia ou paresia dos músculos da mímica facial. As sequelas da PFPI são essencialmente de caracter funcional (assimetria facial, incapacidade de comer, beber e comunicar), afectando igualmente o estado psicossocial dos indivíduos, promovendo o isolamento, a depressão e a ansiedade. Na literatura, diversas modalidades de prevenção secundária têm sido propostas, tal como o treino neuromuscular facial (TNMF) subsistindo a controvérsia científica. O principal objectivo desta dissertação foi avaliar os efeitos do TNMF em doentes com PFPI nas distintas fases de evolução. A dissertação incluiu duas revisões sistemáticas **(estudo I e II)**, seguida de dois estudos originais, observacionais e prospetivos. As revisões sistemáticas, com estudos de natureza aleatória e controlada, analisaram o efeito do TNMF na função e na simetria facial, na fase aguda, subaguda e crónica da PFPI, assim como averiguaram a eficácia do TNMF combinado com os fármacos. O **estudo III** investigou a eficácia do uso de corticosteróides combinados com o TNMF, na fase aguda e subaguda da PFPI, na recuperação dos doentes. O **estudo IV** examinou a eficácia do TNMF na recuperação e na prevenção de ocorrência de sincinesias, durante um período de 12 meses de *follow-up*. Os resultados das revisões sistemáticas não permitiram evidenciar a eficácia do TNMF isolado ou combinado com os fármacos. Os resultados obtidos nos estudos originais demonstraram que nas primeiras seis semanas de evolução da PFPI, a adição dos corticosteróides ao TNMF não trouxe benefícios na recuperação dos doentes. Para além disso, após seis meses de evolução da doença, o TNMF não evidenciou eficácia na reabilitação, assim como não preveniu a ocorrência de sincinesias. Os resultados obtidos revelaram insuficiente evidência terapêutica do TNMF isolado ou combinado com a farmacoterapia.

PALAVRAS-CHAVE: PARALISIA BELL; EXERCÍCIO FACIAL; REABILITAÇÃO FACIAL; SIMETRIA E FUNÇÃO FACIAL; SINCINESIAS.

Abstract

The idiopathic facial paralysis (IPF) is a sudden dysfunction of the facial nerve of unknown etiology, causing paresis or paralysis of the muscles of facial expression. The consequences of IPF are essentially functional character (facial asymmetry, inability to eat or drink and communicate), also affecting the psychosocial status of individuals, promoting isolation, depression and anxiety.
In the literature, various forms of secondary prevention have been proposed, such as facial neuromuscular training (FNMT), and there is scientific controversy about this intervention. The main objective of this dissertation was to evaluate the effects of FNMT in patients with IPF in different stages of evolution. The dissertation included two systematic reviews (**Study I and II**), followed by two original studies, observational and prospective. The systematic reviews, with randomized and controlled nature studies included, analyzed the effect of FNMT in function and facial symmetry, in acute, subacute and chronic of IPF, and also investigated the effectiveness of FNMT combined with drugs therapy. The **Study III** investigated the efficacy of corticosteroids combined with FNMT, in acute and subacute the IPF in the recovery of patients. The **Study IV** examined the effectiveness of FNMT in the recovery and prevention of occurrence of synkinesis over a period of 12 months follow-up. The results of systematic reviews allow no evidence the efficacy of single or combined FNMT with drugs. The results obtained in original studies showed that within the first six weeks of evolution of IPF, the addition of corticosteroids to FNMT no benefits in the recovery of patients. In addition, after six months of disease progression, the FNMT did not demonstrate efficacy in rehabilitation, and did not prevent the occurrence of synkinesis. The results revealed evidence insufficient of therapy alone or in combination with pharmacotherapy FNMT.

KEYWORDS: BELL PALSY; FACIAL EXERCISE; FACIAL REHABILITATION; SYMMETRY AND FUNCTIONAL FACIAL; SYNKINESIS.

ACSM [American College of Sports Medicine]

AF [Actividade Física]

AHA [American Heart Association]

BDNF [Factor Neutrófico Derivado do Encéfalo]

AChE [Acetilcolinesterase]

EF [Exercício Físico]

EMG [Electromiografia]

ET [Exercício Terapêutico]

FaCE [Facial Clinimetric Evaluation]

FDI [Índice de Incapacidade Facial]

HB-FGS [House-Brackmann-Facial Grading System]

HRQOL [Health-Related Quality of Life]

IC [Intervalo de confiança]

ICF [International Classification of Functioning, Disability and Health]

IL [Interleucinas]

PB [Paralisia de Bell]

PFI [Paralisia Facial Idiopática]

PCR [Reação em Cadeia da Polimerase]

PEDro [Base de Dados de Evidência em Fisioterapia]

PFP [Paralisia Facial Periférica]

PFPI [Paralisia Facial Periférica Idiopática]

NGF [Factor de crescimento neural]

RCTs [Estudos Randomizados Controlados]

SB-FGS [Sunnybrook Facial-Facial Grading System]

SNC [Sistema Nervoso Central]

SNP [Sistema Nervoso Periférico]

TNMF [Treino NeuroMuscular Facial]

UM [Unidade Motora]

VHS-1 [Vírus Herpes Simples Tipo- 1]

VS [Versus]

WHO [World Health Organization]

1] CAPÍTULO
INTRODUÇÃO

Introdução

Sabe-se que a prática regular de actividade física (AF) e/ou exercício físico (EF) promove benefícios na saúde física e mental, optimizando a capacidade e a função física em todos os indivíduos (Haskell *et al.,* 2007). A AF e EF são a componente primordial do estímulo biológico que permite manter e/ou incrementar estruturas saudáveis e desenvolver competências funcionais no corpo humano (Vuori *et al.,* 2013). A AF abrange qualquer movimento corporal produzido pelo sistema muscular esquelético resultando no aumento do dispêndio energético; enquanto o EF consiste numa actividade física planeada, estruturada e repetitiva para manter ou melhorar a aptidão física (ACSM, 2011). A aptidão física consiste na capacidade do indivíduo realizar as tarefas motoras com vigor e agilidade, atributos conferidos pela aptidão cardiorrespiratória, força e endurance muscular, composição corporal, equilíbrio, flexibilidade e tempo de reacção (ACSM, 2011).

Há uma forte evidência do EF e AF na prevenção primária e secundária de distintas patologias e doenças crónicas (p.ex., cardiovasculares, diabetes tipo 2, carcinoma do cólon e da mama, hipertensão arterial, obesidade, osteoporose e depressão) (U.S. Department of Health and Human Services, 2008). A redução do risco de desenvolvimento destas condições requer anos de prática de EF e AF (U.S. Department of Health & Human Services, 2008). Porém, o aumento da capacidade cardiorrespiratória e força muscular, assim como a diminuição da pressão arterial e a melhoria do estado depressivo, necessitam apenas de algumas semanas ou meses de prática de EF (U.S. Department of Health & Human Services, 2008). Apesar do EF melhorar o estado de saúde geral, nem sempre esta relação é linear, podendo os potenciais benefícios não serem atingidos, com riscos acrescidos para a saúde (Haskell *et al*., 2007). Por exemplo, o EF vigoroso pode desencadear lesões no sistema muscular esquelético e danos cardiovasculares, principalmente em indivíduos com doença arterial coronária (Pollock *et al.*, 1977; Whang *et al*., 2006; AHA & ACSM, 2007). Segundo a *American College Sports Medicine* (ACSM) (2011), estes riscos são baseados em estudos observacionais e não randomizados (Evidência C).

De acordo com a literatura, a plasticidade neuromuscular obedece ao princípio de sobrecarga do treino físico, devendo este comprometer a homeostasia do tecido muscular e/ou neural sem desencadear danos neuromusculares (ACSM, 2011; Baricich *et al*., 2012). Alguns estudos demonstraram que diferentes tipos de treino aumentam o crescimento de neurónios indiferenciados (Molteni *et al.,* 2004; Sabatier *et al*., 2008; Deumens *et al.*, 2010). Molteni *et al*. (2004), no modelo animal, demonstraram que o treino físico activa o crescimento dos neurónios do gânglio dorsal posterior comparativamente a ratos sedentários. Também Sabatier *et al*. (2008) revelaram maior regeneração axonal com o treino contínuo em tapete rolante de baixa intensidade, de 1 hora, durante 5 dias, ou com o treino intermitente de alta intensidade, de 2 a 10 repetições (2 minutos de corrida e 5 de repouso), em ratos com neurotmesis do nervo fibular comum. O mecanismo de regeneração nervosa, através do EF, parece estar associado ao aumento de níveis de factores de crescimento, estimulando o crescimento neural, tal como o factor neutrófico derivado do encéfalo (BDNF) e o factor de crescimento neural (NGF) (Berchtold *et al.,* 2005). Para além disso, observou-se que o treino de baixa intensidade aumenta a actividade da acetilcolinesterase (AChE) com uma melhoria da transmissão sináptica da junção neuromuscular (Crockett *et al.,* 1976; Tomas *et al.*, 1997). Por outro lado, o treino de força com elevadas cargas promove adaptações neurais e uma melhoria do fenótipo muscular esquelético (Deschenes *et al*., 2000, Lee *et al.*, 2004). Pela exposição anterior, existe a crescente evidência da influência favorável do EF nos fenómenos de plasticidade cerebral, neuroregeneração, neuroadaptação e neuroprotecção (Dishman *et al*., 2006; Cotman *et al.*, 2007) assim como na plasticidade muscular, com adaptação do fenótipo muscular para melhor tolerar a exigência funcional (Marini & Veicsteinas, 2010). Para além disso, é sabido que o EF também influencia a actividade do sistema imunitário, com um efeito anti-inflamatório pela produção das interleucinas (IL-6, IL-1ra e IL-10) pelas fibras musculares, com inibição da produção de citocina pró-inflamatória TNF-α, exercendo assim uma protecção contra doenças crónicas associada a situações pró-inflamatórias, como as doenças cardiovasculares e a diabetes (Petersen & Pedersen, 2005; Bruunsgaard,

2005). Assim, o EF apresenta um caráter multidimensional, com efeitos em todo o organismo (Roberts & Barnard, 2005).

Nas disfunções neuromusculares dos nervos periféricos, a terapia através do exercício físico engloba o treino de força, resistência e potência, sendo adaptado ao estado de saúde, à função física e à resposta do indivíduo ao exercício (Clark, 2003; ACSM, 2011). De acordo com a *National Library of Medicine* (2015), o exercício terapêutico (ET) consiste na planificação estruturada de exercícios, com objectivos específicos, para restaurar a função muscular esquelética causada por patologias e doenças. Assim, os estudos clínicos desenvolveram modalidades de ET, no sistema neuromuscular periférico, nomeadamente na regeneração axonal, na reinervação e na recuperação funcional (Clark, 2003; Lee *et al*., 2012; Vuori *et al*., 2013; Armada-Da-Silva, 2014). De acordo com a literatura, o ET, designadamente o treino neuromuscular, engloba modalidades de exercício passivo (movimento passivo e alongamento), exercício activo assistido, activo e activo resistido (treino de força e resistência), podendo ser combinado com outras modalidades (vibração, estimulação elétrica) e agentes físicos (termoterapia, crioterapia, mobilização dos tecidos) (Brach & VanSwearingen, 1999; Clark, 2003; Armada-Da-Silva, 2014). Estrategicamente, a selecção das modalidades e dos agentes físicos, com objectivos terapêuticos, depende dos sinais das disfunções neuromusculares (p.ex., hipotonia, fraqueza muscular, discinesias) (May & Schaitkin, 2000; Beurskens & Heymans, 2003a, 2003b; Clark, 2003; Coulson *et al*., 2005; VanSwearingen, 2008). Alguns estudos clínicos, realizados no modelo animal, demonstraram implicações destas modalidades (estimulação manual através da mobilização passiva e da vibração) no sistema neuromuscular (Pachter & Eberstein, 1989; Pavlov *et al.,* 2008; Evgenieva *et al.*, 2008, Bendella *et al*., 2011). Os resultados obtidos nestes estudos revelaram o crescimento do nervo e reinervação da placa motora no músculo longo extensor dos dedos, nos músculos da língua e da mímica facial, após lesão do nervo radial, hipoglosso e facial, respectivamente (Pachter & Eberstein, 1989; Pavlov *et al.*, 2008; Evgenieva *et al.*, 2008, Bendella *et al.*, 2011). Por outro lado, demonstraram que o número de motoneurónios

regenerados e a topografia de reinervação dos motoneurónios faciais não se alterava (Pavlov *et al*., 2008; Angelov *et al.*, 2007; Bendella *et al.*, 2011). Acrescentaram, ainda, que a estimulação manual diminuía as pontes de ligação das células de *schwann* conectadas às placas motoras terminais e, consequentemente, a poli-inervação, melhorando igualmente a recuperação funcional sensitiva e motora do sistema trigémino-facial (Pavlov *et al.*, 2008; Angelov *et al.,* 2007; Bendella *et al.,* 2011).

As estratégias de intervenção têm sido desenvolvidas para promover a rápida regeneração axonal do sistema nervoso periférico (SNP) e completa recuperação funcional. Infelizmente, após as lesões dos nervos periféricos, a recuperação funcional permanece frequentemente incompleta (Gordon *et al.*, 2003; Campbell, 2008; Sulaiman & Gordon, 2013). Entre os principais factores que contribuem para a parcial recuperação, contam-se a lenta regeneração dos axónios e células de *schwann* (1milímetro diário), o progressivo declínio da capacidade do motoneurónio em promover o crescimento do axónio, a atrofia muscular, a carência de ligações entre as células de *schwann* e os axónios, a deficiência sensorial e a inapropriada reinervação dos músculos através dos axónios regenerados (Tonge & Golding, 1993; Lee, & Wolfe, 2000; Gordon *et al.,* 2003; English *et al.*, 2009). Na perspectiva de melhorar a recuperação funcional do SNP, principalmente em doentes com paralisia facial periférica idiopática (PFPI) ou de Bell (PB), diversos estudos científicos investigaram as terapias de intervenção como o treino neuromuscular facial (TNMF) e os fármacos. Contudo, a actual controversa clínico-científica versus a prática recorrente destas estratégias de intervenção no contexto clínico, permitiram de seguida aprofundar os conhecimentos sobre as estratégias de intervenção no SNP e analisar os resultados destas intervenções, nomeadamente na PFPI.

As expressões faciais manifestam o silêncio da comunicação e do sentimento interpessoal, enquanto a simetria da face condiciona a sua beleza. As funções da face são multidimensionais, abrangendo aspectos emocionais, físicos e sociais (Prakash *et al*., 2012). E, naturalmente, a disfunção facial afecta dramaticamente a fisionomia, as expressões voluntárias e espontâneas, a

função oral e ocular, com impacto psicossocial (isolamento, baixa autoestima, depressão) (Hadlock, 2008).

A paralisia facial periférica (PFP) é uma mononeuropatia do sétimo par de nervos cranianos que resulta no comprometimento parcial (paresia) ou completo (paralisia) da face ipsilateral (Rath *et al.*, 2007). A PFP abrange múltiplas etiologias, contudo a forma idiopática é fundamentada no diagnóstico diferencial (Beurskens *et al.,* 2005; Anderson, 2006; Rath *et al.,* 2007; Baugh *et al.*, 2013). A incidência da paralisia facial etiológica é de 34% (Peitersen, 2002), incluindo causas traumáticas, neurovasculares, infecciosas, metabólicas, genéticas, neoplásicas, tóxicas, iatrogénicas, obstétricas e congénitas (Pardal-Fernández *et al.,* 2003; Anderson, 2006; Valls-Solé, 2007).

A PFPI é uma afecção aguda comum do nervo facial periférico, de etiologia desconhecida, caracterizada pela súbita instalação (24 a 72 horas) da paralisia ou paresia, unilateral dos músculos da hemiface (Peitersen, 2002; Rath *et al.,* 2007; Lalwani, 2008). A PFPI decorre do comprometimento do neurónio motor inferior, resultando na incompleta oclusão ocular e no “fenómeno de Bell” (a incapacidade de oclusão palpebral resulta na contracção do músculo recto superior com a deslocação do globo ocular superiormente, expondo a esclerótica) (National Institute of Neurological Disorders and Stroke, 2015). Clinicamente, as disfunções dos músculos do quadrante superior da hemiface permite identificar a PFP (Benatar & Edlow, 2004; National Institute of Neurological Disorders and Stroke, 2015). Na fase aguda, entre 0 e 3 semanas (Yanagihara, 2000; Rath *et al.,* 2007), os sintomas e sinais clínicos podem ser manifestados pelo comprometimento das fibras aferentes sensitivas (algia e disestesia periauricular) e somatosensoriais (hipo/disgeusia de 2/3 da região anterior da língua), das fibras eferentes parassimpáticas secretomotoras (hiper/hipossecreção lacrimal, nasal e salivar) e das fibras eferentes motoras (diminuição do tónus e força dos músculos faciais e hiperacusia do músculo estapédio) (Ahmed, 2005).

A PFPI abrange aproximadamente 2/3 de todas as PFP (Hato *et al.,* 2008; Holland & Weiner*,* 2004; Peitersen, 2002). Na europa, a sua incidência oscila entre os 20,2 (Reino Unido) e os 53,3 (Itália) casos por 100.000 habitantes

(Rowlands *et al.,* 2002; Monini *et al.,* 2010) e o risco de desenvolver a PFPI é de 1 em 60 indivíduos (Beal *et al.,* 2004). A recorrência pode atingir os 6,8% dos casos, independentemente da face ipsi ou contralateral afetada, enquanto o factor hereditário representa cerca de 4,1% dos casos (Peitersen, 2002). O estudo de Peitersen (2002), estimou o pico de incidência máxima entre os 15 e os 45 anos de idade. Diversos estudos têm demonstrado prevalências similares entre os géneros e a lateralidade das hemifaces (Piercy, 2005; Peitersen, 2002; Holland & Weiner*,* 2004). O clima, a latitude e as estações climatéricas são preditores independentes do risco de desenvolver a PFPI (Campbell & Brundage*,* 2002; Peitersen, 2002). Mundialmente, desconhece-se a análise custo-benefício do diagnóstico e do tratamento da PFPI, mas segundo Baugh *et al.* (2013), o impacto económico é indubitavelmente significativo nos Estados Unidos da América, com incidência estimada de 35.000 a 100.000 casos anuais.

O mecanismo fisiopatológico da PFPI envolve a inflamação (principalmente o edema) e isquemia por compressão do nervo facial no canal de Falópio, desencadeando inicialmente o bloqueio neural reversível (neuropraxia) e, progressivamente, a degeneração *walleriana* (axonotmesis, neurotmesis) (Adour *et al.,* 1975). Algumas teorias têm sido propostas para explicar a etiologia da PFPI, nas quais se integram a infecciosa (Adour *et al.,* 1975), a imunológica (Abramsky *et al.,*1975) e a vascular (Ikeda *et al.,* 1996).

Na década de 90, os investigadores Murakami *et al.* (1996) e Furuta *et al.* (1998) demonstraram forte evidência da etiologia infecciosa na PFPI, com o isolamento do genoma Vírus Herpes Simples tipo-1 (VHS-1) das células epiteliais orais na população saudável e do fluido endoneural do nervo facial na população com PFPI. De notar, que o genoma do VHS-1 foi identificado entre 31 a 79% dos indivíduos com PFPI (Murakami *et al.,*1996; Furuta *et al.,*1998; Abiko *et al.,* 2002). A segunda causa infecciosa mais comum incluiu a reactivação do vírus Zóster que, apresentando sinais clínicos de disfunção do nervo vestíbulo coclear e exantema vesicular no pavilhão auricular (Furuta *et al.,* 2001; Lee *et al.,* 2012). O método de serologia e de reacção em cadeia da polimerase (PCR) permitiram identificar a presença do vírus Zóster entre 8 a

28% dos indivíduos com PFPI (Furuta *et al.,* 2001). Contudo, alguns estudos contrariam a teoria viral, mantendo indeterminada a etiologia da PFPI (Linder *et al*., 2005; Stjernquist-Desatnik *et al.,* 2006). Os dados anteriores não são suficientes para demonstrar uma relação causal entre reactivação do VHS-1 no gânglio geniculado com a PFPI, pois a inflamação pode de alguma forma ter sido despoletada por outro agente etiológico, com posterior reactivação do vírus previamente alojado.

Os sinais e os sintomas clínicos da PFP dependem da lesão topográfica do nervo facial (Finsterer, 2008; Patel & Tanna, 2009). Se a lesão ocorrer no segmento do meato (meato acústico interno até ao canal de Falópio) fica comprometida a secreção lacrimal, salivar, gustativa, reflexo estapédico e a função motora da face; se ocorrer no segmento labiríntico (infra gânglio geniculado e o nervo estapédio), resulta em alterações gustativas, salivares, reflexo estapédico e disfunção motora da face; se a lesão atingir o segmento timpânico (infra-estapédio e nervo da corda do tímpano), está comprometida a gustação, secreção salivar e função motora da face e, por último, se o dano ocorrer no segmento mastóide (infra cordal) resulta unicamente na disfunção motora da face (Chevalier, 2003; Raimar, 2005; Seok *et al.,* 2008). Seok *et al.* (2008) mostraram que o dano nervoso na PFPI afecta mais o segmento labiríntico, o que está de acordo com a anatomia do canal de Falópio que é mais estreito neste percurso, favorecendo a compressão e isquemia do nervo facial (Dawidowsky *et al*., 2011).

De acordo com Yanagihara (2000), a evolução do edema do nervo na PFPI pode ser subdividida em fase aguda (0-3 semanas), fase subaguda (4-9 semanas) e fase crónica (superior a 9 semanas). No seguimento da PFPI, a interrupção axonal desencadeia redução da força muscular ipsilateral à lesão e estratégias compensatórias de hiperactividade contralateral (Finsterer, 2008), com sequelas crónicas de contracturas, espasmos, atrofia muscular e sincinesias ipsilateral (Pennock *et al*., 1999; Diels, 2000; Cronin & Steenerson, 2003). O estudo de Peitersen (2002) demonstrou que, num período de seis meses, o prognóstico da PFPI compreende a recuperação completa e espontânea em cerca de 71% dos casos. Os restantes 29% dos casos

apresentavam sequelas residuais, disseminadas entre 12% de sequelas ligeiras, 13% moderadas e 4% severas. Resumindo, 29% das sequelas abrangeram a fraqueza muscular ligeira a severa, 17% contracturas, 16% espasmos ou sincinesias e 2% epífora (Peitersen, 2002; Caúas *et al.,* 2004). As sequelas residuais podem igualmente compreender a incapacidade funcional periocular (lagoftalmo e lágrimas de crocodilo) e perioral (disartria, mastigar e deglutir), desencadeada pela hipo e/ou hipertonia muscular (Peitersen, 2002). De acordo com Moldovan *et al.*, (2006), a taxa de maturação e crescimento das fibras motoras e sensitivas mielinizadas são similares durante a regeneração. Assim, estas incapacidades podem ser desencadeadas pelas sincinesias secretomotoras, originadas pela perda de axónio e endoneuro (lesão de grau III/ classificação de *Sunderland*) (Sunderland, 1978) com regeneração caótica dos axónios (crescimento desorganizado e incapacidade dos axónios atingirem os tubos endoneurais originais, inervando outros grupos musculares) (Husseman & Metha, 2008). O prognóstico desfavorável pode depender sobretudo da idade avançada (superior a 65 anos de idade) (Ikeda *et al.,* 2005; Kasse *et al.,* 2005; Finsterer, 2008; Portelinha *et al.,* 2015), do elevado grau de severidade clínico (paralisia) no início da PFPI (Peitersen, 2002; Ikeda *et al.,* 2005; Finsterer, 2008), da ausência de recuperação motora após 3 a 4 semanas de evolução (Ikeda *et al.,* 2005; Finsterer, 2008), da existência de algia retroauricular (Peitersen, 2002; Holland & Weiner, 2004; Berg *et al.,* 2009), da degeneração nervosa (teste electrofisiológico (Portelinha *et al.,* 2015) e género masculino (Pelaz *et al.*, 2008). Segundo Holland & Weiner (2004), os indicadores de mau prognóstico estão igualmente associados às comorbilidades de hipertensão arterial e diabetes *mellitus*, apesar de Peitersen (2002) considerar que a hipertensão arterial poderá não ser por si só um preditor de pior prognóstico, uma vez que a idade avançada parece coincidir com a hipertensão arterial.

O diagnóstico e o prognóstico clínico abarcam a história clínica e o exame físico, assim como outros exames complementares, como sejam testes laboratoriais, audiométricos e vestibulares, electromiografia e electrodiagnóstico, ressonância magnética, tomografia axial computorizada e

ultrassonografia (Raimar, 2005; Murthy & Saxena, 2011; Baugh *et al.,* 2013). No entanto, as orientações na prática clínica para o diagnóstico de PFPI demonstraram insuficiente evidência de exames de imagiologia e testes laboratoriais de rotina na fase aguda, contrariamente ao exame físico que é fortemente recomendado (Baugh *et al.,* 2013). A degeneração *walleriana* principia entre o 3º e o 5º dia e termina entre a 1ª e a 2ª semana após o início dos sintomas, consequentemente, nesta fase precoce, alguns exames complementares são desaconselhados por não serem conclusivos (Chow *et al.,* 2002; Hsieh *et al.,* 2009). De acordo com Baugh *et al.* (2013), o padrão de ouro do diagnóstico e do tratamento não está ainda clarificado, e a inconsistência dos procedimentos da prática clínica dependem da experiência e do conhecimento dos clínicos sobre a evidência científica, e igualmente do interesse e das necessidades de cada doente.

Um grupo internacional de investigadores sugeriu seis dimensões fundamentais na *Health-Related Quality of Life* (HRQOL): função física, psicológica, social, actividades, satisfação geral da vida e percepção do estado de saúde (Berzon *et al.,* 1993). Estes domínios devem ser avaliados com instrumentos de medição específicos e abranger a dimensão objectiva e subjectiva (Testa & Simonson, 1996). De acordo com a *World Health Organization* (WHO) (2001), a *International Classification of Functioning, Disability and Health* (ICF) permite agrupar a evolução das sequelas dos doentes com PFPI, em funcionais (deficiência e incapacidade), correspondendo a sequelas de hipotonia/flacidez (fraqueza muscular) ou hipertonia/sequelas residuais (contractura, sincinesia, espasmo) da hemiface afectada promovendo a incapacidade de mastigar e deglutir, de oclusão ocular, de comunicar; e, por último, em sequelas para a saúde em geral, envolvendo repercussões psicossociais (baixa autoestima, isolamento, ansiedade, depressão).

Os instrumentos de medição universais podem capturar as deficiências e as incapacidades relacionadas com a disfunção facial. A deficiência corresponde às alterações antomofisiológicas da face, tais como: assimetria em repouso e contracção voluntária e sincinesias, avaliadas pelas escalas de *Sunnybrook Facial Grading System* (SB-FGS) (Ross *et al.*,1996; Brach *et al*., 1997; Kayhan

et al., 2000; Cruz *et al.*, 2006) e *House-Brackmann Facial Grading System* (HB-FGS) (House & Brackmann, 1985; Evans *et al*., 1989; Coulson *et al*., 2005). A *American Academy of Otolaryngology-Head and Neck Surgery* considera a escala HB-FGS o padrão de ouro na avaliação da PFPI. Este sistema apresenta limitações na avaliação das sincinesias e de regiões específicas da face. Assim, para complementar a avaliação, a SB-FGS avalia as sincinesias, a simetria estática e dinâmica de forma separada e em distintas regiões da face (Ross *et al.*, 1996; Kayhan *et al.*, 2000). As incapacidades correspondem ao desconforto físico, dificuldades funcionais e sociais, avaliadas pelas escalas faciais Disability Index (FDI) (VanSwearingen & Brach , 1996) e FaCE (Facial Clinimetric Evaluation) (Kahn *et al*., 2001).

Na literatura, diversas terapias de intervenção têm sido propostas na prevenção secundária da PFPI, tal como a cirurgia descompressiva e correctiva, os fármacos e o Treino NeuroMuscular Facial (TNMF) (métodos e técnicas de exercícios terapêuticos) (Beurskens & Heymans, 2003a, 2003b; Manikandan, 2007; Holland & Bernstein*,* 2011; Groseth *et al.,* 2012; Baugh *et al.,* 2013). Durante décadas, as diferentes intervenções têm demonstrado controvérsia e, actualmente, ainda não reúnem o consenso científico. Todavia, recentemente, as orientações reúnem unanimidade científica nos princípios de prevenção geral da córnea (colírios lubrificantes e/ou pomadas oftalmológicas e protectores oculares) e na farmacoterapia (corticosteróides) (Holland & Bernstein*,* 2011; Groseth *et al.,* 2012; Baugh *et al.,* 2013). O consenso assenta no princípio dos cuidados profilácticos da córnea, no qual o encerramento incompleto das pálpebras (lagoftalmo) pode desencadear a queratite e/ou úlcera, na fase aguda da PFPI (Rahman & Sadiq*,* 2007; Finsterer, 2008; Baugh *et al.,* 2013). Adicionalmente, a prevenção de lesões tardias da córnea (infecções), associada às sequelas (sincinesias, hemiespasmos e lagoftalmo) da PFPI, suportam a aplicação de toxina botulínica e a cirurgia correctiva (tarsorrafia e aplicação de pesos de ouro na pálpebra superior) (Beurskens *et al.*, 2005; Finsterer, 2008; Birgfeld *et al.,* 2011; Baugh *et al.,* 2013).

Na década de 30, surgiu a primeira cirurgia descompressiva fundamentada no mecanismo fisiopatológico (compressão do nervo facial) da PFPI, no qual

foram sendo desenvolvidas diferentes abordagens cirúrgicas nas décadas subsequentes (McAllister *et al.,* 2011). Porém, a baixa evidência da intervenção cirúrgica, a afirmação da teoria viral, os elevados custos e riscos cirúrgicos desencadearam a contestação e limitação destes procedimentos cirúrgicos em vários países (McAllister *et al.*, 2011; Baugh *et al.,* 2013; Almeida *et al.,* 2014).

Segundo as orientações Americanas e Canadianas, a intervenção mais eficaz está limitada aos fármacos (Baugh *et al.,* 2013; Almeida *et al.,* 2014). Ambas as orientações recomendaram fortemente o uso de corticosteróides orais nas primeiras 72 horas após o início dos sintomas e em todos os graus de severidade (Baugh *et al.,* 2013; Almeida *et al.,* 2014). No entanto, as orientações Americanas consideraram opcional a terapia combinada de corticosteróides e antivíricos orais em todos os graus de severidade da PFPI na fase aguda, enquanto as orientações Canadianas recomendaram o uso de antivíricos orais no subgrupo de paralisias (Baugh *et al.,* 2013; Almeida *et al.,* 2014).

De acordo com os investigadores, o TNMF assenta em diferentes métodos e técnicas (Kisner & Colby, 2009) tais como, o método *Mime Therapy* (exercícios faciais combinado com termoterapia e mobilização dos tecidos) (Beurskens & Heymans, 2003a, 2003b), Reeducação Neuromuscular Facial (exercícios faciais combinado com mobilização dos tecidos) (Diels, 1995, 2000; Manikandan, 2007), Facilitação Neuromuscular Proprioceptiva (irradiação, estiramento inicial, contrações repetidas) (Barbara *et al.*, 2010); *biofeedback* por electromiografia (EMG) (Cronin & Steenerson, 2003; Nakamura *et al.*, 2003; Dalla Toffola *et al*., 2005, 2012), vídeo (Coulson *et al.,* 2006), estimulação eléctrica (Alakram *et al.*, 2010). O TNMF é acompanhado pelo *feedback* visual (espelho), reforçando o padrão de movimento correto, melhorando o controlo motor e inibindo a co-contracção de outros grupos musculares (Beurskens *et al.,* 2005; Pourmomeny & Asadi, 2014).

O TNMF consiste num processo de (re)aprendizagem ou de (re)educação dos movimentos faciais, no qual facilita a actividade muscular em padrões de movimentos funcionais (simetria facial, função periocular e perioral e inibição dos sinergistas) e promove as expressões emocionais ou espontâneas,

suprimindo sequelas imediatas (fraqueza muscular) e tardias (hipercinesias, sincinesias), usando o *feedback* visual (espelho) (VanSwearingen, 2008; Dorion, 2005). O TNMF engloba estratégias específicas baseadas na actividade analítica dos grupos musculares correspondente ao trajecto do nervo, e ao grau de lesão neuromuscular, permitindo assim restabelecer as funções faciais periorbital e perioral tal como, a fonação, a mastigação, a mimica facial, a sensibilidade, a oclusão ocular, resultando na melhor qualidade de vida (Diels, 2000; VanSwearingen, 2008; Beurskens *et al.,* 2005). Nas paralisias faciais crónicas, o TNMF é baseado no conceito de plasticidade neural, capacidade de adaptação sensoriomotora do sistema nervoso central (SNC) que reaprende ou reorganiza o movimento dinâmico, melhora a resposta fisiológica e a capacidade funcional, promovendo o autocontrolo motor (Ross *et al.*, 1996; Cronin & Steenerson, 2003).

A eficácia do TNMF foi suportada pela especificidade dos exercícios, adaptado às características histoquímicas dos músculos faciais: músculos predominantemente fásicos (orbicular dos olhos, procero e o nasal), intermédios/proporção de fibras fásicas/tónicas de 2:1 (zigomático, levantador do lábio superior, levantador do ângulo da boca, depressor do ângulo da boca, mento, orbicular da boca e platisma) e predominantemente tónicos (bucinador, frontal, corrugador supraciliar e depressor do lábio inferior) (Goodmurphy & Ovalle, 1999; Fa *et al.*, 2000; May & Schaitkin, 2000; Cattaneo & Pavesib*,* 2014). Assim, alguns músculos de expressão facial requerem rápida contracção muscular, enquanto outros músculos com características metabólicas e contratéis lentas proporcionam maior resistência à fadiga (May & Schaitkin, 2000; Perry *et al*., 2011). Os músculos faciais mostram igualmente particularidades anatomofiológicas diferentes comparativamente aos demais músculos esqueléticos (membros superiores e inferiores) (Cattaneo & Pavesib*,* 2014). Especificamente, estes músculos não apresentam ambas as inserções no periósteo (p.ex., pele ou aponevrose epicraniana) (Cattaneo & Pavesib, 2014); possuem uma grande variabilidade intra e intermuscular (p.ex., tecido conjuntivo), sugerindo que cada músculo facial não seja uma única unidade funcional, mas a composição de distintas subunidades funcionais (Cattaneo &

Pavesib, 2014); possuem pequenas unidades motoras (UM), revelando movimentos precisos e complexos (proporção de 25 fibras:1motoneurónio) (Happak *et al.*, 1997; May & Schaitkin, 2000); enviam um *input* sensitivo que é transmitido ao nervo facial motor através da anastomose com o nervo trigémeo (unidade funcional sensoriomotora ou nervo trigémino-facial) (May & Schaitkin, 2000; Cattaneo & Pavesib, 2014) (May & Schaitkin, 2000; Cattaneo & Pavesib, 2014). A literatura tem manifestado dúvidas sobre a presença de órgãos proprioceptivos nos músculos faciais, fundamentada através da ausência de articulações e perda do feedback da visão (informação exteroceptiva) na trajectória do movimento (May & Schaitkin, 2000; Cattaneo & Pavesib, 2014). Todavia, alguns investigadores defendem a inexistência de receptores proprioceptivos (Hosokawa, 1961; Happak *et al*., 1994) (fusos neuromusculares e órgãos tendinosos de Golgi), indicando que a informação estática e dinâmica da posição (cinestesia) e tensão muscular da face é fornecida ao SNC pelos mecanoreceptores cutâneos (Cattaneo & Pavesib, 2014). Sendo assim, a aplicabilidade do TNMF na PFPI parece ser fundamental pelas características singulares dos músculos faciais (Diels, 1995).

O TNMF e os fármacos têm sido amplamente praticados na prevenção secundária da PFPI, sendo estas as terapias mais investigadas comparativamente a outras intervenções (Beurskens & Heymans, 2003a, 2003b; Manikandan, 2007). As revisões sistemáticas demonstraram limitada evidência sobre a eficácia do TNMF com *feedback* visual (espelho), EMG *biofeedback* e electroestimulação na redução do tempo de recuperação e ocorrência de sequelas (Teixeira *et al.,* 2008; Cardoso *et al.,* 2008). Contrariamente, outra revisão sistemática concluiu que o TNMF, com feedback visual, melhorava a funcionalidade (Pereira *et al.,* 2010). Porém, as orientações americanas e canadianas não recomendam os ET na fase aguda, independentemente da severidade, enquanto as orientações canadianas recomendam os ET apenas na fase crónica (Baugh *et al.,* 2013; Almeida *et al.,* 2014). Por outro lado, as orientações indianas, na fase aguda da PFPI, incluíram no algoritmo de intervenção a aplicação dos ET combinado com os corticosteróides (Murthy & Saxena, 2011).

Apesar da carência de consenso sobre as terapias de intervenção na PFPI, recentemente as investigações visam a combinação de fármacos com o ET facial (Penteado *et al.,* 2009; Alakram *et al.,* 2010; Barbara *et al.,* 2010; Nicastri *et al.,* 2013). Apesar de na última década se pesquisarem e desenvolverem distintas estratégias de prevenção secundária, ainda perdura um escasso conhecimento sobre o impacto do TNMF na simetria, no grau de recuperação funcional e na qualidade de vida, entre a fase aguda e crónica da PFPI. E, contrariamente às recomendações, o TNMF continua comummente a ser praticado pelos profissionais de saúde no contexto clínico, sendo a primeira linha de intervenção precoce simultaneamente com os fármacos. Assim, baseada nas escassas investigações científicas, na carência de diretrizes na prática clínica, considera-se primordial investigar os efeitos do TNMF isolado ou combinado com os corticosteróides na PFPI, num período de *follow-up* de 12 meses. No seguimento deste objectivo principal, foram definidos os seguintes objectivos específicos:

1. Analisar, através de duas revisões sistemáticas da literatura, com estudos aleatórios e controlados, o efeito do TNMF no grau de severidade e na simetria facial, entre a fase aguda e crónica da PFPI, assim como averiguar a eficácia da intervenção de corticosteróides agregados ao TNMF.

2. Investigar, numa população de doentes se, durante a fase aguda e subaguda da PFPI, o uso de corticosteróides combinado com o TNMF seria mais eficaz na recuperação dos graus de severidade e na simetria facial comparativamente ao TNMF isolado, assim como averiguar:
   (i) Se os doentes de maior grau de severidade beneficiariam do uso dos corticosteróides;
   (ii) Se o tempo de remissão dos sinais e sintomas seria mais rápido com o uso dos corticosteróides;

(iii) Se a idade, o sexo, o tipo de intervenção e a gravidade inicial do quadro clínico influenciariam a variação do grau de recuperação funcional dos doentes.

3. Investigar, em doentes com PFPI, os efeitos do TNMF durante 12 meses, na fase subaguda e crónica, em relação ao nível funcional e da qualidade de vida, assim como apurar:
   (i) Se os doentes beneficiariam do TNMF durante os 12 meses;
   (ii) Se o TNMF preveniria a ocorrência de sincinesias durante os 12 meses de seguimento do estudo.

O presente documento está dividido em seis capítulos principais. O primeiro capítulo compreende a introdução desenvolvida sobre a incidência, etiologia, fisiopatologia, diagnóstico e prognóstico, instrumentos de medição e terapias de intervenção na PFPI, assim como a descrição do conceito de TNMF na recuperação funcional, na prevenção de sequelas e na melhor qualidade de vida. Este capítulo finaliza com a pertinência e objectivos da investigação fundamentados em questões emergentes da literatura. No segundo capítulo, intitulado de revisão da literatura, são inseridas duas revisões sistemáticas publicadas (estudo I e II) sobre o assunto em questão. O terceiro capítulo engloba as investigações originais (estudo III e IV), com os métodos, resultados e discussão específica de cada um. O quarto capítulo, evidencia os resultados dos artigos originais, com uma discussão geral dos dados apresentados. No quinto capítulo são apresentadas as principais conclusões dos resultados obtidos. O último capítulo engloba as referências bibliográficas que sustentam a introdução e a discussão geral.

2] CAPÍTULO
REVISÃO DA LITERATURA

ESTUDO I

Idiopathic facial palsy and physical therapy: an intervention proposal following a review of practice

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Systematic Review

Idiopathic facial palsy and physical therapy: an intervention proposal following a review of practice

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Background: Idiopathic facial palsy (IFP) or Bell's palsy is a unilateral mononeuropathy of the lower motorneuron of the facial nerve, excluding tumor, infectious or traumatic causes.
Objectives: To evaluate the efficacy of physical therapy on the outcome of IFP.
Search strategy: The electronic databases MEDLINE, Cochrane Database of Systematic Reviews, PEDro and SPORTDiscus, were searched up to December 2009.
Selection criteria: Studies included in this review were selected according to the following set of criteria: (1) the design was randomized controlled trial; (2) all participants had an IFP or paresis; (3) the intervention was any modality of physiotherapy (a combination of modalities was possible) except interventions such as acupuncture and osteopathic; (4) the studies were published between January 2000 and December 2009; (5) English language.
Methods: The review authors extracted and analyzed the data independently, using the PEDro scale to assess the methodological quality of each eligibly study.
Results: Only two eligible studies were identified and included in the review. Both studies were scored 5 out of 10 on the PEDro scale. Both studies found benefits from facial neuromuscular reeducation with mirror feedback in the acute or chronic phase of IFP. The results of these studies could not be pooled for meta-analysis, as the study interventions and assessment were heterogeneous.
Conclusions: The experimental studies demonstrated moderate efficacy in the treatment of facial neuromuscular reeducation with mirror feedback in different phases of the paralysis.

Keywords: Idiopathic facial palsy, Physiotherapy, Systematic review

Introduction

Idiopathic facial palsy (IFP) or Bell's palsy is a unilateral mononeuropathy of the lower motorneuron of the facial nerve, excluding tumor, infectious or traumatic causes.[1,2] Clinical, histological and molecular biology evidence suggests virus etiology, possibly simple herpes virus type I.[3] However, viruses cannot explain all the Bell's palsy cases and this kind of palsy also can be associated with genetic, autoimmune and vasomotor disorders.[4]

The clinical view of IFP ranges from sudden to progressive (48 hours), the injury seriousness from partial to complete and the manifestation can be unilateral or bilateral.[4]

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In England, the IFP incidence is 20 out of 100 000 inhabitants, and of this number, one out of 60 will experience sequelae. The genders are equally affected, though the incidence is higher in pregnant women (45 out of 100 000 inhabitants).[4] The incidence increases between 15 and 45 years old.[5] Spontaneous recovery occurs in two-thirds of the population and 85% recover in the first 3 weeks.[4] Idiopathic facial palsy in the remaining persists for 3–5 months.[4] Idiopathic facial palsy recurs in 7 to 15% of cases; this is known as recidivant (homolateral) or alternant (contralateral) IFP.[1]

During the acute phase (flaccid and recovery) the partial and complete neuromuscular dysfunction of the IFP expresses itself with face asymmetry at rest and during movement.[2] The frontal and nasogenian flap fades, the palpebral opening extends, the lower eyelid droops (lagophthalmos), the consequent tear secretion increases (epiphory), the palpebral closes leading to Bell's phenomenon (synergic contraction

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of the upper rectum with its own ocular globe rotation pointing out the sclera) and the labial commissure droops.[6] The ocular occlusion reflection is reduced or annulled and the voluntary contraction of the muscles of the injured hemifacial is weak or null. The individual has difficulty articulating words, communicating through expressions and keeping solid and liquid food in the mouth.[6] The facial palsy can be equally associated with hypo or hyperacusis, hypo or hyper-tear and saliva secretions, dysphasia or ageusia on the 2/3 fore tongue and pains in the mastoid and retroauricular regions.[2,5]

The chronic or sequelae phase consists of incomplete recovery after 6 months from the beginning of the IFP symptoms. The clinical view includes the combination of synkinesis, atrophy due to disuse and contractures of the injured hemifacial.[7]

Compromised facial expressions can negatively affect life quality, self-esteem and social interaction, creating anxiety, depression, stress, solitude and psychological and social problems.[8]

The factors that negatively influence the prognosis of IFP are: age, arterial hypertension, diabetes mellitus, pregnancy and puerperium, severity and type of virus.[4,6]

Research by Caúas *et al.*[1] showed that sequelae predominance in chronic IFP was linked to muscle spasms (12.8%), partial recovery or motor deficit (10.6%), epiphory (3.3%) and synkinesis (2.8%).

The IFP diagnosis is based on the anamnesis and physical exam. The anamnesis covers personal data (beginning of the palsy, cause and manifestation), risk factors (diabetes, herpes zoster, otitis, poliomyelitis) and family factors (Melkersson-Rosenthal syndrome).[6] The physical exam consists of facial rest observation (tonus), analytic evaluation of the muscle contraction and its function and checking beauty spot existence (logophtalmus, Bell signal, soques, epiphora). To complete the diagnosis the following complementary electrophysiological exams are requested: electromyography (EMG), electroneurography and topographic diagnosis.[2] These diagnosis techniques allow practitioners to spot and quantify the facial nerve injury level.[9,10]

The Seddon's[11] system allows rating of the type of peripheral injury of the nerve as neuropraxis, axonotomesis or neurotomesis. The neuropraxis symptoms are transitory and result in a compression and ischemia. The axonotomesis prognosis depends on the injury extension and severity. The neurotomesis demands nerve reconstruction.[12]

The aims of IFP treatment are facial mime recovery and the complete regeneration of the nerve based on several treatment methods, i.e. medical general measures, medication, surgery and physiotherapy.[13]

During the acute phase the general measures predominate: ocular prevention in order to avoid inflammation and keratitis (regular lubrification, glasses, ocular protection and night ophthalmic cream)[5] and education (anatomy, pathology, clinical manifestations, objectives, treatment strategies and contra-indications).[14] The pharmacologic treatment consists of prednisone administration [(corticosteroid/first 72 hours) and acyclovir (anti-viral)].[15] Corticosteroids are used to decrease the edema and consequently the nerve decompression (avoiding the worsening of ischemia and/or neuropathy) while the antivirals prevent reproduction.[6]

In the chronic or sequelae phase, the palpebral opening extent is indicated by tarsorrhaphy and lateral canthoplasty,[4,9] the hypercynesis is indicated

Table 1 Databases searched

Database	Search terms
Medline	Facial palsy, facial paralysis peripheral, rehabilitation, physical therapy
Central (Cochrane Central Register of Controlled Trials)	Bell's palsy, idiopathic facial paralysis review
PEDro (Physiotherapy Evidence Database)	Facial palsy, facial paralysis peripheral, rehabilitation, physical therapy
SPORTDiscus	Facial palsy, facial paralysis peripheral, rehabilitation, physical therapy, neuromuscular facial retraining

Table 2 Inclusion criteria

Publication type	Randomized controlled trials and full text
Publications of period	January 2000 to December 2009
Language	English only
Study participants	Participants with a diagnosis of Bell's palsy, all degrees of severity, 15 years or older, unilateral Bell's palsy
Intervention	The intervention was any modality of physiotherapy (a combination of modalities was possible), except studies containing interventions such as acupuncture and osteopathic intervention
Outcome measures	The primary outcomes measure was Sunnybrook facial grading system (SB-FGS)[35] The secondary outcome measures were House-Brackmann grading system (HB-FGS)[36] and other specified by author (video).

by the botulinum toxin[9] and the syncinesis by neuromuscular reeducation with EMG and mirror.[14]

The physiotherapy treatment in the different IFP phases aims to reestablish the expression of the facial mime, trophism, strength and muscle function. It also aims to minimize or avoid sequelae[6] to encourage psychic rebalancing and to promote reintegration into society and the job environment.[4] The different techniques applied in IFP treatment include massage, thermotherapy, electrotherapy, facial mime exercises and neuromuscular reeducation with EMG or mirror.[13]

Objectives

The importance of the current systematic review is associated with the lack of intervention protocols in the clinical practice of physiotherapy in IFP. Therefore, our goals consist of determining the efficacy of physiotherapy interventions for IFP between 2000 and 2009 and proposing an intervention plan.

Methods

Search strategy

The authors searched articles in the MEDLINE database, the Cochrane Central Register of Controlled Trials, PEDro and SPORTDiscus via EBSCOhost, between 2000 and 2009. The research strategy of the thematic headings and the key-words were based on the medical terms of the *National Library Medicine* (Table 1).[16] The inclusion criteria list of the current study is in Table 2.

Two of the authors (MF, PS) independently screened titles and abstracts. The full texts of those that were potentially relevant were, independently, evaluated by the authors. Both authors chose the studies to include in the current review. Any disagreement on inclusion criteria was resolved through the consensus of the third author (JD).

Study quality assessment

The studies included in this review were evaluated by the PEDro scale,[17] which allows researchers to rate the methodological quality of the selected studies. This scale is composed of 11 items with a maximum score of 10 points. The scale is based on the Delphi list[18] and it evaluates the internal validity of the randomized controlled trials.[19–21]

Results

Search results

The authors examined articles and identified potentially relevant articles (MEDLINE Database=9, Cochrane Database of Systematic Review=1, PEDro =3 and SPORTDiscus via EBSCOhost=4). Some studies were found in more than one database. From all of these, two articles met the inclusion criteria [Manikandan (2007)[22]; Beurskens and Heymans (2003)[23]].

Eleven studies were excluded from the present study because they were:

1. Systematic reviews [Finsterer (2008)[24]; Quinn and Cramp (2003)[25]].
2. Case reports or series reports [Cederwall *et al.* (2006)[26]; Coulson *et al.* (2006)[27]].
3. Not physical therapy interventions or not only physical therapy interventions [Zhou *et al.* (2009)[28]; Wong and Wong (2008)[29]].
4. Retrospective studies [Dalla-Tofolla *et al.* (2005)[30]; Cronin and Steenerson (2003)[31]].
5. Other outcome measures [Denlinger *et al.* (2008)[32]; Song *et al.* (2008)[33]; Nakamura *et al.* (2003)[34]].

Characteristics of studies included

Populations

The characteristics of each study are summarized in Table 3. One of the studies compared two active interventions [Manikandan (2007)[22]]. The other study included a non-intervention control group and an active intervention experimental group [Beurskens and Heymans (2003)[23]]. One of the studies[22] took place during the acute phase and the other took place in the chronic phase.[23]

Interventions

Manikandan[22] included 59 individuals with Bell's palsy in the study. Subjects were randomly divided into two groups: control group (N=30) and experimental (N=29). The control group was treated with electrical stimulation, gross facial expression exercises and facial massage. Electrical stimulation was given with galvanic current (3 sessions/day, for 6 days per week for a period of 2 weeks, 90 contractions) in each muscle, plus faradic current in each facial nerve trunk (10 contractions) and gross facial expression exercise administered to individuals for 3 months. The experimental group received facial neuromuscular reeducation techniques (exercise program with mirror for visual feedback, exercise at home and facial massage) on a sole basis administered to individuals, 5 to 10 repetitions, 3 sessions/day, for 3 months.

The Beurskens and Heymans study[23] recruited 50 people with long-term (for at least 9 months) peripheral facial nerve paresis. The experimental group received 3 months of mime therapy consisting of facial massage, relaxation, inhibition of synkinesis, and co-ordination and emotional expression exercises. The mime therapy included individual sessions of 45 minutes, once weekly. The control group was placed on a waiting list.

Outcomes assessment

Both studies[22,23] used the same primary outcome assessment Sunnybrook facial grading system (SB-FGS)[35] in the beginning of the treatment and after a period of 3 months. The primary outcome addressed

Table 3 Summary of the characteristics of the included studies

Author (Year)	Study design	Population	Interventions	Outcomes measures	Summary of findings
Manikandan (2007)[22]	Randomized controlled trials	*N*=59 participants; acute Bell's palsy with a mean duration of 2 weeks	1. Exercises (facial neuromuscular reeducation) on a individual basis taught to patients, 5 to 10 repetitions, 3x/day, for 3 months, *N*=29 2. Electrical stimulation (3x/day, for six days in 2 weeks. Galvanic current=90 contractions in each muscle+faradic current=10 contractions in each facial nerve trunk, intensity until minimal visible contraction) plus gross facial expression exercises taught to patients for 3 months, *N*=30.	SB-FGS before and after 3 months	SB-FGS showed that EG [27.5(20–43.77)] improved significantly more than the CG [16.5(12.2–24.7)].
Beurskens and Heymans (2003)[23]	Randomized controlled trials	*N*=50 participants; chronic phase/with sequelae of facial paralysis; HB IV, for at least 9 months	1. Exercises (mime therapy) on a individual basis in sessions of 45 minutes, one weekly, over 3 months (10 sessions) and home program of exercises, *N*=16 CG=waiting list, *N*=18	HB-FGS SB-FGS Before and after 3 months	EG had improved their facial symmetry by 20.4 points on the SB-FGS compared with the CG. In addition, the EG had reduced the severity of their paresis by 0.6 grade on the HB-FGS compared with the CG.

Note: SB-FGS, Sunnybrook facial grading system; HB-FGS, House-Brackmann grading system, EG, experimental group; CG, control group.

three components of facial asymmetry: resting asymmetry, symmetry of voluntary movement, and synkinesis. Burskens *et al.*[23] used primary and secondary outcomes. The secondary outcome measures the severity of paresis and it is measured using the House-Brackmann facial grading system (HB-FGS).[36]

Results after training

Manikandan[22] showed relevant differences in the experimental group (EG) compared to the control group (CG) according to SB-FGS scale (TG=27.5; CG=16.5; $P<0.01$). In this scale the symmetry component of the voluntary contraction was statistically relevant (TG=24; CG=12; $P<0.01$) (Table 3).

The Beurskens and Heymans study[23] noticed relevant statistically significant differences between groups in all the SB-FGS scale components: asymmetry at rest, voluntary contraction symmetry and synkinesis ($P<0.001$). The asymmetry sub-component of the eyes at rest is the only one that was not affected by the intervention of facial neuromuscular reeducation. The EG reduced the IFP severity to 0.6 degrees according to the HB-FGS scale (Table 3).

Quality assessment

The methodological quality of the studies is characterized in Table 4. The two studies did not differ in quality according to the PEDro scale (both scored 5/10). The diversity of interventions and assessments diversity did not allow researchers to undertake meta-analysis of the outcomes of the different studies.

Discussion

In clinical practice, physiotherapists use different treatment techniques in IPF and this review intends to assess the evidence supported in the application of these techniques.

However, between 2000 and 2009 only two experimental studies of moderate quality 5/10 on the PEDro scale were identified. The shortage of investigations, small simple sizes and diversity in groups, study types, and interventions preclude firm conclusions regarding effective techniques for the different phases [critical (flaccid, recovery) and chronic (sequelae)] of the IFP intervention.

The treatment of IPF remains highly controversial. Medical treatment has been proposed in the last decade,[37,38] concerning the virus etiology struggle. Two randomized trials have found significant benefits of medical treatment and concluded that, after treatment, prednisone and acyclovir or valacyclovir may reduce incomplete recovery.[37,38] However, the authors of these systematic reviews on the benefits of corticosteroids recommended future investigations since the results are not sufficient to conclusively recommend drug treatment for IPF.[37,38] Additionally, every treatment is controversial when there is a high rate of spontaneous and complete recovery of the facial nerve.[4] According to Peitersen[4] the IPF has a reasonable prognosis without treatment. In his study, Peitersen[4] found incomplete recovery or some remission (94%) and full recovery (61%) within the first 3 weeks.

The current systematic review showed moderate effectiveness of facial neuromuscular reeducation with mirror feedback[22,23] in the two phases of IFP (acute and chronic). A neuromuscular reeducation program includes analytic and specific exercises of correct motor patterns, facial massage, ocular care and education.[22,23] The moderate coherence of the results in the different study assessments,[22,24] is consistent with other studies,[14,39] which conclude that the neuromuscular reeducation with feedback is effective in preventing and reducing the severity of synkinesis and facial asymmetry. These results of neuromuscular reeducation can be explained through the peripheral and central mechanism based on nervous system plasticity.[31] Manikandan[22] demonstrated the inefficiency of the electric stimulation compared to the neuromuscular reeducation with mirror feedback in the acute phase, after a period of 3 months. The results of Manikandan[22] showed that electric stimulation worsened symmetry facial movement. On the other hand, Diels[39] reported mass action or synkinesis with electric stimulation. However, Manikandan[22] concluded that there was no difference in the Sunnybrook Grading System synkinesis score ($P<0.41$) between groups because this score is difficult to prove in the acute phase, whereas the component

Table 4 PEDro scores

Author (year) Scale PEdro	Manikandan (2007)[22]	Beurskens and Heymans (2003)[23]
Random allocation	1	1
Concealed allocation	0	0
Baseline comparability	1	1
Blind subjects	0	0
Blind therapists	0	0
Blind assessors	0	0
Intention-to treat analysis	0	0
Point measures and variability	1	1
Adequate follow-up (on 85% of subjects)	1	1
Between groups analysis	1	1
Total score (/10)	5	5

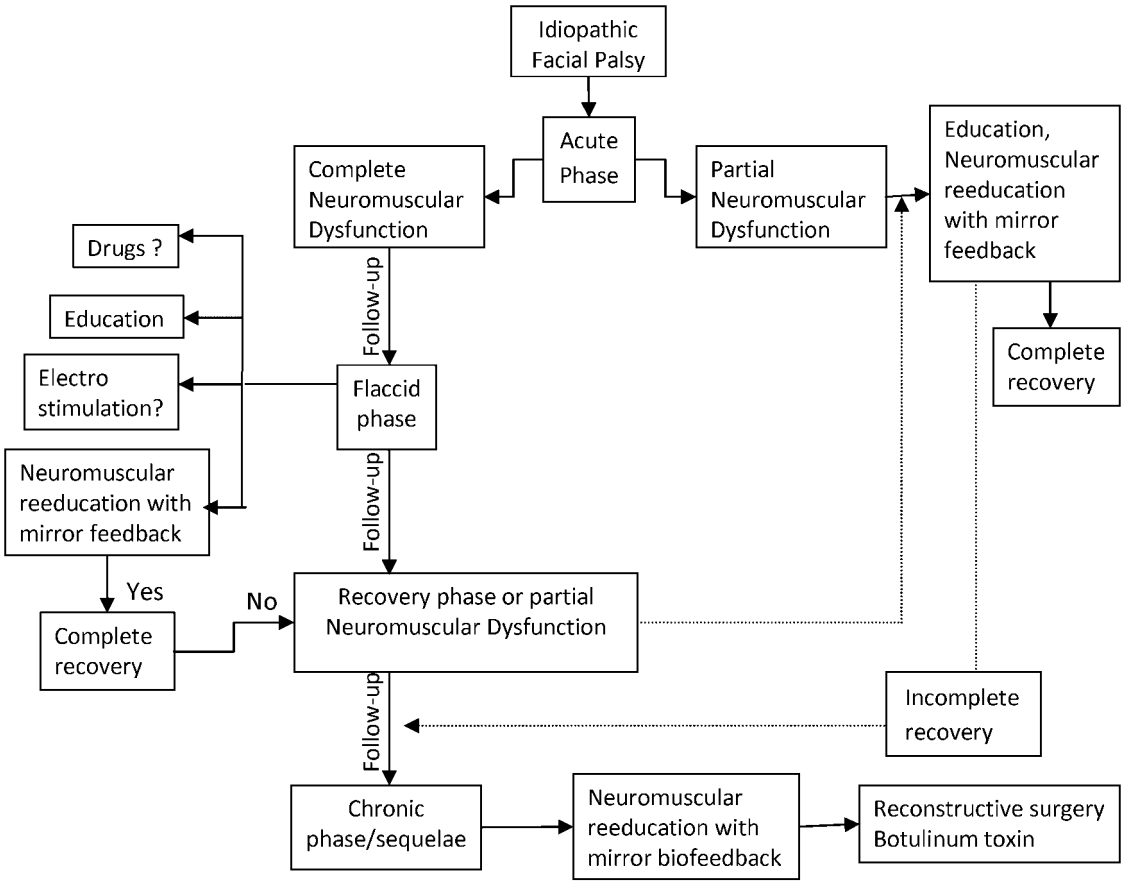

Figure 1 An intervention proposal of idiopathic facial palsy.

movement score showed a significant statistical difference ($P<0.01$) between the two groups. These scores suggest that facial neuromuscular reeducation is more effective and improves facial symmetry. The Manikandan[22] study is limited by the absence of a control group that would allow assessment of spontaneous recovery.

Nearly 30% of the individuals with IFP suffer sequelae of different levels (palsy, contracture and synkinesis). Fifteen per cent of those, with a recovery that begins only after 3 months, suffer from nerve axonal degeneration.[4] Therefore, the chronic phase (sequelae) includes the presence of contractures (17%) and synkinesis (16%) which seems to result in greater discomfort than the palsy (29%).[4] Microscopic evaluation demonstrates that contracture results in a reduction in the number and size of the muscle cells and an increase in the connective tissue and fat, while syncinesis causes multiple growth and defective axonal regeneration, demyelination and microglial scarring.[39] According to House-Brackmann the functional severity level is between IV and V (from severe to complete palsy) and the wallerian degeneration severity that occurs in the nerve includes axonotemesis with wallerian degeneration, endoneurotomesis and perineurotomesis.[40]

Beurskens and Heymans[23] investigated the effectiveness of mime therapy in the reduction of facial asymmetry with sequelae of long-term peripheral facial nerve. After 3 months of treatment mime therapy showed improvements in the Sunnybrook Facial Grading for all three components (resting asymmetry $P<0.001$; symmetry voluntary movement, $P<0.001$ and synkinesis, $P<0.001$) compared to the group on the waiting list. Mime therapy also reduced the severity of paresis by 0.6 grade on the HB-FGS. More research is necessary to confirm these results and the efficacy of this intervention. Lastly, we recommend physiotherapy treatment techniques for use in the different IFP phases based on the author's opinion, to be employed once these interventions are supported by moderate evidence in the literature (Fig. 1).

Conclusions

The conclusions of this systematic review were restricted by a small number of randomized trials, the sample size and intervention diversity. However, two studies demonstrated moderate efficacy in the treatment of facial neuromuscular reeducation with mirror feedback, in the different phases of the palsy. Based on moderate evidence, facial neuromuscular reeducation may reduce asymmetrical movement and synkinesis, in acute and chronic phases respectively. The authors concluded that future high quality investigations of distinct interventions for IFP,

during different phases and with larger simple sizes are necessary.

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ESTUDO II

Physical Therapy with Drugs Treatment in Bell Palsy: A Focused Review

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FOCUSED REVIEW

Physical Therapy with Drug Treatment in Bell Palsy

A Focused Review

ABSTRACT

Ferreira M, Marques EE, Duarte JA, Santos PC: Physical therapy with drug treatment in bell palsy: a focused review. Am J Phys Med Rehabil 2015;94:331–340.

The physical therapy (PT) associated with standard drug treatment (SDT) in Bell palsy has never been investigated. Randomized controlled trials or quasirandomized controlled trials have compared facial PT (except treatments such as acupuncture and osteopathic) combined with SDT against a control group with SDT alone. Participants included those older than 15 yrs with a clinical diagnosis of Bell palsy, and the primary outcome measure was motor function recovery by the House-Brackmann scale. The methodologic quality of each study was also independently assessed by two reviewers using the PEDro scale. Four studies met the inclusion criteria. Three trials indicate that PT in association with SDT supports higher motor function recovery than SDT alone between 15 days and 1 yr of follow-up. On the other hand, one trial showed that electrical stimulation added to conventional PT with SDT did not influence treatment outcomes. The present review suggests that the current practice of Bell palsy treatment by PT associated with SDT seems to have a positive effect on grade and time recovery compared with SDT alone. However, there is very little quality evidence from randomized controlled trials, and such evidence is insufficient to decide whether combined treatment is beneficial in the management of Bell palsy.

Key Words: Rehabilitation, Facial Muscle Recovery, House-Brackmann, Randomized Controlled Trial, Physical Therapy

Idiopathic peripheral facial nerve palsy or Bell palsy (BP) refers to an acute onset of lower motor neuron type of facial paralysis (complete palsy) or paresis (partial palsy), resulting in an inability to control facial muscles on the affected side. BP is the most frequent form of peripheral palsy of the facial nerve, and the reported annual instance is between 11 and 53.3 new cases per 100,000 persons.[1,2] It leads to a considerable disturbance in social activities.[3] The etiology of BP is unknown, but it is widely accepted as being due to the reactivation of latent herpes simplex type 1 virus within geniculate ganglion, followed by the ethiopathologic mechanism that involves inflammation and entrapment of the nerve at the meatal foramen that leads to demyelination of the axons and possible ischemia by disruption of blood supply.[4,5]

The aims of any treatment in acute-stage BP are to promote speedy recovery and prevent sequelae. Thus, the most effective evidence-based treatment that entails

the fewest side effects or risks should be prescribed. Considerable knowledge has been accumulated concerning the significance of pharmacologic treatment based on the presumed pathophysiology of BP, namely, inflammation and viral infection. On the basis of evidence, some physicians prescribe corticosteroids as a primary treatment because of their potential to reduce swelling and inflammation, whereas the aim of antiviral treatment is to inhibit herpes simplex type 1 virus replication through viral DNA polymerase. Several studies have demonstrated somewhat conflicting results about the effectiveness of corticosteroids only or combined with antiviral treatment. The meta-analysis by Nunthavaj et al.[6] suggests that corticosteroids combined with antiviral treatment may lead to slightly higher recovery rates at 3 and 6 mos compared with treating with corticosteroids only, although this difference is not statistically significant. Corticosteroids remain the strongest evidence-based monotherapy treatment, whether compared with placebo or antiviral treatment.[6,7] On the other hand, one systematic review[8] included three studies with 117 patients who demonstrated no benefit from using corticosteroids only compared with placebo/vitamin. The American College of Neurology currently recommends the use of oral corticosteroids only.[9]

For the past decades, some methods and physical agents of facial physical therapy (PT), such as functional neuromuscular reeducation associated with or without mirror, mime therapy, electrical stimulation, surface electromyography biofeedback, and video self-modeling, have been used to treat facial paralysis, but the significance of PT is controversial.[10–12] Most previous studies evaluated the effects of PT or drug therapy only. Thus, the combined effect of PT with corticosteroids and/or antivirals on patients' recovery rates has been poorly investigated. In addition, it should be highlighted that BP has a high rate of spontaneous recovery, thus making it difficult to establish a strong cause-effect association between treatment and recovery, even in controlled trials. Peitersen[13] suggested a favorable prognosis of spontaneous recovery within 3 wks in 85% of patients, and 70% had a complete recovery within 6 mos. However, patients with inappropriate treatment may experience longstanding paralysis and develop sequelae, contractures, partial recovery of motor function, and synkinesis, affecting 31% of BP patients.[14]

The conclusion of the literature review was that, although standard drug treatment (SDT) seems to reduce edema and secondary inflammation damage, it does not influence the amount of long-term damage. As the only alternative to no treatment, PT seems to be effective in improving facial expression and function. Strategies of PT have been developed to control the symmetry of the face, through slow movements and voluntary control of synkinesis, particularly with specific exercises. The central question in this research is, "Do PT and SDT have positive effects on grade and time recovery in BP?" Given the emergence of this clinical practice and lack of evidence of the benefits, this is the first systematic review to present the evidence for prescribing PT associated with SDT.

METHODS

Criteria for Considering Studies for This Review

Studies and Participants

A study was included in the review only when the following criteria were met: (1) there were randomized trials (RCTs) or quasi-RCTs, (2) the study population consisted of patients diagnosed with BP of all degrees of severity, (3) the efficacy of PT plus drugs treatment was evaluated, (4) there were at least 15 days of follow-up, (5) the outcome measure was motor function recovery by a recognized scoring system such as the House-Brackmann (HB) facial grading system,[15,16] (6) there was a comparative control group (CG), and (7) it included adults older than 15 yrs. The authors did not include studies on pregnant women, patients experiencing recurrent or bilateral BP, and studies comparing PT or drugs therapy only. No language restrictions were used.

Types of Interventions

Included studies compared interventions with any PT (except acupuncture and osteopathic) combined with SDT (corticosteroids and/or antiviral agents) against a CG. The accepted intervention in the comparison group was SDT only or SDT (similar in the experimental group [EG]) plus a distinctive PT to assess which PT technique is the most beneficial. PT in BP can include functional neuromuscular reeducation with or without mirror, mime therapy, video self-modeling, electromyography biofeedback, and electrical stimulation with or without thermal or massage agents.

SDT was accepted if administered orally and started immediately after the diagnosis of BP.[9,17,18]

Types of Outcome Measures

The primary outcome of the present study was complete or partial facial muscle recovery, defined by HB grade 1 or 2. This scale analyzes the

symmetry, synkinesis, stiffness, and global mobility of the face. It is divided into six categories (normal, mild dysfunction, moderate dysfunction, moderately severe dysfunction, severe dysfunction, and total paralysis) and is a 1- to 6-point scale with 6 representing total paralysis.[15,16]

Secondary outcome measures were adverse events (side effects of interventions); compound motor action potential amplitude and percentage activity as measured in the orbicular oculi and frontal and orbicular oris muscles, the both sides of the face [(electroneurography (%) = 100 - 100*(amplitude on the affected side/amplitude on the healthy side)]; no residual symptoms (synkinesis, hemifacial spasm, contractures, epiphory); and Sunnybrook facial grading system (SB). The SB system has three components of facial asymmetry: resting asymmetry (scored from 0/asymmetry to 4/symmetry), symmetry of voluntary movement (0/asymmetry, 5/symmetry), and synkinesis (0/better, 3/worst).[19] A total score of 100 points represents normal facial symmetry.

Search Methods for Identification of Studies

The search strategy was applied to the following databases: MEDLINE, Academic Search Complete, MedicLatina, CINAHL, SPORTDiscus, Scopus, and PEDro from their inception to August 1, 2013. The search method incorporated National Library of Medicine Medical Subject Headings,[20] combining the following terms: (1) type of disease, "idiopathic facial palsy" or "facial paralysis" or "Bell's palsy," and (2) types of intervention, "physical therapy" or "physiotherapy" or "mime therapy" or "exercise movement techniques" or "facial exercises" or "facial expression" or "physical rehabilitation" or "Biofeedback" or "electrical stimulation" or "massage" and ["drug therapy" or "anti-viral agents" or "acyclovir" or "valacyclovir" or "famciclovir" or "anti-inflammatory agents" or "cortisone" or "prednisone" or "corticosteroids" or "steroids"].

Selection of Studies and Data Extraction

Abstracts and full texts identified by computerized database searches were screened by two reviewers (MF, JD), using predetermined eligibility criteria to ascertain potentially relevant trials to be included in the review, as defined in the National Health and Medical Research Council classification guidelines.[20,21]All relevant information was collected in data extraction form, which included the following: study design, authors and year of publication, country and setting, sample size, patient demographics, number of patients in each treatment group, type of antiviral and/or steroids used and dose, type and frequency of PT, length of follow-up, type of facial muscle recovery outcome scale used, definition for facial recovery, proportion of patients with facial recovery at each follow-up time point, and methodologic quality of included studies. Disagreements regarding trial eligibility were

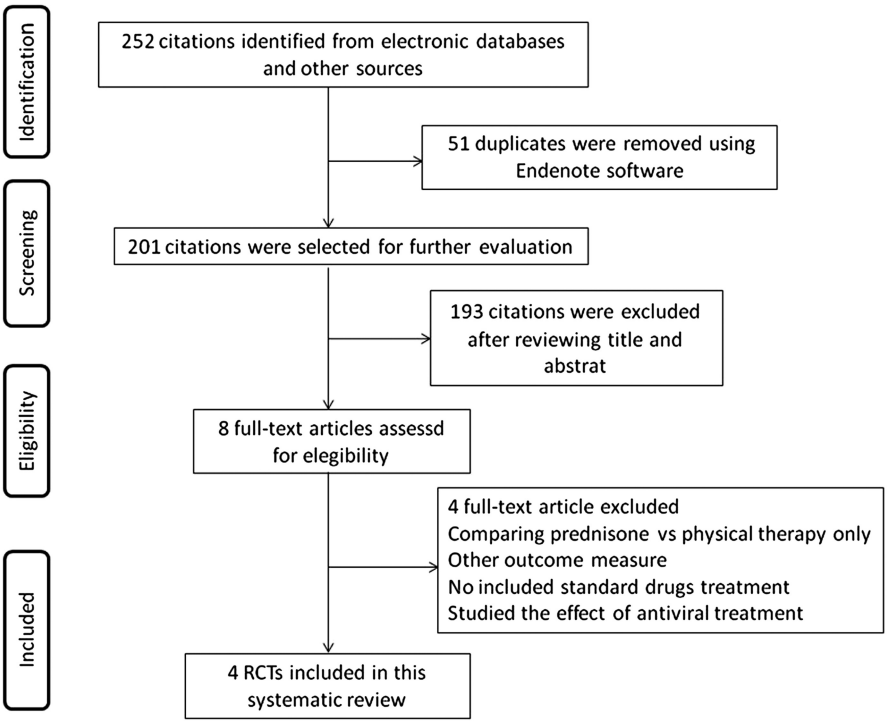

FIGURE 1 *Flow diagram of the study selection process.*

resolved by discussion and consultation by a third reviewer (ME).

Assessment of Methodologic Quality

The PEDro scale was used to rate the methodologic quality of each study. The scale contains 11 items, of which ten items assess internal validity.[22,23] One criterion was omitted among the studies (eligibility criteria), because such criterion refers to the generalization of the results. Each item was graded 0 or 1 (point), with a maximum score of 10 points. PEDro scores were interpreted as follows: a score of 9 or more indicated excellent methodologic quality, 6–8 was good methodologic quality, 4–5 was fair methodologic quality, and <4 was poor methodologic quality. Two reviewers (MF, JD) assessed quality independently. Any disagreement between the two reviewers was discussed and resolved by consensus with a third author (EM).

RESULTS

Description of Studies

Selected Studies

The search strategy retrieved 252 abstracts (Fig. 1). As some studies were found in more than one database, duplicates were removed. A total of 244 studies were excluded because they did not match the inclusion criteria. Of these, eight trials were identified as highly relevant, although four were subsequently excluded: one study[24] compared the intervention with prednisone alone *vs*. PT alone, another study[25] used different outcome measures, another study[26] did not include SDT, and the last analyzed the effect of antiviral treatment.[27] Four studies satisfied the inclusion criteria and were included in the current review.

Included Studies

In total, four studies[28–31] were included in the systematic review (Table 1). Of these, three studies[28–30]

TABLE 1 Characteristics of included studies

Study	Country, Setting	Participants
Nicastri et al.[28] (2013)	Italy University Hospital "Umberto I"	Total of 87 patients with severe grade (HB ≥ IV) on the tenth day after the onset of palsy; follow-up, 6 mos; CG, 48 patients (22 men, 26 women); age, 51.3 yrs; EG, 39 patients (22 men, 17 women); age, 47.1 yrs
Barbara et al.[29] (2010)	Italy University Hospital "Sant´Andrea"	Total of 20 patients with moderate-to-severe grade (HB ≥ 3) on the third day after onset, follow-up of 2 wks; CG (nonrehabilitation), 11 patients (five men, six women); age, 42 yrs; EG (rehabilitation), nine patients (five men, four women); age, 35 yrs
Penteado et al.[30] (2009)	São Paulo (South America) Hospital University	Total of 20 patients with moderate-to-severe grade (HB ≥ III–V) on the fourth mo of the episode of BP were followed for 1 yr; CG, ten patients (18–60 yrs); EG, ten patients (18–60 yrs)
Alakram et al.[31] (2010)	South Africa Hospital Complex (three hospitals)	Total of 16 patients in early stages of BP, follow-up of 3 mos; CG, eight patients (three men, five women); age, 41.4 yrs; EG, eight patients (five men, three women); age, 3.6 yrs

evaluated SDT (corticosteroids + antiviral agents) plus PT *vs*. SDT alone. The other study[31] evaluated a monotherapy drug (prednisolone) plus conventional PT *vs*. prednisolone plus conventional PT and electrical stimulation.

The four trials included an overall sample of 143 patients (between 16 and 87 patients). The length of follow-up varied between studies and ranged from 2 wks to 12 mos. Trials were conducted in three countries and on three continents. Three studies[28,29,31] were published in English, and one study[30] was published in French.

The study by Nicastri et al.[28] was designed for 6 mos, was single-blind, and was an RCT. It included 87 patients with BP, distributed in two treatment groups: an EG (39) received SDT (prednisone + valacyclovir) combined with PT, and the CG (48) received SDT. The eligibility criteria were as follows: age between 15 and 70 yrs, unilateral BP clinically diagnosed, and severe (grades IV–VI) facial palsy assessed by HB on the tenth day after the initial symptoms of BP. Both groups were treated with oral prednisone (1 mg/day for 10 days) plus valacyclovir (500 mg three times per day for 6 days). In addition, the EG was treated with a neuromuscular retraining program that consisted of facial muscle physiology and massage education, active motion exercises with or without mirror feedback, stretching, and specific facial exercises. Each patient of EG was treated in the outpatient clinic by means of individual sessions lasting 45 mins each, twice a week for the first 3 mos and once a week thereafter, until the follow-up was completed. All patients were assessed by HB on their first visit to the clinic, 10 days thereafter, and then monthly until the end of follow-up (6 mos).

Barbara et al.[29] published a study of a randomized trial: 20 patients with moderate- to severe-grade

Interventions	Outcome	Results/Conclusions
CG: patients who received only SDT (oral prednisone of 1 mg/10 days + valacyclovir of 500 mg three times a day for 6 days). EG: patients who received the same SDT plus PT (neuromuscular retraining program with or without mirror feedback; individual sessions lasting 45 mins each/two times a week for the first 3 mos and once a week thereafter, until the follow-up was completed or at the end of the 6 mos).	The primary outcome was the HB-FGS (reaching a grade of II or less). The secondary outcomes were the time to reach a HB-FGS grade of II or less, the differences over time in the mean SB-FGS total score, and the proportion of patients having a synkinesis subscore of 0 (i.e., no synkinesis).	The results demonstrated that the EG experienced a significant effect in grade and time to recovery only among patients presenting with severe facial palsy (HB grade V/VI). The reduction of synkinesis was not significant between the groups.
CG: patients were submitted to SDT (oral prednisolone of 40 mg/day for 10 days and then tapered within the next 5 days + acyclovir of 400 mg three times per day for 15 days). EG: patients received the same SDT and Kabat rehabilitation or proprioceptive neuromuscular facilitation (stretching, maximal resistance, manual contact, verbal input).	HB-FGS (grades I and II) and electroneurography (amplitude of the compound motor action potential); normal range was considered to be between 2 and 4.5 mV.	Kabat rehabilitation patients achieved a better and faster recovery in comparison with nonrehab patients, in early stages.
CG: received SDT (oral prednisone of 1 mg/day for 15 days + valacyclovir of 500 mg three times a day for 5 days). EG: patients received the same SDT and rehabilitation facial or Chevalier method, which consisted of analytic muscle exercises and undesirable movement inhibition by stretching, for 15 mins, two times per day and five-to-ten repetitions for each exercise, from days 1 to 15 after symptom onset.	HB-FGS (grades I and II), SB-FGS	The facial rehabilitation method described by Chevalier showed improvement in function recovery than CG.
CG: patients were treated with drug monotherapy (oral prednisolone of 2 mg daily) weaned off within 2 wks and combined conventional PT (5 mins of hot packs, 10 mins of massage, and ten repetitions of exercises once a week/home exercise). EG: patients received the same drug monotherapy and conventional PT with electrical stimulation (30 mins/TENS unit).	HB-FGS (recovery defined, 80%)	The improved percentage of HB-FGS in the EG was not significant compared with the CG.

(HB ≥ III–VI) early-stage BP who submitted to SDT (prednisolone + acyclovir) for 15 days were included. Drugs treatment was immediately started, combining oral prednisolone (40 mg/day for 10 days and then tapering off within the next 5 days) plus acyclovir (400 mg three times per day for 15 days). After that, they were divided into two groups. The rehabilitation group (rehab group) of nine patients underwent Kabat rehabilitation with one session per day for 6 days, sustained for 15 days. The nonrehabilitation group (nonrehab group) of 11 patients did not submit to physical rehabilitation. Kabat rehabilitation or proprioceptive neuromuscular facilitation started from day 4 after BP onset and included stretching, maximal resistance, manual contact, and verbal input. This method considers the harmony, coordination, and optimal strength of body movements through a global pattern. The evaluation was carried out by measuring the amplitude of the compound motor action at days 4, 7, and 15 after onset of BP as well as by observing grade House-Brackmann within 3, 4, 7, and 15 days.

Penteado et al.[30] had 20 patients with moderate-to-severe grade (HB ≥ III–V) on the fourth month after onset of BP, who were followed for 1 yr. All patients received SDT oral prednisone (1 mg/kg/day for 15 days) plus valaciclovir (500 mg three times per day for 5 days). The EG included ten patients treated according to the facial rehabilitation method described by Chevalier between the 1st and 15th days after the installation of BP and having developed sequelae during their recovery. Facial rehabilitation consisted of analytic muscle exercises on the palsy face and inhibition of undesirable movements by stretching. The CG received a nonrehabilitation facial. All patients were evaluated weekly during the first month and then monthly until the end of the study by HB and SB scales.

The study conducted by Alakram and Puckree[31] had 16 patients with BP with less than 30-day duration, randomized into two intervention groups with eight patients each. Both groups were treated with oral prednisolone (2 mg/kg daily, weaned off within 2 wks). The researcher treated each patient in both groups (CG and EG) with 5 mins of heat, 10 mins of massage, and ten repetitions of exercises once a week, and each patient was also given an illustrated home exercise handout with instructions: ten repetitions of each exercise, three times daily. The EG also received electrical stimulation of the facial muscles (30 mins/pulse and frequency of 10 Hz/pulse width and duration of 10 μsecs). All patients were objectively evaluated with the HB scale until recovery, for a maximum of 3 mos after onset of BP.

Methodologic Quality of the Studies

PEDro scores ranged between 2 and 8 (Table 2), with one study[28] considered to have good methodologic quality (i.e., PEDro score of 6–8). All studies[28–31] were conducted with no blind patients, therapists, and concealed allocation, which reduced the maximum score achieved. On the other hand, all studies[28–31] satisfied the criteria of baseline similarity between groups and point estimates and variability. Three studies[28–30] observed the follow-up of greater than 85%, and two studies[30,31] did not use random allocation.

Effects of Interventions

Primary Outcome Measure

All studies reported satisfactory recovery for PT and medical treatment. Nicastri et al.[28] showed that the EG (PT plus SDT) had a significant effect in function recovery ($P = 0.038$) and time of recovery ($P = 0.044$) compared with the CG (SDT) on patients with HB grade V/VI, at the end of the 6-mo follow-up period.

The study by Barbara et al.[29] showed that the rehabilitation group (Kabat rehabilitation combined with SDT) had significant improvement only at day

TABLE 2 Methodologic quality of studies

	PEDro Criterion											
Study	1	2	3	4	5	6	7	8	9	10	11	Total/10
Nicastri et al.[28] (2013)	1	1	0	1	0	0	1	1	1	1	1	7/10
Barbara et al.[29] (2010)	1	1	0	0	0	0	0	1	0	1	1	4/10
Penteado et al.[30] (2009)	1	0	0	1	0	0	0	1	0	1	1	4/10
Alakram et al.[31] (2010)	1	0	0	0	0	0	0	0	0	1	1	2/10

PEDro criteria: (1) eligibility criteria, (2) random allocation, (3) concealed allocation, (4) baseline comparability, (5) blind subjects, (6) blind therapists, (7) blind assessors, (8) follow-up > 85%, (9) intention-to-treat analysis, (10) between-group comparisons, and (11) point estimates and variability.

Item scoring: 1, present; 0, absent. Criterion 1/eligibility criteria does not contribute to total score.

15 ($P = 0.028$) compared with the nonrehabilitation group (SDT). At day 15, the worst grade of paralysis was HB III and affected 44% of the rehab group, whereas 10% of patients in the nonrehab group were affected by HB V. Conversely, HB grade I (normal function) was observed in 22% of the rehab group and in 20% of the nonrehab group.

The Penteado et al.[30] study showed better facial recovery of motor function (HB, 87 values or grades I and II) with the Chevalier method plus SDT compared with SDT (HB, 69 or grades III and IV).

Alakram and Puckree[31] compared two interventions and reported rate recovery of motor function in the CG between 17% and 50% with a mean of 30%, whereas that for the EG ranged from 17% to 75% with a mean of 37%. The difference between the groups was not statistically significant ($P = 0.36$).

Secondary Outcome Measure

The Nicastri et al.[28] study reported a significant difference between two groups for SB final scores: 60 and 79 values for the CG and EG, respectively ($P = 0.021$).

The Barbara et al.[29] study showed no significant variation in compound motor action potential amplitude.

The Penteado et al.[30] study revealed a difference between groups for SB final scores: 89 values for the Chevalier method plus medical treatment group and 69 values for medical treatment.

Residual Symptoms

Nicastri et al.[28] demonstrated that synkinesis was found in 25 patients (29%), and in most cases, it started after the fourth month of follow-up. There were no differences between the two treatment groups in the proportion of patients with a synkinesis subscore of 0 at the end of the study period.

The Penteado et al.[30] study also showed that sequelae were developed approximately the fourth month after onset of palsy, in both groups.

Three studies[29–31] did not evaluate synkinesis.

Adverse Events

All studies did not report side effects of pharmacologic treatment, but Sullivan et al.[18] reported peptic ulceration, hypertension, and state-of-confusion effects.

DISCUSSION

Many physicians prescribe antiviral and steroid drugs to treat BP, despite the unclear benefits of antiviral therapy.[32] Recent evidence from large RCTs indicates that the complete recovery rate with oral prednisolone is approximately 85%–94% within 9–12 mos.[18,33] In the present review, all studies[28–31] had anti-inflammation interventions (prednisone or prednisolone), administered within 48–72 hrs of the onset of BP. In opposition to medical treatment, PT is an alternative and is one of the most commonly used in clinical practice. This review included modalities of facial rehabilitation in the form of Kabat[29] and Chevalier,[30] electrical stimulation,[31] neuromuscular retraining[28] with or without massage, and hot pack. The efficacy of facial rehabilitation has been shown in patients with permanent sequelae or long-standing facial paresis (at least 9 mos) by several observational studies.[34–37] In contrast, the efficacy of facial rehabilitation in early/acute stages is more complex to calculate because of the high rate of spontaneous recovery.[13] Presently, there are scarce studies about conservative treatment in the early stage of BP.[38,39] Three systematic reviews[11,12] demonstrated that the ideal modality of PT has not yet been established or that no clear consensus exists. According to the previous literature, reviews focused on the monotherapy of SDT or PT effects of interventions, and so the combined therapy effects of interventions remain unknown.

In the present systematic review, three studies[28–30] indicate that facial rehabilitation associated with SDT is slightly superior in recovery of motor function than SDT alone. One RCT[28] showed a significant effect on grade and time to recovery in patients presenting with severe BP (HB $\geq$ IV) compared with SDT alone. In addition, through secondary outcomes, two studies[28,30] reported significant facial symmetry by Sunnybrook with the neuromuscular retraining and rehabilitation method described by Chevalier. Only one study[28] showed that combined treatments are effective in fighting synkinesis. On the other hand, one study[31] did not find the kind of technique in PT for the recovery motor function of BP; this study concluded that electrical stimulation did not greatly influence the recovery rate of BP.

Thus, the studies covered in this systematic review support improvements with respect to drugs treatment, which might include the following:

(1) Corticosteroids reduce the inflammatory process in BP, and this facilitates remyelination of the facial nerves. This theory made good physical sense based on the length of the canal and relatively small caliber and subsequent decompression of the nerve.[6,18]
(2) The addition of antiviral treatment such as acyclovir or valacyclovir is aimed at the eradication of herpes simplex type 1 infection.[6,7]

This prescription therapy is based on primary etiology; it is quite plausible when it involves the viral agents' herpes simplex type 1 or varicella-zoster virus.

In addition, the possible explanations for the incremental effects of PT might include the following:

(1) External feedback techniques such as specific instructions and mirror are adjuvant techniques to control the correct pattern of responses that the patient will learn to self-regulate.[40]
(2) Soft-tissue mobilization and hot pack preserve muscle trophism, increase circulation, and reduce involuntary contraction induced by relaxation.[14]
(3) Electrical stimulation has been discouraged in the early stages of BP to avoid potential interference with neural regeneration.[39] It is difficult to produce an isolated contraction of the facial muscles using electrical stimulation due to their small size and close proximity to each other. The contraction produced causes mass action, which reinforces abnormal motor patterns and can be painful.[41,42]
(4) The neuromuscular rehabilitation, Kabat and Chevalier rehabilitation, included the active assistive movement to guide the movement pattern and to promote axonal regeneration by improving the neuronal connection and facilitating new motor patterns.[43] Owing to the lack of somatosensory afferents that constitute the main intrinsic feedback in relearning movements is particularly important in facilitating the proprioceptive inputs by PT techniques.[44]
(5) The stretching can influence the length-tension relationship of muscles, avoiding mass movement patterns and synkinesis.[44]

These combined modalities of BP should be centralized in the degenerative lesion of the facial nerve, which may be the most important risk factor for incomplete recovery. The time course for improvement and the extent of recovery are significantly different in patients presenting with an incomplete (paresis) at the onset of BP. Patients with incomplete BP should start to improve their facial function within 1–2 wks after onset of BP and are expected to recover completely within 3 wks.[13] These patients have a spontaneous recovery of BP; it does not seem that any treatment adds benefits because of the only partial degeneration and blocking of nerve conduction (neuropraxia).[13] One study[31] included patients with slight dysfunction in the onset of BP (corresponding HB = II), which showed improvement in function recovery after 2 wks, and no significant differences between the groups. On the other side, in the patients' subgroup with moderate-to-complete paralysis (corresponding HB grade ≥ III) at the onset of BP, complete recovery is more uncertain. Optimum therapy remains a crucially important issue for the 30% of patients who experience a varying degree of complications, including permanent paresis, pain, and synkinesis, which can be highly stressful.[45] Three studies[28–30] demonstrate that PT plus SDT approaches seem to be more effective in the severe and early/acute stages of BP.

Limitations

To the authors' knowledge, this is the first systematic review examining the effectiveness of combined PT with SDT in the early stage of BP.

First, as with any systematic review, there is the potential for selection bias; however, the authors used an ample search strategy in which the authors included publications in any language as well as independent reviewers; exclusion criteria were clearly documented.

Second, the PEDro scores were lowered by a lack of insufficient randomization and allocation concealment; appropriate blinding of patients, therapists, and assessors; and substantial losses in intention-to-treat analysis. Third, there was heterogeneity among studies, particularly the sample size, grades severity at baseline, time of duration of the intervention, delay in receiving treatment of PT, and different types of modalities. Finally, a few studies were included. This diversity prevented us from conducting a meta-analysis and highlights the need for further research.

CONCLUSIONS

The present review suggests that the current practice of BP treatment by PT associated with SDT seems to have a positive effect on grade and time recovery compared with SDT alone. However, there is very little quality evidence from RCTs, and this is insufficient to decide whether combined treatment is beneficial in the management of Bell palsy. Further research is required to evaluate the efficacy of PT associated with SDT and to determine the better modality to reduce the time of recovery and occurrence of synkinesis.

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CME Self-Assessment Exam Answers

CME Answers

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Arneja et al.

1. D
2. B
3. B
4. A
5. A

3] CAPÍTULO
ESTUDOS ORIGINAIS

ESTUDO ORIGINAL III

Oral intake of corticosteroids in the early stage of Bells' palsy has no additional benefit then facial neuromuscular training

Under review in *Acta Oto-Laryngologica* with minor revisions

Title: Oral intake of corticosteroids in the early stage of Bells' palsy has no additional benefit then facial neuromuscular training

Short running title: Corticosteroids with exercise and Bell´s Palsy

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Abstrat

Objectives: The main aim of this study was to investigate whether the use of corticosteroids paralleled with neuromuscular training (C+FNT) is more effective than facial neuromuscular training (FNT) applied alone, in terms of recovery degree and facial symmetry during the early phase of Bell's palsy (BP).

Methods: Seventy three patients with BP were included. The patients were systematically treated with corticosteroid plus facial neuromuscular training (C+FNT, n=42) or with facial neuromuscular retraining (FNT, n=31) only, within 10 days of onset. Patients were assessed before and six weeks after treatment by outcome measures House-Brackmann (HB-FGS) and Sunnybrook Facial Grading System (SB-FGS).

Results: Recovery degree and facial symmetry improved significantly in both groups ($p<0.001$), without differences between groups ($p<0.05$). However, the C+FNT group displayed better outcomes for check ($p=0.004$) and mouth ($p=0.022$) resting symmetry of SB-FGS comparing to FNT group. The corticosteroid had no significant effect in all recovery degree ($p=0.992$) and remission time ($p=0.995$). Multiple linear regression analysis showed that type of intervention was not a significant predictor for recovery degree ($p=0.917$).

Conclusions: Our results provide preliminary evidence that the addition of corticosteroid was not effective in all grades of dysfunction and remission time at early phase of BP, highlighting the need to define standard and rigorous criteria to prescribe corticosteroids in these patients.

Keywords: facial palsy; medical therapy; muscle training; Sunnybrook Facial Grading System; House-Brackmann Facial Grading System

Introduction

The most common type of facial paralysis is the Bell's palsy (BP), which represents about 66% of all peripheral facial paralysis.[1] BP is defined as an acute unilateral paralysis or paresis of the facial nerve without any associated disorders.[1,2] There are several conditions that can cause facial paralysis such as, congenital disorders, traumas, neoplasms, autoimmune diseases and local infections,[3] which must be discharged before a diagnosis of BP.

Facial functions are multidimensional, providing emotional, social, and physical features of personal health.[4,5] Therefore, incomplete recovery from facial nerve damage has significant social and psychological consequences.[4] Although the prognosis of BP is generally good, with a high rate of recovery, 29% of patients with BP lack to achieve a satisfactory recovery.[1] Moreover, patients with complete facial palsy and absence of recovery within 3 weeks may experience poor outcomes.[6,7]

The prognosis and outcomes of the BP are highly dependent on the severity of nerve impairment as well as the management of this disorder. More recently, BP has been attributed to viral etiologies, principally herpes simplex virus type 1 (HSV‑1).[8] Pathologically HSV-1 (re)activation results in an inflammation of the seventh facial nerve, which leads to compression within the bony canal fallopian and nerve demyelination.[9,10] Based on this, in 2012, the American Academy of Neurology[11] established that powerful anti-inflammatory agents, such as oral corticosteroids, are effective in improving facial function outcomes in BP. Furthermore, Sullivan *et al.*[12] reported a significant improvement of facial nerve function in patients treated with prednisolone within 72 hours of onset. On the other hand, oral antiviral therapy in addition to oral steroids is considered more beneficial for patients with new-onset BP than oral antiviral therapy alone. [2]

At present, evidence suggests that there are no beneficial effects of physical therapy in the treatment of BP[2]. Nevertheless, several studies showed advantages in facial symmetry and quality of life in people with BP after several therapy modalities, such as thermal treatment, electrotherapy, massage, facial exercise, and biofeedback.[7,13-17] Several Cochrane Systematic Reviews[18-20] have concluded that the recommendation for optimal physical therapy of BP is difficult due to limited number and low quality of trials and the heterogeneity of results.

The recent American and Australian Guidelines[2,21] recommend the use of corticosteroids for all patients with BP; on the other hand, the use of facial exercise for acute phase of BP of any severity was not recommend. The Australian Guidelines only suggest facial exercise for patients with persistent weakness. Moreover, for acute phase of BP, the Indian Guidelines[22] include physical therapy and corticosteroids for targeting the speed recovery. Thus, while recent practice guidelines include corticosteroids in the treatment of BP, the use of physical therapy is not unanimously recognized. However, there are no data regarding the effects of corticosteroids treatment versus facial neuromuscular training only, in early phase of BP.

In this study, the main goal was to investigate whether the use of corticosteroids allied with neuromuscular training is more effective than the facial neuromuscular training applied alone, in terms of recovery degree and facial symmetry during the early phase of BP. Four main hypotheses were tested: (1) corticosteroid treatment influences positively of recovery degree and facial symmetry; (2) patients with a high degree of BP severity have more benefits with the use of corticosteroids; (3) the remission time is faster with the administration of corticosteroids; and (4) predictors, such as age, sex, baseline HB-FGS, and intervention type, influence the recovery degree.

Methods

Subjects and Experimental Design

A prospective and single-blinded trial, performed in patients diagnosed with peripheral facial paralysis, screened from January 2009 to May 2013 (Fig 1). The first clinical visit included examinations by a clinical physician, an otolaryngologist, and a physiatrist, according to the routine protocol of the XXXX hospital, XXXX. In the urgency department, all outpatients were referred to Physical Medicine and Rehabilitation (PM&R) unit at XXXX hospital by the clinical physician. This study was implemented according to the rules of the CONSORT statement.[23] The protocol was approved by the hospital ethics committee, and written informed consent was obtained from all studied patients. An initial sample composed by 123 patients with peripheral facial paralysis was examined by a physiatrist, in the PM&R department. The eligibility criteria for this study included: patients diagnosed with unilateral BP of both gender, age 18 years and older, onset of oral corticosteroid treatment within 72 hours after the initial symptoms

of BP, and facial neuromuscular retraining treatment within 10 days after the initial symptoms of BP. Patients were excluded if they had recurrent facial nerve palsy, a central nervous system disease, traumatic facial nerve injury, metabolic, infective, cancer, psychiatric condition, neuropathy or neuromuscular disease, antiviral treatment therapy, corticosteroids treatment for others diseases and, inability to speak or read Portuguese language.

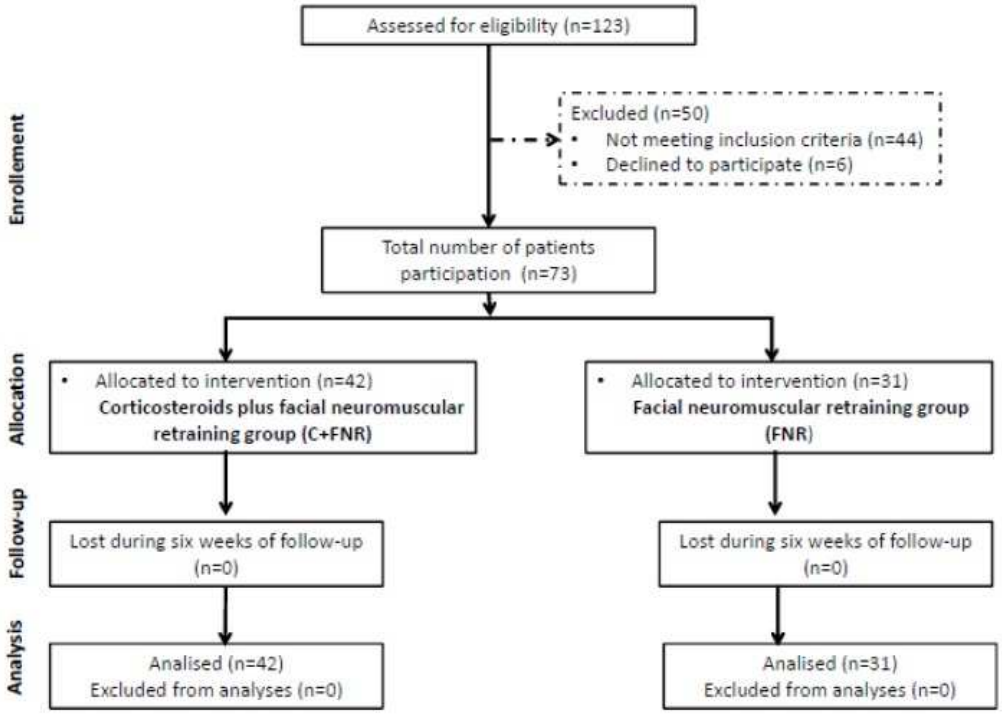


Fig.1 CONSORT diagram summaring the flow of participants

BP was diagnosed when no other cause was identified through medical history and physical examination by a physiatrist at PM&R department. In case of a diagnostic disagreement, radiology and laboratory testing were performed. A questionnaire was applied to all selected patients and included demographic data, side of palsy, symptoms, date to first consultation, and medical and personal history. According to the prescription of several clinical physicians, 73 eligibility patients were divided into two treatment groups: Corticosteroid plus Facial Neuromuscular Training (C+FNT) group or Facial Neuromuscular Training (FNT) group. The prescription criteria for corticosteroids administration were unknown and without any apparent uniformity among the physicians, allowing obtaining subjects with different severity levels of BP,

with and without prescription of corticoids, in the final sample. Blinding to treatment allocation of participants and physical therapists was not possible due to the nature of the interventions. However, clinical physicians and investigators were blind to the allocated intervention.

Intervention

The C+FNR group was composed by patients receiving oral prednisolone, within 72 hours of BP onset, at a dose of 1mg/kg per day (maximum 60mg/per day) for 5 days, then tapered over 5 days (10mg/per day). Both groups were treated with FNT individually by five trained physical therapists in accordance to the facial neuromuscular training principles[24-28]. Each patient was treated in the outpatient hospital, 5 days a week, 20 minutes a day, for 6 weeks or until complete recovery. In the case of complete recovery, FNT was no longer performed, although assessment continued until the sixth week.

A standard program of FNT included different muscle groups supplied by each branch of the facial nerve in both sides of the face by using a mirror to promote symmetry and feedback. The FNT was based in principles of strength training, overload and specificity.[29] Table 1 shows the detailed description of each training phase.

Table 1 Facial neuromuscular training components of intervention

Phase 1 Information	All patients were educated on facial muscle physiology, facial functions and changes induced by paralysis
Content of the standardized education[24,28]	✓ Postural correction information was given for to increase awareness of the head position and its effect on facial tone ✓ Relaxation training was taught to increase the participant's awareness of the hyperactivity of the unaffected face by breathing and relaxation exercises ✓ Tissue mobilization was taught to improve circulation and sensory stimulation by combination of "effleurages" and "kneading", in both side of the face and neck during 5 to 10 min ✓ Strategies were instructed for to avoid mass facial movements (excessive chewing on the affected side), eye protection (wear glasses, an eye shield and ointment) and oral hygiene
Phase 2 Training components and techniques intervention	All patients were treated individually by trained physical therapist and biofeedback method (mirror)
Standardized training components[24,28,29]	✓ The basis exercises consisted of seven facial muscles/motion (Frontalis/wrinkling; Corrugator supercili/wrinkles of forehead; Orbicularis oculi/closure of eyes; Procerus/snarl; Orbicularis oris/whistling; Risorius/smile; Zigomaticus/laugh) with variations of speed, amplitude, force, repetitions (from 5 to 20), series (from 1 to 2) per each facial muscle, selective and coordination motion and other muscles innervated by the facial nerve. Patients were also taught expression exercises (e.g. to open the eyes wide/surprise, lift the upper Lip/disgust, tighten the lips/anger, lips pucker/kiss or laugh/happy) and facial function (eat, drink, speak)
Techiniques intervention[24,28,30]	✓ *Neuromuscular facial training* had two different interventions according to the House-Brackmann-Facial Grading System assessment. Patients who had severe facial asymmetry at rest or flaccid facial regions, and who were unable to initiate movement on the affected side were given instructions on small and controlled movement by passive and active assistive exercises. On the other hand, patients who had mild to moderate facial asymmetry at rest and were able to initiate at least slight movement in any or all regions of the face were given instructions in the isolated movement and controlled by active assistive and resistive exercises
Homework	✓ In addition, when the patients performed correct movements and symmetry of facial expression were instructed to practice a home-based exercise program, 2 times a day, for no more than 10 minutes per day. Adherence to the home exercise was formally registered daily in standard document by patients and it was weekly controlled by physical therapists.

Outcome measures

Assessment of patients was performed using two of the routinely used systems in clinical practice:[13-17] the House-Brackmann facial grading system (HB-FGS)[31-33] and the Sunnybrook facial grading system (SB-FGS).[34-36] The first system was selected to measure the global degree of paresis/paralysis while the second system (SB-FGS) was used to obtain detailed data on symmetry at rest and during motion in regional facial function.

The HB-FGS consists of six grades, where grade I represents normal facial function in all areas, and grade VI represents total paralysis. The scale analyzed the symmetry, synkinesis, stiffness, and mobility of face.[31] It has been shown to have good inter-rater

reliability however, the sensitivity to variation in facial symmetry is low.[32,33] Complete recovery was defined as the achievement of HB-FGS grade I.

Facial symmetry was measured using the 13-item SB-FGS.[34] This system is divided into three components of facial asymmetry: resting asymmetry (scored from 0/symmetry to 4/asymmetry), symmetry of voluntary movement (1/asymmetry to 5/symmetry), and synkinesis (0/better to 3/worst). Resting symmetry evaluates the eye, cheek (nasolabial fold), and mouth. Symmetry of the voluntary movements evaluates the forehead wrinkle, gentle eye closure, open mouth smile, snarl, and lip pucker. Synkinesis during the voluntary movements evaluates the forehead wrinkle, gentle eye closure, open mouth smile, snarl, and lip pucker. A combined facial symmetry score is calculated as [(4 × symmetry of voluntary movement) – (5 × resting asymmetry) + (1 × synkinesis)] with 100 points representing normal facial symmetry. The SB-FGS has been tested for validity and reliability.[35,36] In the present study, the synkinesis component could not be established due to the absence of synkinesis in the early phase of BP (score 0/none synkinesis).

Outcome measurements were assessed at baseline and after a 6-week follow-up period. The evaluator, experienced in musculoskeletal facial evaluation, was blinded to group allocation.

Data Analysis

Categorical variables are presented as absolute and relative frequencies while continuous variables are presented as absolute values, using means and standard deviations, or medians and interquartile ranges for variables with skewed distributions. Differences between two interventions (i.e., C+FNT vs FNT) in baseline characteristics were tested using the χ^2 test and the Mann-Whitney U test, as appropriate. HB-FGS and SB-FGS scores were analyzed with Kruskall-Wallis test to compare differences between and within groups. The median variation of recovery degree i.e., Δ HB-FGS and Δ SB-FGS (final value-initial value), was tested among groups using the Mann-Whitney test. χ^2 test was used to analyze differences in proportions of patients between groups (C+FNT vs. FNT groups) who experienced full recovery (HB-FGS grade I) as well as after stratifying patients according to their baseline HB-FGS grades (slight to moderate severity grade II, III, IV; severe severity grade V, VI). The remission time,

assessed every 1 week by the number of days to reach HB-FGS grade I, was analyzed with hazard curves with differences among groups tested using Log-Rank Test. Multiple linear regression was performed to test an association between the predictor intervention group and the outcome variable of the Δ HB-FGS, adjusting for confounding variables (age, sex, and severity baseline of HB-FGS). P values less than 0.05 were considered as significant. Analyses were performed using SPSS, version 22.0.

Results

All demographic and baseline clinical measures were similar in both groups (p>0.05) (Table 2).

Table 2 Demographic and clinical data in both groups

	C+FNT group (n=42)	FNT group (n=31)	p-value
Sex, n (%)			
Male	19 (45.24)	16 (51.61)	0.593
Female	23 (54.76)	15 (48.39)	
Face Side, n (%)			
Right	20 (47.62)	13 (41.94)	0.632
Left	22 (52.38)	18 (58.06)	
Age (years), Median (IQR)	37.5 (26)	49.0 (33)	0.053
Baseline HB-FGS, n (%)			
Grade II	5 (11.90)	3 (9.68)	
III	12 (28.57)	9 (29.03)	
IV	5 (11.90)	4 (12.90)	0.944
V	4 (9.52)	5 (16.13)	
VI	16 (38.10)	10 (32.26)	

IQR (interquartile range); HB-FGS, House-Brackmann facial grading system; SB-FGS, Sunnybrook facial grading system; C+FNT, corticosteroids plus facial neuromuscular training group; FNT, facial neuromuscular training group

According the HB-FGS, the median paresis severity at baseline was grade 4 for both groups. On the SB-FGS, median score at baseline was 26 points in C+FNT group and 30 points in FNT group (Table 3). As shown in table 3, both groups significantly improved all components of facial symmetry (within group p<0.05). However, after interventions the C+FNT group displayed better outcomes for check (p=0.004) and mouth (p=0.022) resting symmetry compared to FNT group (Table 3). Combined facial symmetry improved on median 74 points in the C+FNT group compared with 70 points in the FNT group.

Table 3 Baseline and after intervention expressed by HB-FGS and SB-FGS components, in both groups

SCALES	C+FNT group			FNT group			p-value+
	Baseline	**After intervention**	**p-value***	**Baseline**	**After intervention**	**p-value***	
HB-FGS (I to VI grade)	4.00 (3.0-6.0)	1.00 (1.0-3.0)	**<0.001**	4.00 (3.0-6.0)	1.00 (1.0-2.0)	**<0.001**	0.665
Composite facial symmetry score (0 to 100)	26.00 (5.0-60.8)	100.00 (83.8-100)	**<0.001**	30.00 (10.0-60.0)	100.00 (79.00-100)	**<0.001**	0.794
Eye (0-1)	1.00 (0.0-1.0)	0.00 (0.0-0.0)	**<0.001**	1.00 (0.0-1.0)	0.00 (0.0-1.0)	**0.001**	1.000
Check (0-2)	0.00 (0.0-1.0)	0.00 (0.0-0.0)	**<0.001**	1.00 (0.0-1.0)	0.00 (0.0-0.0)	**0.001**	**0.004**
Month (0-1)	0.00 (0.0-1.0)	0.00 (0.0-0.0)	**<0.001**	0.00 (0.0-1.0)	0.00 (0.0-0.0)	**0.002**	**0.022**
Resting asymmetry score 0-20)	5.00 (0.0-15.0)	0.00 (0.0-0.0)	**<0.001**	10.00 (0.0-15.0)	0.00 (0.0-5.0)	**<0.001**	0.686
Forehead wrinkle (1-5)	2.00 (1.0-3.8)	5.00 (5.0-5.0)	**<0.001**	2.00 (1.0-2.0)	5.00 (5.0-5.0)	**<0.001**	0.399
Gentle eye closure (1-5)	2.00 (1.0-3.0)	5.00 (5.0-5.0)	**<0.001**	2.00 (1.0-2.0)	5.00 (4.0-5.0)	**<0.001**	0.553
Open mouth smile (1-5)	2.00 (1.0-4.0)	5.00 (5.0-5.0)	**<0.001**	2.00 (1.0-2.0)	5.00 (4.0-5.0)	**<0.001**	0.331
Snarl (1-5)	2.00 (1.0-3.0)	5.00 (5.0-5.0)	**<0.001**	2.00 (1.0-2.0)	5.00 (4.0-5.0)	**<0.001**	0.587
Lip pucker (1-5)	2.00 (1.0-3.0)	5.00 (5.0-5.0)	**<0.001**	2.00 (1.0-2.0)	5.00 (4.0-5.0)	**<0.001**	0.498
Symmetry voluntary movement (20-100)	40.00 (20.0-68.0)	100.00 (92.0-100)	**<0.001**	36.00 (20.0-60.0)	100.00 (84.0-100)	**<0.001**	0.528

*Median and interquartile range differences within groups; + Median and interquartile range differences between groups, C+FNT corticosteroids plus facial neuromuscular training; FNT facial neuromuscular training; SB-FGS, Sunnybrook facial grading system; HB-FGS, House-Brackmann facial grading system

The clinical data at follow-up (after 6 weeks) indicate that both groups had significantly improved the recovery degree (ΔSB-FGS), without significant differences between groups ($p>0.05$) (Table 4). Thus, a similar recovery degree was found in both groups of approximately 2 degree HB-FGS, while the median ΔSB-FGS at report approximately 54.50 points in C+FNT and 47.0 in FNT group.

Table 4 The Δ of HB-FGS and Δ of SB-FGS, after intervention-baseline intra-groups and between groups

Scales	C+FNT	FNT	p-value+
HB-FGS (I to VI grade)	-2.00 (-3.0. to -2.0)	-2.00 (-3.0 to -2.0)	0.996
Composite facial symmetry score (0 to 100)	54.50 (28.0 to 77.3)	47.00 (16.0 to 76.0)	0.476
Eye (0-1)	-1.00 (-1.0 to 0.0)	0.00 (-1.0 to 0.0)	0.889
Check (0-2)	0.00 (-1.0 to 0.0)	-1.00 (-1.0 to 0.0)	0.761
Month (0-1)	0.00 (-1.0 to 0.0)	0.00 (-1.0 to 0.0)	0.921
Resting asymmetry score (0-20)	-5.00 (-15 to 0.0)	-5.00 (-15.0 to 0.0)	0.648
Forehead wrinkle (1-5)	3.00 (1.0 to 3.0)	2.00 (1.0 to 3.0)	0.490
Gentle eye closure (1-5)	2.00 (1.0 to 3.0)	2.00 (1.0 to 3.0)	0.371
Open mouth smile (1-5)	2.00 (1.0 to 3.0)	2.00 (1.0 to 3.0)	0.631
Snarl (1-5)	3.00 (1.0 to 3.0)	2.00 (1.0 to 3.0)	0.575
Lip pucker (1-5)	2.00 (1.3 to 3.0)	2.00 (1.0 to 3.0)	0.532
Symmetry voluntary movement (20-100)	50.00 (28.0 to 66.0)	44.00 (16.0-64.0)	0.487

+Change after intervention-baseline between groups; C+FNT, corticosteroids plus facial neuromuscular training; FNT, facial neuromuscular retraining; HB-FGS, House-Brackmann facial grading system; SB-FGS, Sunnybrook facial grading system; Δ, final values-initial values

No significant effect of both interventions was found between groups. Similarly, no differences were found after stratifying patients according to their baseline HB-FGS grades (II-IV and V-VI). As shown in Table 5, at the end of the 6-week follow-up period, 27 (64.28%) patients in C+FNT group and 20 (64.54%) in FNT group experienced full recovery (p=0.992).

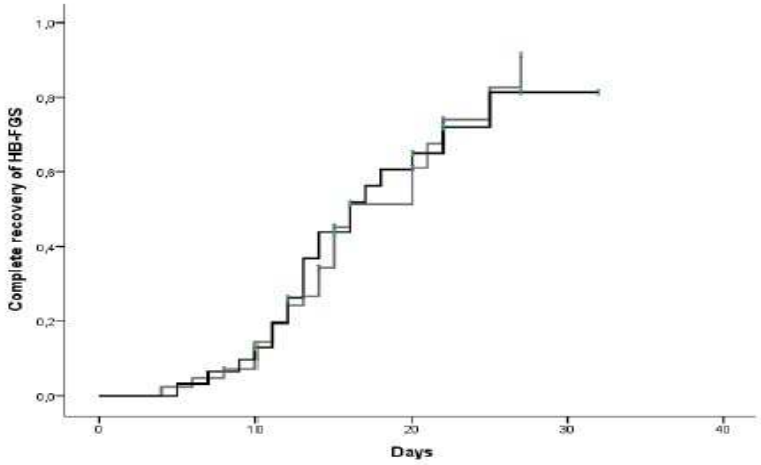
Table 5 Patients' distribution among HB-FGS grades at the beginning and after 6 weeks of intervention

HB-FGS	C+FNT (n=42)		*p-value	FNT (n=31)		*p-value	+p-value
	Baseline	After six weeks		Baseline	After six weeks		
HB grade I	0 (0%)	27 (64.28%)	**p<0.001**	0 (0%)	20 (64.52%)	**p<0.001**	0.992
HB grade II-IV	22 (52.38%)	18 (81.82%)	**p<0.001**	16 (51.61%)	15 (93.75%)	**p<0.001**	0.777
HB grade V/VI	20 (47.62%)	7 (35.00%)	**p<0.001**	15 (48.39%)	4 (26.66%)	**p<0.001**	0.703

C+FNT, corticosteroids plus facial neuromuscular training; FNT, facial neuromuscular training; HB-FGS, House-Brackmann facial grading system;* intra-group p≤ 0.001; + between groups

There were no differences in remission time (reaching HB-FGS grade I) between groups (p=0.952) (Fig. 2). The average remission time was 17.86 days (95%, CI=15.68-20.03) in the C+FNT group and 18.43 days (95%, CI=15.23- 21.63) in the FNT group.

Fig 2 Hazard curves for complete recovery, according to intervention group



Incomplete recovery	d0	d≤10	d≤20	d≤30
C+FNT group	42 (100%)	3 (85.7%)	19 (45.2%)	15 (35.7%)
FNT group	31 (100%)	27 (87.1%)	14 (41.9%)	11 (35.5%)

C+FNT, corticosteroids plus facial neuromuscular retraining; FNT, facial neuromuscular training; HB-FGS, House-Brackmann facial grading scale

Considering the recovery degree (ΔHB-FGS) in all patients, a multiple linear regression model was performed adjusted for variables such as age, sex, baseline HB-FGS, and intervention groups. Age, sex and baseline HB-FGS were significant confounding variables ($p<0.004$, $p<0.003$ and $p<0.001$, respectively). The type of intervention was not a significant predictor of recovery degree ($p=0.917$).

After adjusting for age, sex and baseline HB-FGS, the type of intervention was not a significant predictor of recovery degree (ΔHB-FGS; $p=0.917$).

Table 6 Relationship between the independent and predictive variables

Independent variables	Unstandardized Coefficients		Standardized Coefficients	
	B (95% CI)	SE	ß	p-value
Constant	2.615 (1.352-3.878)	0.633	_____	**<0.001**
Intervention groups	0.024 (-0.440-0.488)	0.233	0.010	0.917
Age	-0.018 (-0.030-0.006)	0.006	-0.285	**0.004**
Sex (male)	-0.705 (-1.154-0.255)	0.225	-0.292	**0.003**
Baseline of HB-FGS	0.393 (0.241-0.545)	0.076	0.480	**<0.001**

B, Unstandardized Coefficient; ß Standardized Coefficient; SE, Standard Error; Independent variables: age, sex, baseline HB-FGS and intervention groups; Predictor: Δ of recovery degree (HB-FGS)

Discussion

The results of the present study show that oral administration of corticosteroids does not bring advantageous effects in terms of recovery degree and facial symmetry in the early phase of BP. Moreover, we found some heterogeneity regarding corticosteroids prescription among physicians, since they were not prescribed to all patients with the same level of BP severity.

This study showed that after 6 weeks, both interventions reduced the degree of BP severity in a similar way. At the pre-intervention phase, both groups had similar distribution of facial grades' severity, which supports the concept that post-treatment values provided a reliable evaluation of each treatment efficacy. After interventions there were no significant differences between groups for all components of facial symmetry at rest and with voluntary movement, except for two parameters (resting symmetry component of check and mouth), revealing that corticosteroids only had positive effects on rest symmetry with droop corner of mouth and increased of nasal labial fold. Our results do not support the present treatment guidelines which advocate the use of potent anti-inflammatory agents, such as oral corticosteroids, for all patients with BP to decrease recovery time and improve facial nerve functional recovery.[2,11,21,22] These guidelines were based on the assumption that an early administration of corticosteroid might reduce nerve's swelling and subsequent unblocking of nerve conduction, in the fallopian canal.[1] The lack of superior results after corticosteroid use observed in the present study may suggest that the administered dose was insufficient to promote anti-inflammatory effects in the fallopian canal. In addition the oral administration has a systemic effect, which may have compromised the local effect at the fallopian canal. Another explanation includes the timing for corticosteroids intake; an initial intake within 72 hours after BP onset, might follow the earlier occurrence of nerve´s swelling. Independently of the underlying reasons, our results suggest that the criteria to prescribe corticosteroids in BP must be revised.

The identical distribution of BP severity among the groups at beginning of the interventions clearly suggests the absence of uniform criteria to prescribe corticosteroids by clinical physicians, once there are slight to moderate degrees (HB-FGS/grade II-IV) and severe degree (HB-FGS/grade V-VI) of BP with and without corticosteroid therapy. Fortunately, this absence of uniform criteria allows us obtaining a great homogeneity in

the distribution of BP severity between groups at the beginning of experimental protocol, which also allows demonstrating that both interventions had similar effects in recovery degree in all patients, independently of severity level at baseline (p=0.992). Our results diverge from those obtained in other study showing that drugs therapy (corticosteroids and valacyclovir) plus facial exercise had significant effect on grade (p=0.038) and time (p=0.044) of full recovery in patients with severe facial palsy (HB-FGS/grade V-VI).[37] However, differences in the characteristics of the enrolled patients (HB grade IV and V-VI vs II-IV and V/VI), intervention types and biased variables' control (drugs therapy + FNR and drugs therapy vs C+FNR and FNR only), and length of follow-up (6 months vs 6 weeks) limit a direct comparison between studies.

Although both interventions showed positive results (HB-FGS and SB-FGS), the occurrence of spontaneous recovery in the acute phases of BP may have influenced our results. In fact, an early study demonstrated that spontaneous recovery of the facial nerve follows a predictable time course after an injury, reporting a complete recovery of 85% of patients within 3 weeks. These results were explained by the facial nerve motor fibers ability to regenerate their injured axons.[1] However, Peitersen[1] used a different facial grading system and the definition of recovery was unclear. Independently of the methodological differences, Peitersen [1] showed that full spontaneous recovery may not occur in all patients with facial nerve paralysis and, for this reason, various therapies have been designed to enhance functional recovery and reduce sequelaes of BP.[12-17,30] Facial exercise is a conservative intervention for this condition and is considered to be an effective form of treatment[13-17]although its effects have been found debatable according to different guidelines.[2,21,22] FNT provides specific exercises and strategies based on individual function, muscle characteristics and degree of facial neuromuscular damage (symptoms and clinical signs).[30,38] This approach integrates the fields of therapeutic, behavioral, and educational science with the goal of restoring muscular function and prevent irregular muscular activity, as much as possible, in order to improve facial functions (eating, drinking, speaking clearly and expressing emotions).[24,28,30,38] Although there is no compelling evidence about the effectiveness of FNT intervention, some studies have recognized efficacy of functional recovery on early stage of BP.[15,16] Some studies demonstrate that the patients with FNT in the early phase, performed the muscle actions more symmetrically within movement pattern

compared control group, reduced severity of their paresis and synkinesis.[13-15] Additionally, FNT reduces the frequency of patient visits, and thereby it is cost effective and less time-consuming.[30] Additionally, it has other advantages such as being a noninvasive procedure, easily available in clinical setting, easily implemented as a daily home exercise program, and has no contraindications. Theoretically, manual mechanism stimulation directly affects the denervated muscles fibers by increasing the circulation, maintaining membrane properties and consequently improving the motor response.[32] Using animal model, Angelov and colleagues showed that manual stimulation may synthesize fewer growth factors, limit inappropriate intramuscular axonal sprouting and reduce polyneuronal reinnervation of motor endplates.[39]

Finally, our results showed that age, sex and level of baseline HB-FGS might be useful to predict the recovery degree, irrespective of the intervention groups. Similarly to our results, other studies have also reported that old patients have a poor prognosis, which may be due to an age-related increase in brain cytokine activity that impairs the ability of cell repair.[1,40] Regarding the influence of gender, and in contrast with other studies showing no association between sex and grade of functional recovery, [1,41] our results showed a better prognosis for females then males, which might be explained, among others factors, by the influence of the endocrine environment, once the anti-inflammatory role with favorable effects of estrogens in many diseases are well known.[42,43] Consequently, this subject requires further research to clarify the potential effect of gender as a predictor factor to full recovery of BP.

This study had both strengths and limitations. The strengths of the study included the rigorous control to reduce bias through blinded assessment and patient's selection (homogenous population with exclusion of many co-morbid). The limitations of the study were the lack of a placebo group to assess spontaneous recovery, which restricts the analysis of FNT effectiveness. However a control group was not included due to ethical reasons.

Our results provide preliminary evidence that oral intake of corticosteroid was not effective in all grades of dysfunction and remission time at the early phase of BP, highlighting the need to reanalyze the criteria to prescribe corticosteroids in these patients.

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ESTUDO ORIGINAL IV

Long Effects of Facial Neuromuscular Training in Bell's palsy: A Prospective Longitudinal Study

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Title: Long-term Effects of Facial Neuromuscular Training in Bell's Palsy: A Prospective Longitudinal Study

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Abstrat

Objectives: The main aim of this study was to evaluate the long-term effect of facial neuromuscular training (FNT), in terms of grade of function, symmetry movements, occurrence of synkinesis, and quality of life, in patients with Bell's palsy (BP), during 10.5 months of follow-up.

Study design: Prospective longitudinal study.

Participants: After six weeks of BP onset, 26 non recovered patients, with grade II to VI of House Brackmann Facial Grading System (HB-FGS), were included in this study.

Interventions: All patients received individually FNT intervention by a physical therapist; the intervention comprised techniques of tissue mobilization, relaxation strategies, synkinesis control, symmetry promotion of the face at rest and during voluntary and spontaneous movement, and coordination, for 15 minutes, once a day for a period of 10.5 months.

Outcome measures: The impairments outcomes were assessed by HB-FGS (grade of functional recovery) and Sunnybrook Facial Grading Systems (SB-FGS) (facial symmetry resting, voluntary movements, and synkineses), being the disability outcome measured by the FaCE scale (quality of life). Patients were evaluated at baseline (6 weeks after BP onset) and after 3, 6 and 12 months after BP beginning. A full recovery was defined as grade I by HB-FGS.

Results: During the follow-up period, 50.0% patients achieved the complete recovery at 6 months. From these, only 1 patient had grade ≥ IV of HB-FGS at baseline, in contrast with the remained 12 patients, which grade at baseline was <IV of HB-FGS. Nevertheless, all non-recovered patients achieve some degree of recovery function at 6 months ($p<0.05$). The facial symmetry and quality of life were significantly improved until 6 months of follow-up in all patients ($p<0.05$). The synkinesis was started at 3 months after BP onset and 12 patients showed persistent synkinesis at the end of the study.

Conclusions: During the first 6 months of disease evolution, patients showed improvements with FNT intervention but, after this time the FNT did not show advantages for recovery, moreover, it did not appear to prevent the occurrence of synkinesis.

Keywords: Neuromuscular Training, Synkinesis, Facial impairments, Facial disabilities.

Introduction

According to the International Classification of Functioning, Disability and Health of the World Health Organization (WHO),[1] facial neuromuscular dysfunction in patients with Bell Palsy (BP) can be described on three levels: i) functioning (impairment) level, expressed by hipotonicity/flaccid (facial weakness) or hipertonicity/sequelae (stiffness, synkinesis, spasms) on the affected side of the face; ii) disability level, manifested by difficulty with eye closure, eating, drinking, speaking clearly and expressing emotions; and iii) health level, with repercussions on emotional well-being (social isolation, decreased self-esteem, anxiety, depression).

BP is an idiopathic, unilateral and acute paresis or paralysis of facial movement caused by dysfunction of the lower motor neuron.[2,3] Most people with muscular paresis make a spontaneous recovery within 3 weeks.[2,3] Up to 30% of patients, typically with paralysis (complete palsy), have a delayed or incomplete recovery,[4] being assumed that full functional recovery is mainly dependent from the initial level and severity of injury.[3,5] After the primary injury, the distal part of the motor axons degenerate, leaving to a slow atrophy of the skeletal muscles.[5,6] The reinnervation process tends to occur slowly (during months), through the growth of new neurons from the area of the injury, or distally through the growth of branches from remaining axons,[5,6] which taking aberrant redirections may lead to synkinesis.[4] It is also assumed that denervation of any skeletal muscle for over a year will lead to an irreversible atrophy of the motor endplates, and therefore to a total inability to reestablish the nerve-muscle synapses and their function.[5] More recently, facial neuromuscular training (FNT)[7-14] was addressed to promote the complete recovery and reduce the severity of synkinesis. Facial muscles exercise may improve blood flow and oxygen exchange, stimulating angiogenesis and arteriogenesis, increase the size of muscle fibers or increase motor control, leading to improvements in muscle performance.[15,16] On the other hand, when the quality of the performed movements is repeated many times, increasing the awareness of the movements of the facial muscles and avoiding the muscle activity of abnormal patterns of movement, the acquire motor skills could become automated and be used spontaneously in daily life.[14,17] Unlike other skeletal muscles, the information about the position and stretch of the facial muscles is not accessible to the central nervous system through visual

feedback or by proprioceptive information conveyed by muscle spindles or tendon and joint receptors, of which the facial muscles are devoid.[5,6,16]

The literature on the FNT intervention is still controversial.[4,17,18] The recent Canadian Guidelines recommend facial training for patients with persistent weakness, contrasting with no recommendations of American Guidelines.[19,20] Some intervention studies proved the effectiveness of FNT for recovery and to avoid the severity of synkinesis in the late stage of BP.[10-14] However, there have been no reports on FNT intervention for long-term. To our knowledge, this is the first study examining the clinical effects of FNT during 10.5 months of follow-up after BP onset. Our main aim was to evaluate the long-term effect of facial neuromuscular training, in terms of grade of function and symmetry movements, occurrence of synkinesis, and quality of life.

Methods

Study Design and Participants

This was a prospective longitudinal study with 4 repeated measurements over 10.5 months of follow-up. From January 2009 to May 2013, 73 patients with BP were diagnosed by the hospital of XXX-XXX, being treated with FNT (alone or with corticoids) in the physical medicine and rehabilitation (PMR) service. Six weeks after the BP onset, all non-recovered patients (n=26) were integrated in this study to assess the long-term effect of facial neuromuscular training in their recovery. Patients showed the following characteristics: unilateral BP of both gender, age 18 years or older, grade II to VI HB-FGS. Their facial nerve palsy was idiopathic and not recurrent, and patients were not submitted to any treatment with steroids and non-steroids anti-inflammatory drugs.

All the 26 patients continue the previous treatment of FNT applied individually, which comprising techniques of tissue mobilization, relaxation strategies, synkinesis control, promote symmetry of the face at rest and voluntary and spontaneous movement, and coordination for 15 minutes, once a day, during 5 sessions per week until 12 month of BP onset. All patients were evaluated at 6 weeks (baseline), and 3, 6 and 12 months after BP onset (Figure1).

The hospital ethics committee had given its approval and all patients were informed as to the nature of the study, giving their informed consent.

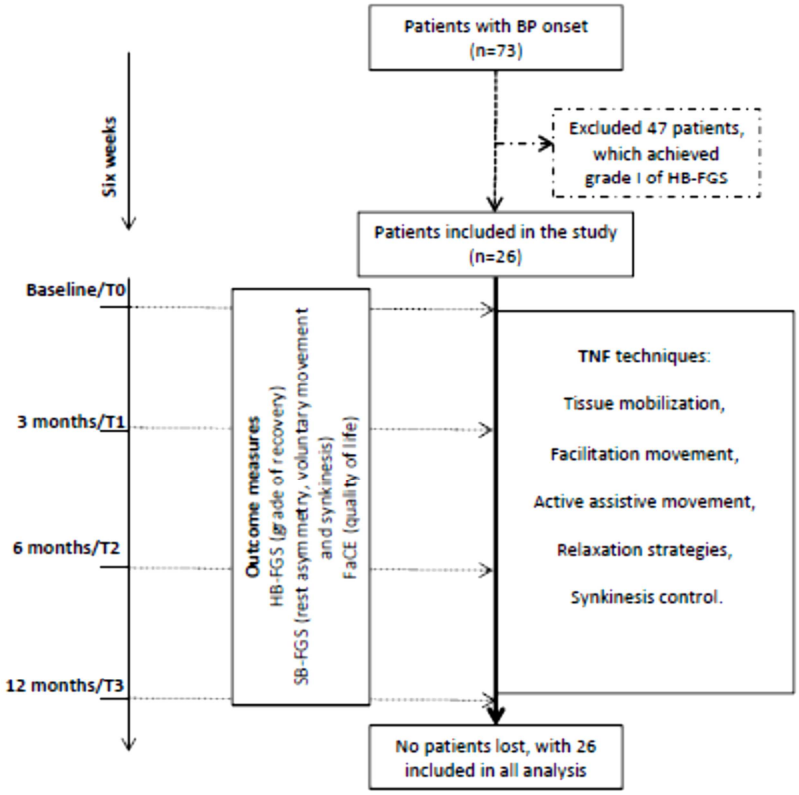

Figure 1. Study design

Intervention

Facial Neuromuscular Training

All patients were treated with FNT individually by five trained physical therapists and in accordance with the neuromuscular training principles.[21,22] Each patient was treated in the outpatient hospital for 15 minutes per day, 5 days per week during 12 month. A standard program of FNT included different muscle groups supplied by each branch of the facial nerve in both sides of the face by a mirror. The FNT included all facial muscles of motion (e.g. frontalis/wrinkling; corrugator supercili/wrinkles of forehead; orbicularis oculi/closure of eyes; procerus/snarl; orbicularis oris/whistling; risorius/smile; zigomaticus/laugh) and other muscles innervated by the facial nerve. The parameters of FNT included variations of speed, amplitude, force, repetitions (from 5 to 10), series (from 1 to 3) per each facial muscle, selective and coordination motion. Patients were also taught expression exercises (e.g. to open the eyes wide/surprise, lift

the upper lip/disgust, tighten the lips/anger, lips pucker/kiss or laugh/happy) and facial function (eating, drinking, speaking).

The FNT had different interventions according to the individual assessment level of BP (Table 1). Patients who had severe facial asymmetry at rest or flaccid facial regions (HB-FGS scores ≥V grades), and who were unable to initiate movement on the affected side were given instructions on small and controlled movement by combined passive and active assistive exercises with soft tissue mobilization. For these patients, the strategy used were to avoid mass movement patterns in front of a mirror (i.e., avoid overuse of the uninvolved side).[6,10,18] On the other hand, patients who had mild to moderate facial asymmetry at rest and were able to initiate at least slight movement in any or all regions of the face (HB-FGS scores II-IV grades) were given instructions to perform isolated and controlled movement by combining active assistive and resistive exercises with soft tissue mobilization. Patients were instructed to perform slow, controlled, graded facial expressions to generate symmetry between of face sides.[6,10,18]

All participants who developed synkinesis were used stretching-relaxation to perform slow, controlled, graded facial expressions to generate symmetry between the sides of the face while simultaneously controlling synkinesis movements in other regions of the face (Table 1).[6,10,18]

Table 1. Algorithm of facial neuromuscular training

Patient education	Postural correction information was given for to increase awareness of the head position and its effect on facial tone; Relaxation training was taught to increase the participant's awareness of the hyperactivity of the unaffected face or synkinesis in affected side by breathing and relaxation exercises; Tissue mobilization was taught to improve circulation and sensory stimulation by combination of "effleurages" and "kneading", in face and neck during 5 minutes.			
Measurements	**HB-FGS**	**Score VI grade**	**Score≤V grade**	**Score ≥II grade**
	Tonus	Hipotonicity		Hipertonicity and Synkinesis
	Symmetry rest, voluntary movement and synkinesis	Flaccid muscles; Asymmetry of rest (e.g., a drooped face, including lower eyelid, depressed cheek, and drooped mouth corner); Unable to initiate movement on the affected side.	Active motion; Mild to moderate facial asymmetry at rest; Initiate slight movement (marked asymmetry with voluntary movement or spontaneous expressions).	Initiate at least slight movement in any or all regions of the face; Synkinesis (e.g., eye closure with smile, and retraction of the corner of the mouth and deepening of the cheek fold with a raise of the brow); Tightening, spasms and twitches of the muscles; Asymmetry of face (narrowed aperture between the eyelids, a deepened cheek fold, and shifted laterally toward the involved side of the face.
	Physical and social function	More dificult for speaking, drinking, eating, closing the eye and emotional expessions; Decreased self-esteem, anxiety and depression	Incomplete facial functions and expressions; Negative impact on psychosocial well-being and daily interpersonal interactions.	More difficult for speaking, drinking, eating, closing the eye and expressions; Decreased self-esteem, anxiety and depression.
Treatments	Facial neuromuscular retraining	1) Soft tissue mobilization (combination effleurage and kneading) in affected side of face and neck and effleurage only in uninvolved side ; 2) Passive and active assistive movement; 3) Avoid mass movement patterns; 4) Facilitation of the movement in front of a mirror.	1) idem 2) Active assistive movement; 3) and 4) idem 5) Performed small movement, controlled intensity to promote symmetry between the sides.	1) Tissue mobilization (effleurage) in both side of face and neck; 2) Active assistive movement; 3) and 4) idem 5) Relaxation exercises (Jacobson and breathing); 6) Sinkinesis control; 7) Stretching exercises in affected side of face and neck.

Abbreviations: HB, House-Brackmann Facial Grading System

Outcome Measures

All patients were evaluated at baseline (Bas - 6 weeks after the beginning of BP) and after 3 (t1), 6 (t2), and 12 months (t3) after BP onset.

The impairments outcomes were assessed by HB-FGS (grade of recovery of function), Sunnybrook Facial Grading Systems (SB-FGS) (facial symmetry resting, voluntary movements and synkineses) and disabilities outcomes were measured by FaCE scale (quality of life). The HB-FGS is classified as a universal scale by the American Academy of Otolaryngology Committee of Disorders of the Facial Nerve.[23]The HB-FGS consists of six grades, from grade I, representing normal facial function in all areas, to grade VI, representing total paralysis. The scale analyzed the symmetry, synkinesis, stiffness and mobility of face. It has been shown to have good inter-rater reliability.[24,25] Complete recovery was defined with the achievement of HB-FGS I grade.[23-25]

The SB-FGS[26] is a regionally system of evaluations that includes 4 regions of face (forehead, peri-orbicular, nose and perioral region). The system measures are divided into three components of facial symmetry: resting symmetry (scored from 0/symmetry; 4/asymmetry), symmetry of voluntary movement (0/asymmetry; 5/symmetry) and synkinesis (0/better; 3/worst). Resting symmetry evaluates the eye (aperture between the eyelids), cheek (nasolabial fold) and mouth (drooped corner). Symmetry of the voluntary movements evaluates the forehead wrinkle, gentle eye closure, open mouth smile, snarl and lip pucker. Synkinesis during the voluntary movements evaluates the forehead wrinkle, gentle eye closure, open mouth smile, snarl and lip pucker. The synkinesis was absent at the baseline assessment (score 0/none synkinesis). A composite facial symmetry score is calculated as [(4 × symmetry of voluntary movement score) – (5 × resting asymmetry score) + (1 × synkinesis score)] with a total score of 100 points representing normal facial symmetry.[27,28]

The FaCE questionnaire[29] is a quality-of-life instrument that is used to assess facial impairment and disability perception in patients with BP. It involves 15 domains, each using a 5-item Likert scale whereby 1 corresponds to the lowest function and 5 corresponds to the highest function. These domains are subsequently grouped into 6 independent subdomains scores: Facial Movement, Facial Comfort, Oral Function, Eye Comfort, Lacrimal Control, and Social Function. A total score of 0 represents worst

quality-of-life and 100 represents the best quality of life. The FaCE questionnaire has demonstrated excellent internal consistency as well as test-retest reliability.[29]

Statistical Analysis

Categorical variables are presented as absolute and relative frequencies, and continuous variables were expressed as means and standard deviations, or medians and interquartile range for variables with normal or skewed distributions, respectively. To test the existence of differences on HB-FGS, SB-FGS and FaCE scale, we used ANOVA for repeated measures with Bonferroni post hoc test or the Friedman's Test in the cases of skewed distribution. Severity of synkinesis outcome was investigated in the global sample and after stratifying patients according to their baseline synkinesis grade (3 months after BP onset) component of SB-FGS. All the patients were graded as having mild (1 point for each question with a maximum of 5 points) and moderate to severe synkinesis (2 or 3 points for each question, with a maximum of 15 points), according to sum these questions of SB-FGS were obtained the total score of 1 to 15 points. χ^2 test was used to analyze differences in patients' distribution with synkinesis.

P values less than 0.05 were considered significant. Analyses were performed using SPSS, version 22.0.

RESULTS

Outcomes of HB-FGS

Twenty six patients with residual paresis defined as II to VI HB-FGS grades were included in this study. During the follow-up period, 13 (50.0%) patients achieved the complete recovery (HB-FGS/I grade). From these, only 1 patient had grade ≥ IV of HB-FGS at baseline, in contrast with the remained 12 patients, which grade at baseline was <IV of HB-FGS. Table 2 showed that 10 (38.5%) patients recovered completely at t1 (3 months) and 3 (11.6%) patients at t2 (3 to 6 months) (Table 2). Of note that all patients achieve some degree of recovery function as depicted in Table 2.

From all the non-recovered patients, 11 (42.3%) had still a slight to moderate dysfunction and null patients had severe or total paralysis, at the final follow-up period.

Table 2. Absolute and relative frequencies of patients according to HB-FGS levels during the follow-up period.

Severity stratification HB-FGS	Grades HB-FGS	t0 n (%)	t1 n (%)	t2 n (%)	t3 n (%)
				n=26	
	Grade I - Normal	----	10 (58.8)	12 (70.6)	12 (70.6)
HB-FGS≤III (n=17)	Grade II - Slight Dysfunction	7 (41.2)	3 (17.6)	2 (11.8)	4 (23.5)
	Grade III - Moderate Dysfunction	10 (58.8)	4 (23.5)	3 (17.6)	1 (5.9)
	Grade I - Normal	----	----	1 (11.1)	1 (11.1)
	Grade II - Slight Dysfunction	----	1 (11.1)	2 (22.2)	2 (22.2)
	Grade III - Moderate Dysfunction	----	3 (33.3)	3 (33.3)	4 (44.4)
HB-FGS≥IV (n=9)	Grade IV - Moderate Severe Dysfunction	3 (33.3)	------	3 (33.3)	2 (22.2)
	Grade V - Severe Dysfunction	4 (44.4)	4 (44.4)	----	----
	Grade VI-Total paralysis	2 (22.2)	1 (11.1)	----	----

Abbreviations: HB-FGS, House-Brackmann facial grading scale; t, time

The median severity of the paresis on admission to the study was grade 3 for the HB-FGS (Fig. 2). The median variation of grade of the severity between t0-t3 showed significant improvement, decreasing from grade 3 at t0 to grade 1 at t3 ($p<0.05$) (Fig. 2).

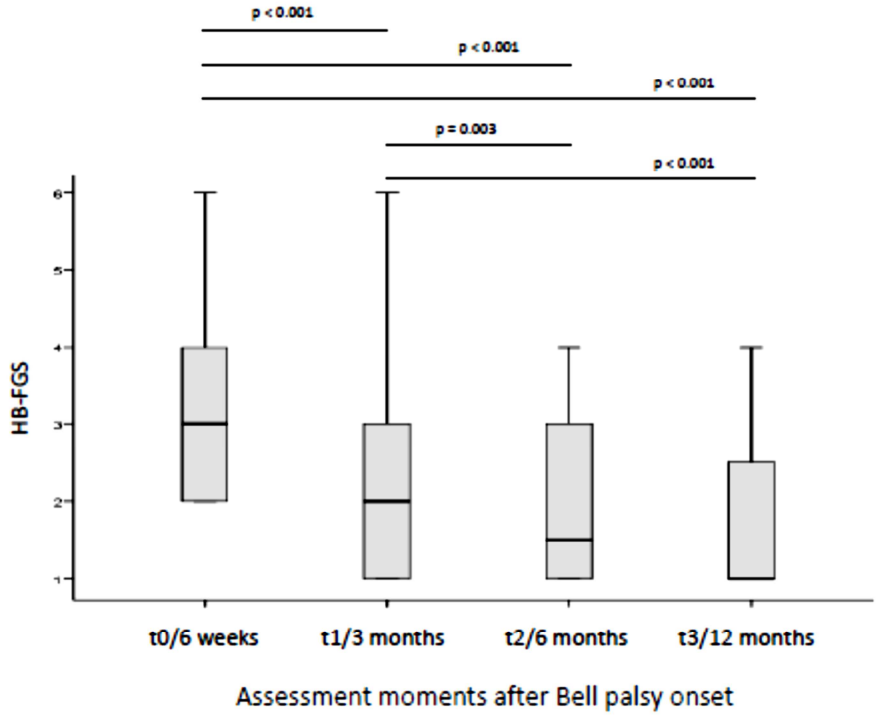

Figure 2. Median and interquartile values of HB-FGS considering the total sample in the different assessment moments.

When stratification of patients according to HB-FGS was considered (Table 3), both subgroups of severity showed significant decrease of HB-FGS grade between t0-t2 ($p<0.05$). However, between t2-t3 over the last 6 month follow-up period, the differences were not significant in both subgroups.

Table 3. Median and interquartile values of HB-FGS during the follow-up period.

HB-FGS	t0	t1	t2	t3	p-value t0-t1	p-value t1-t2	p-value t2-t3
	n=26						
HB-FGS≥IV (n=9)	5.00 (4.00-5.50)	5.00 (3.00-5.00)	3.00 (2.00-4.00)	2.00 (1.50-3.00)	**0.034**	**0.024**	0.100
HB-FGS≤III (n=17)	3.00 (2.00-3.00)	1.00 (1.00-2.50)	1.00 (1.00-1.50)	1.00 (1.00-1.00)	**0.001**	**0.046**	0.100

Abbreviations: HB-FGS, House-Brackmann facial grading scale; t, time

Outcomes of SB-FGS

The median of the composite facial symmetry score on baseline was 75.5 points for the SB-FGS (Table 4). A significant increase in this score was observed over time ($p<0.05$), except between t2 and t3 assessments. The composite facial symmetry score was significantly improved in 11.5 (15.2%) points until t2 period, which showed slight continuous improvements at the end of the study. In contrast, no differences were demonstrated on resting asymmetry score ($p>0.05$) over time. Table 4 showed significant improvement on symmetry voluntary movement (respectively forehead, eye region, nasolabial fold, and mouth region) between t0-t1 ($p<0.05$). Symmetry voluntary movement components were significantly improved on eye and snarl region between t1-t2 period. During the last 6-month follow-up period, the symmetry voluntary movement of the SB-FGS score revealed no significant differences between t2 and t3 ($p=0.51$). Synkinesis started three months after BP onset and persisted at the end of the study. Severity of synkinesis score had significant increase in t1-t2 ($p<0.05$). An increase of synkinesis severity was observed in eye closure and lip pucker movements (Table 4).

Table 4. Median and interquartile values of SB-FGS during the follow-up period.

SB-FGS	t0 (n=26)	t1 (n=26)	t2 (n=26)	t3 (n=26)	p-value t0-t1	p-value t1-t2	p-value t2-t3
Composite facial symmetry score (0-100)	75.5 (26.6-90.3)	91.0 (71.8-100)	87.0 (81.8-100)	100 (81.8-100)	**<0.001**	**0.019**	0.722
Eye (0-1)	0.5 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-0.25)	0.0 (0.0-0.25)	0.157	0.435	0.161
Cheek (0-2)	0.0 (0.0-0.0)	0.0 (0.0-0.25)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.166	0.327	0.538
Month (0-1)	0.0 (0.0-0.25)	0.0 (0.0-0.25)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.405	0.538	0.739
Resting asymmetry score (0-20)	5 (0.0-6.5)	0.0 (0.0-5.0)	0.0 (0.0-5.0)	0.0 (0.0-5.0)	0.280	0.502	0.096
Forehead wrinkle (1-5)	4.0 (2.0-5.0)	5.0 (4.0-5.0)	5.0 (4.75-5.0)	5.0 (4.75-5.0)	**0.002**	0.161	0.090
Gentle eye closure (1-5)	3.5 (2.0-4.0)	4.5 (3.0-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	**<0.001**	**<0.001**	0.425
Open mouth smile (1-5)	4.0 (2.0-5.0)	5.0 (3.75-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	**<0.001**	0.086	0.083
Snarl (1-5)	4.0 (1.0-5.0)	5.0 (3.0-5.0)	5.0 (4.0-5.0)	5.0 (4.0-5.0)	**<0.001**	**0.016**	0.185
Lip pucker (1-5)	4.0 (2.0-4.0)	4.0 (3.0-5.0)	5.0 (3.75-5.0)	5.0 (3.75-5.0)	**<0.001**	0.119	0.170
Symmetry voluntary movement score (20-100)	78.0 (35.0-92.0)	94.0 (76.0-100)	100 (91.0-100)	100 (95.0-100)	**<0.001**	**0.025**	0.733
Forehead wrinkle (0- 3)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.100	0.161	0.057
Gentle eye closure (0-3)	0.0 (0.0-0.0)	0.0 (0.0-0.25)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.445	**0.011**	0.538
Open mouth smile (0-3)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	**0.002**	0.425	0.161
Snarl (0-3)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.100	0.100	0.096
Lip pucker (0-3)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.098	**0.004**	0.103
Synkinesis score (0-15)	0.0 (0.0-0.0)	0.0 (0.0-1.25)	0.0 (0.0-3.0)	0.0 (0.0-3.0)	**<0.001**	**<0.001**	0.569

Abbreviations: SB-FGS, Sunnybrook facial grading scale; t, time; n.a., not applicable

Outcomes of FaCE scale

The median of total FaCE score at baseline was 63.3 points (Table 5). The variation of total FaCE score showed significant increased quality of life in 23.8 (37.6%) points ($p<0.001$) between t0-t2, whereas at the end of follow-up (t2-t3) no significant differences was showed ($p=0.060$). Subdomains facial movement, oral function and eye comfort, between t0-t1 and t1-t2 showed significant improved ($p<0.05$). All six subdomains of the FaCE revealed significant differences ($p<0.05$), except for facial comfort ($p=0.94$) between t1-t2. At the last 6 months, facial comfort subdomain was the only subdomain of FaCE scale showing significant improvements ($p=0.018$) (Table 5).

Table 5. Median and interquartile values of FaCE scale during the follow-up period.

FaCE Scale	t0	t1	t2	t3	p-value t0-t1	p-value t1-t2	p-value t2-t3
	n=26						
FaCE score total	63.3±21.3	75.8±23.5	87.1±17.7	90.8±16.8	**0.001**	**0.001**	0.060
Facial movement	50.00 (31.25-83.33)	83.33 (50.0-100.0)	100.0 (75.0-100.0)	100.0 (75.0-100.0)	**0.001**	**0.029**	0.470
Facial comfort	88.33 (72.92-91.66)	95.83 (75.0-100.0)	100.0 (70.83-100.0)	100.0 (77.10-100.0)	0.100	0.940	**0.018**
Oral function	75.00 (43.75-100.0)	100.0 (59.38-100.0)	100.0 (75.0-100.0)	100.0 (87.50-100.0)	**0.017**	**0.038**	0.170
Eye comfort	56.25 (25.0-87.50)	87.50 (37.50-100.0)	100.0 (96.88-100.0)	100.0 (100.0-100.0)	**0.004**	**0.004**	0.100
Lacrimal control	62.50 (0.00-75.0)	61.54 (18.75-100.0)	100.0 (93.75-100.0)	100.0 (56.25-100.0)	0.180	**0.010**	0.820
Social function	87.50 (71.88-100.0)	100.0 (79.69-100.0)	100.0 (100.0-100.0)	100.0 (100.0-100.0)	0.054	**0.034**	0.660

Abbreviations: t, time

Synkinesis was found in 12 (46.2%) patients and majority of cases persisted or worst at the end of the study. The results of synkinesis severity scale showed that 9 (34.62%) patients had mild synkinesis at 3 months, 12 (46.15%) patients at 6 months and 12 months. One patient was started moderate to severe synkinesis at 6 (t2) months, increasing for 3 patients at 12 (t3) months. Regarding each subgroup analyzed (mild and moderate to severe synkinesis), the proportion of patients along time did not change significantly from t1 to t3 (Table 6).

Table 6. Absolute and relative frequencies of patients according to the development and severity of synkinesis during the follow-up period.

SB-FGS- Synkinesis	t1(3 months) n (%)	t2 (6 months) n (%)	t3 (12 months) n (%)	p-value t1-t2	p-value t2-t3	p-value t1-t3
Mild synkinesis	9 (34.62)	11 (42.3)	9 (34.62)	0.52	0.47	0.22
Moderate to severe synkinesis	0 (0.00)	1 (3.84)	3 (11.54)			

Abreviations: SB-FGS, Sunnybrook facial grading system;

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Discussion

The present study reports the effects of FNT intervention on BP patients with grade II to VI HB-FGS during 10.5 mouths of follow-up. FNT intervention showed favorable effects on patients' recovery during the first 6 months after BP onset but after this

period, the FNT was not effective to improve recovery. Moreover, FNT intervention did not delay the onset of synkinesis nor reduced their severity.

This is the first study including non-recovered patients after six weeks of BP onset, following a long period of treatment with FNT. Based on the study of Peitersen[4], it is known that spontaneous recovery occurred within 3 weeks after BP onset in 85% patients. These patients who showed improvement in the first 3 weeks had only partial degeneration and blocking of nerve conduction whilst patients who showed improvement after 3–5 months had total degeneration.[4] Based on Petersen's data, the design of our study tried to excluded all these patients with spontaneous recovery, avoiding the influence of this biased variable for the FNT intervention outcome.

Specific exercises have been implemented and developed for controlling the symmetry of the face, through slow movements and voluntary control of synkinesis.[7,8,11] Recent systematic reviews reported that FNT with a mirror was the most effective technique in patients with BP.[30,31]FNT was designed based on the fact that facial muscles do not have proprioceptors, being muscles characterized by specific morphological features, i.e., beyond their thinness, any minimal contraction has a high risk to change movement pattern.[32,33] Moreover, the techniques of FNT must be selected based on the individual patient's assessment over time.[34]

Our study showed that during in the first six months after BP onset, FNT intervention is effective to promote facial recovery of function and symmetry of facial expression, when compared with last 6 months of follow-up. This results on efficacy of facial exercise are in agreement with those described by Barbara et al.[35] However, comparison with this study is limited due to differences in the characteristics of the enrolled patients (HB grade III-IV vs II-VI), intervention procedures (kabat vs FNT), and length of follow-up (15 days vs 12 months).

Our results demonstrated improvements in the facial symmetry of SB-FGS, mainly during voluntary movements. The voluntary movement showed that eye and nose areas (eye closure and nose frowning) improved much better than other regions. Asymmetrical regeneration of facial nerve trunks could be a possible reason for this.[36] However, asymmetry in the face at rest tended to decreased in all the 3 facial investigated areas, even though these improvements were not significantly evident in the SB-FGS resting score. These results can be explained by low number of patients

with high severity (>IV of HB-FGS baseline), since at the beginning of this study the facial symmetry at rest was moderately affected, continuing to improve slightly along the follow-up. Besides that, these low results of resting score in the SB-FGS may be also due to the absence of specific FNT procedures aiming the improvement of resting posture.[8]

Considering all sample, our results showed that synkinesis score in the SB-FGS increased significantly between 3 to 6 months after BP onset. However, only 12 patients were affected by synkineses, which were greatest for the mouth and eye regions, possibly explained by increased tension in the mimetic muscles, not allowing the symmetry of orbicular voluntary movement. In the affected patients, it appears that synkinesis did not influence their facial symmetry during the voluntary movement of eye region. In fact, it may be less difficult to control movements of complete eye closure in comparison with the mouth/cheek region's movements due to the existence in the former region of several muscles for selective contractions or expressions to focus upon.

In comparing scores obtained on the SB-FGS and the FaCE scale, our study found that although overall SB-FGS and FaCE scores were, as expected, significantly related with each other, the facial comfort domain of the FaCE scale was not significantly improvement with the SB-FGS at 6 months. This suggests that patient's disability on facial comfort domain measured by question: ''my face feels tired or when I try to move my face, I feel tension, pain, or spasm'' may not be the best information of symptoms at early stage of BP. Similarly to our results, other studies also reported that impairments improvement have an impact on a patient's quality of life.[37] Other studies, found that the amount of improvement on the HB-FGS or SB-FGS did not correlate well with that on certain domains of the FaCE scale, including facial comfort, lacrimal control, and social function.[29,38]

In our study, synkinesis was started at 3 months after BP onset, and almost patients were developed it until 12 months after BP onset. Some other studies demonstrate that the usual timing for synkinesis onset occurs between third to sixth month, showing several degrees of variation.[4,39] These findings are in agreement with our results, reporting that more than an half of patients developed persistent synkinesis even when using FNT therapy. Therefore, early FNT interventions do not appear to prevent or

reduce synkinesis severity. Of note that our results are in disagreement with the RCT study of Beurskens et al.[12], which reported a reduction of synkinesis severity with FNT intervention. Nevertheless, while Beurskens et al.[12] aimed to assess the efficacy of FNT treatment in patients with synkinesis, our goal was mainly to see the influence of FNT on synkinesis development (efficacy of FNT prevention), which beyond the differences in experimental protocols of both studies may explain the different results.

Our study has several limitations that need to be acknowledged: 1) the limited sample size due to a high recovery after six weeks of BP onset and 2) the absence of a control group, not included due to ethical reasons, which restricts the analysis of FNT effectiveness. Indeed, the absence of a control group does not allow establishing a confident cause-effect relationship between FNT and patients' improvements, because it cannot be excluded that the observed recovery may have also occurred spontaneously.

Conclusions

During the first 6 months of disease evolution, patients showed improvements with FNT intervention but, after this time the FNT did not show advantages for recovery, moreover, it did not appear to prevent the occurrence of synkinesis.

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4] CAPÍTULO
DISCUSSÃO

Discussão

Os principais resultados das revisões sistemáticas apresentadas nesta dissertação sugerem que o TNMF, isolado ou combinado com os fármacos, parece ter efeitos positivos na recuperação funcional na fase aguda e crónica da PFPI, porém a carência e a qualidade dos estudos incluídos não dão grande evidência científica a estas intervenções. Os resultados dos estudos originais revelaram que, nas primeiras seis semanas, a adição de corticosteróides ao TNMF não foi eficaz na melhoria dos diferentes graus de severidade nem no tempo de remissão da PFPI. O TNMF não evidenciou igualmente benefícios nos últimos seis meses de evolução da doença, não prevenindo a ocorrência de sincinesias.

Os estudos randomizados controlados (RCTs) (Beurskens & Heymans, 2003a; Manikandan, 2007; Nicastri *et al.,* 2013) e uma revisão sistemática (Pereira *et al*., 2010) reconheceram os benefícios do TNMF, através do método de *Mime Therapy* (Beurskens & Heymans, 2003a, 2003b) e da técnica de Reeducação Neuromuscular Facial (Manikandan, 2007) combinados com o *feedback* visual (espelho) na prevenção secundária da PFPI. Todavia, estes resultados foram baseados na qualidade metodológica entre o grau II e IV, segundo a classificação da *American Academy of Neurology* (Gronseth & Paduga, 2012). A revisão sistemática de Pereira *et al.* (2010) incluiu seis RCTs, baseada nas recomendações da *Cochrane Collaboration Handbook* (Higgins & Green, 2008) para a avaliação do risco de viés, e através de um estudo, concluíram que o TNMF apresentava melhoras significativas de funcionalidade (SB-FGS=13.90/100 pontos; IC-95%, 4.31-23.49; p=0.005; coeficiente de *kappa*=0.8). Enquanto a revisão sistemática de Teixeira *et al.* (2008) demonstraram escassa evidência do TNMF, pela redução da qualidade dos estudos e heterogeneidade dos resultados. Estas últimas conclusões corroboram com os resultados da primeira revisão sistemática desta dissertação (Estudo I). Embora os dois RCTs incluídos no Estudo I demonstrassem benefícios do TNMF na simetria facial durante os primeiros 3 meses (Manikandan, 2007) e após 9 meses de evolução da PFPI (Beurskens &

Heymans, 2003a, 2003b), a qualidade metodológica foi de 5/10 pontos da escala PEDro (Maher *et al.,* 2003; Physiotherapy Evidence Database, 2010).

Durante décadas, a farmacoterapia (antivírica e corticosteróide) foi outra das terapias igualmente debatida, sendo baseada nas distintas conclusões das meta-análises (Quant *et al.,* 2009; Salinas *et al.,* 2009; Numthavaj *et al.*, 2011). Actualmente, as investigações científicas demonstraram resultados favoráveis da farmacoterapia na recuperação completa, assentando na hipotética etiologia (agente infeccioso) e na subsequentemente fisiopatologia (inflamação e compressão do nervo facial) (Gronseth & Paduga, 2012; Baugh *et al*., 2013). Porém, 31% dos indivíduos com PFPI desenvolvem sequelas residuais relacionadas com a contractura, paresia motora e discinesias (sincinesia e hipercinesia) (Peitersen, 2002), exigindo novas estratégias de intervenção para minimizar as sequelas. Na generalidade, os estudos avaliaram os efeitos da farmacoterapia e do TNMF isoladamente, desconhecendo o efeito da terapia combinada e a possibilidade desta combinação potenciar a recuperação completa e melhorar as discinesias. Escassos RCTs demonstraram que o TNMF combinado com fármacos eram mais eficazes comparativamente à farmacoterapia isolada (Penteado *et al.*, 2009; Barbara *et al*., 2010; Nicastri *et al*., 2013). A revisão sistemática (estudo II) acrescentou insuficiente evidência do TNMF combinado com os fármacos e com a modalidade de estimulação eléctrica na PFPI, sendo estas conclusões consistentes com a revisão de Teixeira *et al.* (2008). De acordo com a literatura, a estimulação eléctrica pode interferir com a regeneração neural pela proximidade e pela reduzida dimensão dos músculos faciais, promovendo a hiperactividade muscular e consequentemente as sincinesias (Diels, 2000; Targan *et al.*, 2000; Manikandan, 2007; Teixeira *et al.,* 2008; Alakram *et al.*, 2010). De facto, ambas as revisões sistemáticas (estudo I e II) demonstraram baixa a moderada qualidade dos RCTs incluídos, nomeadamente pela natureza do estudo (doentes, investigadores e fisioterapeutas não eram cegos e carência de análise de intenção na intervenção). Aliada a esta análise, os estudos I e II comprovaram carência de RCTs, diversidade metodológica, heterogeneidade das avaliações e intervenções, inconsistência dos instrumentos de medição,

não permitindo consolidar a eficácia do TNMF isolado ou combinado com os fármacos.

Ainda no que respeita à farmacoterapia, as investigações demonstraram uma ampla disparidade de prescrições médicas tal como, via de administração (sistémica ou oral), terapia combinada (corticosteróide e antivírico) ou monoterapia (corticosteróide), agente especifico antivírico (aciclovir, valaciclovir, famciclovir), agente específico do corticosteróide (dexametasona, prednisolona, prednisona, metilprednisolona), posologia da corticoterapia (50 a 80mg diária reduzindo nos últimos 5 dias/ total de 10 dias) e o início da acção da corticoterapia (24 horas a 7 dias) (Lagalla *et al.*, 2002; Roy *et al*., 2005; Sullivan *et al.,* 2007; Engström *et al*., 2008; Berg *et al*., 2009). Os resultados evidenciaram que a corticoterapia oral tinha uma taxa de recuperação acumulada entre 85 a 94%, entre os 6 e os 12 meses (Sullivan *et al.*, 2007; Engström *et al.,* 2008). Contudo, a taxa de recuperação foi sobrestimada porque os investigadores incluíram no desenho de estudo todos os graus de severidade e dilataram a definição de recuperação completa (grau I e II de HB-FGS) (Roy *et al.*, 2005; Sullivan *et al.*, 2007; Engström *et al.*, 2008; Berg *et al.*, 2009). Por outro lado, estas investigações analisaram a eficácia da farmacoterapia comparativamente ao grupo controlo (sem intervenção, placebo ou medicação). Recentemente, a *Guideline Development Subcommittee of the American Academy of Neurology* (2012) e a *American Academy of Otolaryngology, Head and Neck Surgery Foundation* (2013), fundamentadas nos RCTs, publicaram directrizes para a prática clínica dos fármacos na PFPI, recomendando a corticoterapia por via oral, durante as primeiras 72 horas, independentemente da severidade da PFPI e nos doentes com faixa etária superior a 16 anos, em oposição ao carácter opcional da administração antivírica (Gronseth & Paduga, 2012; Baugh *et al.*, 2013). Apesar da forte recomendação da corticoterapia na fase aguda, actualmente ainda se desconhece a taxa de recuperação completa da PFPI severa, sendo este (gravidade de atingimento da doença) um preditor de prognóstico negativo (Shathirapanya *et al*., 2008). Assumindo que os corticosteróides modelam o processo inflamatório na fase aguda, a redução do edema e

consequentemente a descompressão do nervo, favorecendo a recuperação neural (condução nervosa) e motora (aumento do tónus e força muscular), algumas hipóteses foram por nós formuladas. Assim, no estudo III, testámos a hipótese que a adição de corticoterapia ao TNMF seria mais eficaz nos graus mais severos e numa mais rápida remissão da PFPI, comparativamente ao TNMF isolado. Curiosamente, os resultados do estudo III atestaram que o grau de recuperação funcional e simetria facial com a intervenção da corticoterapia eram semelhantes ao TNMF isolado, independentemente do grau de severidade da PFPI. Estes resultados mostram que a dose e a via de administração de corticosteróides utilizadas não adicionaram benefícios na recuperação da disfunção facial. Apesar do estudo III não poder ser comparado com outros estudos, pelo distinto desenho que possui, as meta-análises existentes na literatura demonstraram forte evidência da corticoterapia, independentemente da posologia, tipo, via de administração, quando comparada com o grupo controlo (placebo, monoterapia/antivírica e sem tratamento) (Quant *et al.*, 2009; Numthavaj *et al.*, 2011). Por outro lado, e apesar da controvérsia do TNMF nas distintas fases da PFPI, os estudos precedentes têm evidenciado que o TNMF na fase aguda e em doentes com maior severidade (≥ grau III/HB-FGS) tem efeitos benéficos comparativamente aos fármacos isoladamente, nomeadamente na recuperação funcional (Barbara *et al*., 2010; Nicastri *et al.,* 2013), no aumento da simetria facial (Penteado *et al.,* 2009; Nicastri *et al.,* 2013) e na rápida remissão das disfunções (Barbara *et al.,* 2010; Lindsay *et al.*, 2010; Nicastri *et al*., 2013). Na literatura existem dois paradigmas opostos sobre a intervenção do TNMF na fase aguda da PFPI, principalmente em doentes com grau VI/HB-FGS (máxima severidade). Assim, enquanto alguns investigadores (Balliet, 1989; Nakamura *et al.,* 2003) recomendam a intervenção do TNMF unicamente após a presença de sinais clínicos de reinervação, suportados pela hiperactividade contralateral e, consequentemente, com o agravamento da assimetria facial, outros investigadores (Manikandan, 2007; Cai *et al.*, 2010) defendem a intervenção precoce do TNMF para aumentar a circulação sanguínea, retardar a atrofia muscular, activar as fibras nervosas intactas e manter o tónus muscular. As

recentes orientações internacionais mostram igualmente controvérsia sobre o início da intervenção do TNMF mas, enquanto as orientações americanas não recomendaram o TNMF na fase aguda e crónica, com evidência de grau D, baseadas na classificação do *Centre for Evidence-Based Medicine The Oxford* (2011), as orientações canadianas, baseadas na classificação da *British Medical Journal* (Guyatt *et al.,* 2008), recomendam o TNMF na fase crónica da PFPI. Assim, os resultados obtidos no estudo III estão em discordância com as orientações americanas, demonstrando que tal como os corticosteróides, o TNMF melhora a recuperação funcional e a simetria facial na fase aguda da PFPI. Prévios estudos demonstraram que o TNMF tem uma taxa de recuperação completa do quadro clínico de 88 e de 64% na primeira e segunda semana respectivamente (Manikandan, 2007; Kim *et al.*, 2011). Cronin & Steenerson (2003) acrescentaram ainda que a intervenção precoce do TNMF pode potenciar a recuperação quase completa de graus severos/HB-FGS em doentes com PFPI. A literatura refere que a eficácia do TNMF pode ser argumentado pela selecção das componentes da técnica, sendo inicialmente ajustada e estruturada conforme o grau de disfunção/severidade e/ou sinais clínicos, e igualmente suportada pela performance e capacidade de resposta do doente (Ivona *et al.*, 2010; Lindsay *et al.*, 2010). Nos doentes de grau V e VI/HB-FGS, o TNMF facilita a contracção muscular selectiva através do movimento passivo, activo assistido dos músculos faciais ipsilateral (estimulação da hemiface lesada) e controlo motor contralateral (inibição da hiperactividade contralateral), sustentado pela inervação independente das hemifaces (Diels, 2000; VanSwearingen, 2008). Os doentes com graus de severidade inferior a V/HB-FGS manifestando sinais de reinervação (parcial recuperação funcional e simetria facial), o TNMF abrange os princípios de treino de força e resistência muscular, permitindo inicialmente a adaptação neural (aumento do numero e frequência de activação das UM) e muscular (aumento do tamanho das fibras musculares) (Perry *et al.,* 2011). A recuperação funcional só pode ocorrer com o aumento da força dos músculos da face, fundamentado nos princípios fisiológicos do treino, nomeadamente no princípio da sobrecarga, através de exercícios de elevada resistência/baixas

repetições ou baixa resistência/elevadas repetições (Duffy, 2005). Todavia, a recuperação funcional sucede ainda pela integridade das fibras aferentes do nervo trigémeo (inervação sensitiva da face), permitindo aumentar os *inputs* sinápticos dos motoneurónios, sugerindo o incremento de estímulos sensoriais e mantendo, assim, os níveis de actividade adequado do nervo trigémeo e facial (Pavlov *et al.,* 2008*)*. É de aditar ainda que na fase aguda da PFPI, a literatura menciona elevada taxa de recuperação espontânea (Peitersen, 2002), todavia no contexto clínico os doentes não podem aguardar pela recuperação espontânea. Alguns estudos demonstraram que a inactividade prolongada dos músculos faciais nos doentes com PFPI enfraquece e/ou degenera as estruturas orgânicas, aumentando as irregularidades metabólicas, promovendo a incapacidade funcional e desenvolvendo complicações clínicas (Booth *et al*., 2007; U.S. Department of Health and Human Services, 2008). Beurskens & Heymans (2003a) motivaram os doentes com sequelas (sincinesias) a realizarem exercício facial regularmente, contribuindo para a eficácia clínica comparativamente ao grupo controlo (sedentário). Outro investigador (VanSwearingen, 2008) salientou que o TNMF deve ser usualmente praticado no domicílio bi-diáriamente, 5 a 10 repetições, 3 a 5 exercícios e integrado nas tarefas diárias, tal como os outros músculos, permitindo adquirir competências motoras com a prática regular do exercício facial.

O estudo III demonstrou que, nas primeiras seis semanas de evolução da doença, o grau de recuperação funcional depende do género (feminino) e da idade (jovens) dos doentes. Relativamente ao género, os nossos resultados demonstraram um prognóstico favorável para o género feminino, podendo este achado ser explicado, entre outros, pelo efeito anti-inflamatório dos estrogénios circulantes (Hilsinger *et al.*, 1975; Straub, 2007). Não existe consenso na literatura em relação à influência da idade na recuperação. Enquanto alguns investigadores demonstraram que, particularmente os jovens tinham melhor prognóstico (Peitersen, 2002; Axelsson *et al.*, 2011), outros defenderam que a idade biológica não é um factor relevante na recuperação destes doentes (Takemoto *et al.,* 2011; Marsk *et al.,* 2012). No entanto, no nosso estudo, observamos que o grau de recuperação funcional está relacionado com a

idade, sendo mais efectivo em doentes jovens, reforçando as investigações de Peitersen (2002) e Axelsson *et al.* (2011). Os nossos resultados estão de acordo com o conceito de que o processo de envelhecimento influencia negativamente a recuperação orgânica, quer pela degeneração vascular, com diminuição da irrigação sanguínea periférica, quer pela morosidade na regeneração axonal, resultando em discinesias (Devriese *et al.,* 1990; Kovacic et al*.,* 2009). Os movimentos discinéticos estão presentes nos movimentos voluntários, nas expressões espontâneas e nas funções da face com implicações marcadamente negativas no âmbito psicossocial (VanSwearingen, 2008). Mancini *et al.*, (2014) revelaram que a idade avançada e o elevado grau de severidade (V e VI/HB-FGS) aumentam três vezes mais o risco de desenvolver sincinesias. Esta controvérsia está presente na literatura, tendo, por exemplo, Ikeda *et al.*, (2005) encontrado uma associação directa entre a idade e o desenvolvimento de sincinesias, enquanto outros investigadores consideraram que a idade não tinha influência na ocorrência das sincinesias (Takemoto *et al.,* 2011; Nicastri *et al.,* 2013). Ainda assim, são necessárias mais investigações para consolidar os preditores de recuperação completa. Todavia, os potenciais preditores de recuperação são controversos, principalmente pelo viés dos critérios de selecção (distintas etiologias e graus de severidade) e do desenho de estudo (estudo retrospectivo, série de casos) (Ikeda *et al*., 2005; Kanaya *et al.*, 2009), início e a terapia de intervenção (Sullivan *et al.*, 2007; Engström *et al*., 2008; Nicastri *et al.*, 2013), a duração do estudo (Sullivan *et al.,* 2007; Engström *et al.,* 2008) e os instrumentos de avaliação (Kasse *et al.*, 2005; Mancini *et al*., 2014). Resumindo, nas primeiras seis semanas de evolução da PFPI, o nosso estudo demonstra que o TNMF melhorou o grau de recuperação e a simetria facial dos doentes, enquanto a corticoterapia por via oral combinada com o TNMF não trouxe benefícios adicionais. Os nossos resultados evidenciam ainda que o grau de recuperação é influenciado pela idade, pela gravidade inicial da doença e pelo género.

Os resultados obtidos no estudo IV demonstraram que nos doentes com grau de atingimento ligeiro e moderado (<IV/HB-FGS), às seis semanas, houve uma recuperação completa (I/HBFGS) em 70.6% dos doentes, comparativamente

aos 11.1% observado naqueles com grau severo (>III/HB-FGS). De acordo com alguns estudos, o grau II e III do HB-FGS está associado a uma ligeira degeneração *walleriana*, a qual não resulta em manifestações neurológicas (paresia, discinesia) (Kanaya *et al.*, 2009; Kim *et al.*, 2010). O nosso estudo IV revelou ainda redução significativa da disfunção facial em 1.5 graus/HB-FGS, consequentemente melhorando a recuperação funcional da face, durante o período de seis meses de intervenção do TNMF. Estes resultados corroboraram com o estudo de Barbara *et al.,* (2010). Contudo, esta comparação está limitada pelas diferentes características dos doentes incluídos (grau III-IV vs. II-VI/HB-FGS), procedimentos de intervenção (*kabat* vs. TNMF) e duração do estudo (15 dias vs. 12 meses).

Os resultados do estudo IV demonstraram ainda que o TNMF não influenciou significativamente a subcomponente "simetria em repouso" da escala SB-FGS nos primeiros seis meses, tendo sido encontrados resultados similares aos nossos estudos (House & Brackmann, 1985; Pourmomeny & Asadi, 2014). Este resultado foi sustentado na amostra reduzida de doentes do subgrupo com grau de severidade elevado, resultando numa menor assimetria em repouso e, adicionalmente, pelo facto do TNMF não incluir técnicas de intervenção na postura estática, ou seja, de simetria em repouso (Manikandan, 2007). Teoricamente, a predominância da assimetria dinâmica em algumas regiões da face, comparativamente a outras regiões, pode estar relacionada com a diferenciação da taxa de regeneração axonal (Gagnon & Molina-Negro, 1989, Campbell, 2008; kim *et al.,* 2010), o que está de acordo com os resultados que obtivemos no estudo IV. Neste estudo, após os 6 meses do TNMF, observámos melhoras significativas em alguns movimentos ou expressões/músculos da região da face, com o desenvolvimento de simetrias faciais dinâmicas na região periorbital (oclusão ocular/orbicular do olho) e nasal (cheirar/nasal). De acordo com alguns investigadores, os sinais clínicos das sincinesias surgem entre os 3 e os 4 meses após o início dos sinais e sintomas da PFPI (Peitersen, 2000; Kim *et al.*, 2010; Nicastri *et al.*, 2013) e, neste contexto, o estudo IV demonstrou a presença de ligeiras sincinesias aos 3 meses, aproximadamente em 34.6% dos doentes, sendo o padrão da

sincinesia mais comum a contracção involuntária do orbicular do olho associado ao movimento voluntário do orbicular da boca. Contrariamente, a investigação de Kim *et al*., (2010) identificou que o padrão mais comum era a contracção involuntária do orbicular do olho associado ao movimento intencional do zigomático e risório. Contudo, o estudo de Kim *et al.*, (2010) apresentava uma metodologia diferente da nossa, concretamente, no instrumento de avaliação das sincinesias (escala binária/presente e ausente), na etiologia (PB, fractura temporal, parotidectomia, herpes zóster) e na terapia intervenção (procedimentos cirúrgicos, farmacoterapia e TNMF), dificultando a comparação dos resultados. Segundo a literatura, o mecanismo fisiopatológico das discinesias é originado pelo processo de reinervação caótica irreversível, designadamente a síndrome de autoparalisação e sincinesias, desencadeando a incapacidade funcional (Beurskens *et al.*, 2005). O registo electromiográfico (EMG) demonstrou que a autoparalisação pode ser desencadeada pela activação simultânea de músculos agonistas e antagonistas (cocontração) no esfíncter oral e/ou no orbicular proporcionando uma resposta paradoxal de paresia funcional. Os sistemas esfincterianos apresentam inervação independente, mas com a regeneração anómala das fibras nervosas, a autonomia funcional de ambos os esfíncteres fica comprometida, resultando em sincinesias (Beurskens *et al.*, 2005; English *et al.,* 2009). Durante 12 meses de seguimento do estudo IV, as sincinesias agravaram-se em 3 (11.45%) doentes, podendo ser consequência da contínua degeneração axonal e regeneração caótica dos axónios (Holland & Weiner, 2004; Mancini *et al*., 2014). Os resultados do estudo IV podem deduzir que o TNMF não evita a ocorrência das sincinesias, consequência do processo de desnervação-reinervação. Teoricamente o processo de desnervação pode desencadear depósitos de filamentos de colagénio nos capilares e entre as fibras musculares, redução de dendrites e células satélites, atrofia das miofibrilas e reinervação paradoxal, decorrendo sinais de hiperactividade muscular como as sincinesias, os espasmos e as contracturas (Lee & Wolfe, 2000; May & Schaitkin, 2000; Beurskens *et al.*, 2005). Todavia, apesar do TNMF não evitar a incidência das sincinesias, parece atenuar a severidade das mesmas

(Beurskens & Heymans, 2003a, 2003b; Lindsay *et al.*, 2010), baseado na plasticidade neural, na capacidade do SNC modificar e reorganizar novas redes neuronais, resultando na recuperação funcional (Beurskens & Heymans, 2003a, 2003b, Beurskens *et al.*, 2005; VanSwearingen, 2008). O TNMF permite melhorar o padrão do movimento pela reaprendizagem de contracções voluntárias e de inibição da hiperactividade, numa face dinamicamente assimétrica, pela restrição do movimento e/ou movimento involuntário, logo facilitando a dissociação e selectividade dos movimentos e aumentando gradualmente a amplitude, a força e o controlo motor (Beurskens & Heymans, 2003a, 2003b, Beurskens *et al.*, 2005; VanSwearingen, 2008). Outras investigações têm demonstrado a eficácia do TNMF na redução da severidade das sincinesias, baseada em exercícios de facilitação, relaxamento, alongamento e controlo motor (Brach *et al*., 1997; Beurskens & Heymans, 2003a, 2003b; VanSwearingen, 2008; Lindsay *et al.*, 2010). Adicionalmente, outros estudos demostraram que a adição prévia da injecção de toxina botulínica potenciava o efeito do TNMF (Monini *et al.,* 2011). Todavia, independentemente das terapias de intervenção, a literatura tem demonstrado que em indivíduos com elevado grau de severidade do nervo facial com uma disfunção facial caracterizada pela paresia e sincinesia, cerca de 15% apresentaram sequelas permanentes e irreversíveis (Beurskens *et al*., 2005; Finsterer, 2008).

As disfunções da PFPI também se repercutem no âmbito psicossocial. As assimetrias estáticas e dinâmicas dos músculos periorais e orbitais interferem nas funções básicas das actividades diárias, tal como, dificuldade na alimentação, na ingestão de líquidos, na comunicação e na protecção do globo ocular (Schmidt *et al*., 2005). Estas incapacidades básicas na vida diária do indivíduo revertem na atenuação das interacções sociais e no stress psicológico, criando sentimentos de vergonha, medo da reacção dos outros, baixa autoestima, perda de identidade e rejeição da fisionomia (Prakash *et al.,* 2012). De acordo com Testa & Simonson (1996), a medição da HRQOL deve incluir a percepção subjectiva dos doentes na função física e social nas actividades diárias. As recomendações incidem numa medição específica da

qualidade de vida, tendo a FaCE sido por nós seleccionada pela sua validação para a versão portuguesa, por ser um indicador de elevada fiabilidade e pela abrangência dos domínios funcionais da face (Kahn *et al.*, 2001; Maciel & Mimoso, 2007). O estudo IV evidenciou que os doentes que recuperaram a função e simetria facial tiveram repercussões significativas de boa qualidade de vida geral, principalmente nos primeiros seis meses. Estes resultados estão em sintonia com outros estudos que aplicaram a mesma escala (Lee *et al.*, 2007; Mehta & Hadlock, 2008). O estudo retrospectivo de Lee *et al.,* (2007) incluiu doentes com PFP pós cirurgia do *schwannoma* vestibular, concluindo que a função facial normal (I/HB-FGS) estava relacionada com elevada qualidade de vida comparativamente aos doentes com disfunção facial (≥II/HB-FGS). O estudo prospectivo de Mehta & Hadlock, (2008) incluiu doentes na fase crónica com intervenção de toxina botulínica para as sincinesias, tendo os investigadores verificado uma associação benéfica na qualidade de vida dos doentes. Relativamente aos subdomínios da FaCE, o estudo IV demonstrou que nem todos os subdomínios acompanharam as melhoras significativas da recuperação funcional e simetria facial até aos seis meses, nomeadamente o subdomínio do conforto facial. As três questões do subdomínio do conforto facial focam as sequelas (espasmo, contracturas, sincinesias) que não estão presentes até aos três meses (Kahn *et al.,* 2001). Curiosamente, este subdomínio teve melhoras significativas nos últimos seis meses (presença das sincinesias), sugerindo que as sincinesias não eram suficientemente severas para provocar o desconforto da face. Outros estudos demonstraram que nem todos os subdomínios têm correlação com a recuperação funcional/HB-FGS e simetria facial/SB-FGS, principalmente o conforto facial, o controlo lacrimal e a função social (Kahn *et al*., 2001; Hui & Seng, 2013). Contudo, os escassos estudos e os distintos desenhos dos estudos não permitem comparações e conclusões seguras.

No que respeita às limitações dos nossos estudos, importa referir que a maior é a ausência de um grupo controlo, sem qualquer tipo de tratamento, mas tal não era possível por motivos éticos. Assim sendo não é possível estabelecer uma relação segura de causa e efeito entre o TNMF e a recuperação observada nos

doentes, podendo esta ser uma consequência de uma recuperação espontânea. Outra limitação a apontar poderá ser a reduzida amostra em estudo. Para além da baixa incidência da PFPI na população em geral, limitando a inclusão de uma ampla amostragem, importa referir que comparativamente à maioria dos estudos da literatura (Beursken *et al.*, 2003a; Manikandan, 2007; Penteado *et al.*, 2009; Barbara *et al.*, 2010), a nossa amostra foi muito superior, fornecendo uma maior segurança dos resultados obtidos. Uma outra limitação a referir poderá ser o uso de métodos de avaliação baseados na subjectividade do avaliador. No entanto, a *American Academy of Otolaryngology-Head and Neck Surgery* considera a escala de HB-FGS o padrão de ouro na avaliação das PFP. Por ultimo, o nosso estudo não incluiu instrumentos de medição de diagnóstico e de severidade da PFPI, para predizer com confiança a etiologia e o prognóstico de cada doente, tendo-se baseado apenas em critérios de avaliação clínica, desta forma, o critério para o diagnóstico da PFPI foi de presunção e não de precisão.

Implicações na prática clínica

Os nossos resultados demonstram que há uma grande heterogeneidade entre os critérios de prescrição médica dos corticosteróides, sendo necessário medidas iminentes de uniformidade. Para além disso, permitem inferir que a posologia, via de intervenção, início da acção e o agente específico dos corticosteróides devem ser reconsiderados ou então deve ser repensada a fisiopatologia da PFPI, não dando tanto enfase à teoria isquémica. Recomenda-se o TNMF durante os primeiros seis meses da PFPI, porém após os seis meses de evolução da PFPI, a continuidade deste treino parece não beneficiar a recuperação dos doentes com PFPI.

5] CAPÍTULO
CONCLUSÕES

As revisões sistemáticas documentam efeitos benéficos com o TNMF isolado e combinado com a farmacoterapia, mas não permitem afirmar que são eficazes na recuperação da PFPI, pois carecem de mais estudos controlados e randomizados e de elevada qualidade metodológica.

O primeiro estudo original demonstra que num período de seis semanas ambas as intervenções, corticosteróides combinados com o TNMF e o TNMF isolado, são eficazes na reabilitação dos doentes com PFPI, revelando ainda que os corticosteróides não aditam melhoras no grau de recuperação funcional e na simetria facial. Estes resultados permitem acrescentar, que os preditores de recuperação são o género, a idade e o grau de severidade no início da doença. Este estudo confirma também a heterogeneidade no critério de prescrição médica dos corticosteróides por via oral, havendo doentes graves sem prescrição e doentes com gravidade ligeira com prescrição, reflectindo a falta de uma evidência clara sobre a sua eficácia nestes subgrupos. O segundo estudo original mostra a continuidade da eficácia do TNMF no grau de recuperação funcional e na simetria facial, repercutindo-se numa boa qualidade de vida até aos seis meses de evolução da doença, no entanto, neste período o treino não previne a ocorrência de sincinesias. Nos últimos seis meses de *follow-up* o TNMF não foi eficaz na remissão da doença, revelando que os potenciais efeitos clínicos do TNMF são obtidos até aos seis meses e mais ainda, a recuperação completa ou aquisição da função normal da face é atingida neste período de tempo.

Os resultados obtidos nesta tese científica enfatizam a necessidade de futuras investigações direccionadas para a identificação de outras causas fisiopatológicas para se entender melhor os mecanismos que contribuem para o dano do nervo facial, permitindo estabelecer com rigor o tratamento adequado. Por esta razão, a diversidade de critérios nas prescrições suscitam duvidas sobre o tipo de tratamento na fase aguda da PFPI, variando entre a terapia antivírica e/ou corticosteróides ou outra terapia, nomeadamente o TNMF. Além do mais, os critérios de prescrição dos corticosteróides devem ser uniformizados, avaliando melhor a posologia, o agente específico, a via do imunossupressor que melhor contribui para a rapidez de remissão da doença e a redução de complicações a longo prazo. Seria pertinente atestar com firmeza os factores de risco que podem caracterizar os grupos de doentes com mau prognóstico e analisar a eficácia da farmacoterapia isolada ou combinada com o TNMF nestes grupos específicos.

A limitada evidência sobre a eficácia do TNMF na redução do tempo de recuperação e na prevenção de sequelas nas diferentes fases da PFPI, sugere mais estudos randomizados e controlados para confirmar as vantagens do treino na fase aguda e crónica. Novos estudos deveriam igualmente analisar os parâmetros de frequência semanal e de duração da sessão do TNMF para melhorar a relação custo-efectividade. E por ultimo, desenvolver métodos específicos para avaliar a disfunção neuromuscular (força e tónus) porque a observação/subjectividade não descreve com rigor a variação destes parâmetros.

6] CAPÍTULO
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