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FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

MESTRADO INTEGRADO EM MEDICINA

2019/2020

Maria Inês Portugal Rodrigues

Treatment of Idiopathic Overactive Bladder with Botulinum Toxin: Real-life Results and Patients' Expectations/ Tratamento da Bexiga Hiperativa Idiopática com Toxina Botulínica: Resultados da Prática Clínica e Expectativas das Pacientes

Março, 2020

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Mestrado Integrado em Medicina

Área: Ciências Médicas e da Saúde- Medicina Clínica

Tipologia: Dissertação

Trabalho efetuado sob a Orientação de:

Professor Doutor Carlos Silva

E sob a Coorientação de:

Dr. Pedro Abreu Mendes

Trabalho organizado de acordo com as normas da revista:

Porto Biomedical Journal

Março,2020

FMUP

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UC Dissertação/Projeto (6º Ano) - DECLARAÇÃO DE INTEGRIDADE

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UC Dissertação/Projeto (6º Ano) – DECLARAÇÃO DE REPRODUÇÃO

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Ciência Médicas e da Saúde> Medicina Clínica

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Treatment of Idiopathic Overactive Bladder with Botulinum Toxin: Real-life Results and Patients' Expectations

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É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
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Faculdade de Medicina da Universidade do Porto, 01/02/2021

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Dedicatória

Para a minha avó, Olga: dedico-lhe todo o meu trabalho nos últimos seis anos e, particularmente, esta dissertação. Qualquer que seja a distância, estará para sempre comigo.

Quero agradecer ao meu orientador, o Professor Carlos Silva, por ter aceitado orientar-me e pela sua disponibilidade e ao meu coorientador, o Dr. Pedro Abreu Mendes, por ter feito deste trabalho dele e pela sua dedicação.

Aos meus pais, Ivone e Antero, pela paciência inesgotável e amor incondicional. Foi um percurso muito longo, que teria sido impossível sem eles. Nunca lhes poderei agradecer o suficiente tudo aquilo que fizeram por mim, mas vou tentar. Agradeço também ao meu irmão, Miguel.

Ao Carlos, o meu companheiro de todas as viagens, principalmente desta tão longa, e porto seguro. És o meu preferido. “Era capaz de imaginar a vida, sem ela? E posso dizer que não sei como iria viver. Viveria evidentemente, mas não sei como.” José Saramago.

Aos meus amigos e colegas, que tornaram estes seis anos inesquecíveis e contribuíram para esta conquista.

Treatment of Idiopathic Overactive Bladder with Botulinum Toxin: Real-life Results and Patients' Expectations

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Abstract

Background

Overactive bladder (OAB) is a prevalent syndrome affecting 11%-16% of the adult population. When first-line pharmacological therapy is not effective, intradetrusorial injections of Onabotulinumtoxin A (BTX-A) might have an important role in symptoms control. The aim of this study was to access the efficacy and safety of intra-detrusor injections of 100U BTX-A in real clinical practice, among women with idiopathic OAB (iOAB).

Methods

A retrospective study, based on clinical diaries in 136 iOAB female patients, with or without urinary incontinence, submitted to BTX-A injections, between 2005 and 2018 in a tertiary university hospital. A positive response was considered only when the patient mentioned having great improvement after the injection, otherwise, it was considered negative.

Results

A positive response was obtained in 90 patients (66%) after the first injection. Women with positive response after the first treatment had 7.5 times more chances to improve with the second (p=0.01). Discontinuation of the therapy after the first injection was not dependent on the presence of incontinence at baseline (p=0.73) nor it was related to age (*p*=0.6). On univariate analyses, none of the parameters evaluated was useful of predicting successful response, although there was a trend in women who had had a previous midurethral sling (MUS) surgery for stress urinary incontinence (SUI), to have a lower chance of having a positive response after the first injection (*p*=0.06)

Thirty-nine women (29%) had at least one adverse event, urinary tract infection (UTI) and straining to void were the most frequent. Women above 65 y.o. had less risk of developing a UTI (p=0.04).

Conclusion

In real clinical practice, BTX-A injection is an effective and safe treatment, capable of improving patients' quality of life. Moreover, responding to the first injection seems to predict good clinical outcomes in the second treatment. This procedure can be done with minimal restrictions.

Introduction

Overactive bladder (OAB) is a prevalent syndrome affecting 11%-16% of the adult population and can even be more overwhelming in the elderly (1). It has a significant impact on the quality of life, particularly in sleep disturbance, mental health-related issues and decreased work productivity (2, 3). OAB is characterized by urgency, the core symptom, with or without urgency urinary incontinence, usually with increased daytime frequency and nocturia (4). Although urgency urinary incontinence (UI) may suggest detrusor overactivity, it is not necessary to urodynamically demonstrate involuntary contractions of the muscle (5). OAB is coined as idiopathic (iOAB) when a specific metabolic or pathologic condition that can be the cause is not identified (3).

OAB first-line treatment includes lifestyle changes and behavioural therapy. When these measures are insufficient, the pharmacological prescription is the next step (2). The first-line pharmacologic option is monotherapy with antimuscarinics or β3-adrenoceptor agonists, while a combination of drugs from both classes can be effective after its failure (6, 7).

In patients with refractory or intolerant to antimuscarinics or β3-adrenoceptor agonists, evidence supports the use of intravesical injection of 100U of onabotulinumtoxinA (BTX-A) as second-line therapy (8-12). The injections, in between 10 to 20 sites, are done directly into the detrusor muscle, preventing its contractility modulating both efferent and afferent pathways, resulting in a decrease of frequency and number of incontinence episodes (13, 14). This treatment has a success rate ranged from 60% to 80% (15) and is considered safe, durable and cost-effective(11, 13, 16). However, some adverse events (AE) might happen, such as urinary tract infection (UTI) and urinary retention (16-18).

Unfortunately, not every patient benefit from this minimally invasive therapeutic option (19). Therefore, it is important to understand if there are any clinical or non-clinical parameters predicting a good outcome when offering it (20).

Our aim was to access the efficacy and safety of intra-detrusor injections of 100U BTX-A in real clinical practice. Additionally, another objective was to pursuit predictors of positive response and to identify risk factors associated with AE, in order to level-up the selection of patients proposed to BTX-A treatment.

Materials and Methods

This was a retrospective study including 136 iOAB women, with or without UI (OAB wet/DRY) who were treated with an intravesical injection of 100 U of BTX-A, between 2005 and 2018, in a tertiary university hospital. All patients were above 18 years old and could have initiated and/or ended the treatment at any point in the above-mentioned timeframe. Patients whose OAB could have a potential identifiable cause were excluded: neurologic conditions, metabolic conditions (e.g. diabetes mellitus type I or type 2 insulin-treated) or other related pathologic conditions. Data were extracted from electronic health records.

Demographic and clinical data obtained were age, gynecologic and urologic previous history (recurrent UTI, OAB wet *versus* OAB dry, presence of mixed urinary incontinence (MUI), previous midurethral sling (MUS), previous pharmacological treatments, number of intravesical injections performed, treatment benefit according to the patient reports ("greatly improved", "partially improved, not relevant", "worsened", "not changed"), reason to abandon therapy and AE after each procedure. Since treatment response was measured as a dichotomous variable, a positive response was considered only when the patient

mentioned “greatly improvement”, otherwise it was considered negative. Age was also considered a dichotomous variable (<65 *vs* ≥65 years).

The interval between BTX-A injections was measured from the date of the last injection until the patient asked for the next one.

All the statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). To identify baseline variables associated with the effect of the first BTX-A injection (dichotomous outcome) and the occurrence of AE (dichotomous outcome), logistic regression models were fit for each potential predictor. Initially, each baseline variable was modelled individually to assess the association with each of the two outcomes. Subsequently, multivariate backward stepwise regression analysis was performed using all variables from the univariate analysis. For proportional comparisons, a chi-square test was used, unless otherwise stated. Mean and standard deviations (SD) were used for reported parametric continuous variables. A p-value <0.05 was considered significant.

Ethical approval for this study was provided by the Ethical Committee CES of Centro Hospitalar Universitário de São João, Porto, Portugal on July 2019 (Nº 224/19).

Finally, this study was conducted in accordance with the ethical guidelines mandated by the Declaration of Helsinki all ethical questions have been fulfilled, as well as all sources that provided the theoretical support have been properly referenced.

Results

A total of 136 female patients with iOAB refractory or intolerant to oral pharmacological treatment were submitted to an intra-vesical injection of BTX-A. The mean age at first injection was 60.7±15.3 years, minimum 22 and maximum 87 years old. Globally, 268

treatments were performed and the mean number of injections per patient was 1.96±1.32 (1-8).

OAB Wet was present in 121 (89%) women and MUI was found in 99 (72.8%) patients. Nearly one third (n=33) of women with MUI had previously done a MUS surgery for stress urinary incontinence (SUI). A total of 28 patients (22.1%) had a history of recurrent UTI before the injection (Table 1).

Concerning the number of treatments, 66 (48.5%) were submitted to a single treatment (n=66), 28.7% discontinued at the second treatment (n=39) and 11% at the third 3 (n=15). The remaining 11.8% of the patients discontinued after 4 or more injections. All patients could ask for a new BTX-A treatment at the time of reappearance or worsening of OAB symptoms.

The mean timeframe between the first and second treatment was 17.5±11.7 months and the interval between the second and the third was 19.6±14.8 months. No significant difference was found between these two intervals (p=0.4).

Regarding previous pharmacological therapies, 30.9% (n=42) of the patients had tried exclusively an antimuscarinic drug, while 7.4% of them (n=10) had tried exclusively the β3 agonist. Combination therapy with 2 antimuscarinic was tried in 25.7% (n=35), while 27.9% (n=38) tried the combination of an antimuscarinic with the β3 agonist.

Likewise, there was no statistically significant difference when analyzing age (<65 or ≥65 years old) of women who went for the first injection (p=0.6). Additionally, no difference was found regarding incontinence: OAB wet was present in 61 (44.9%) women above 65 years old and 59 (43.4%) bellow 65, although OAB dry was present in more women <65 years old (*p*=0.052). MUI was more common in the elderly group (p= 0.03) (Table 2).

Efficacy

Concerning the treatment efficacy, 90 out of the 136 patients (66.2%) had great clinical improvement, 41 (30.1%) reported a suboptimal improvement or even worsened their complaints and 5 (3.7%) were not evaluated in any appointment after the procedure, having no clinical records.

Analyzing the 66 patients who were submitted to only one treatment, the reasons given to not repeat the injection were multiple, such as 14 reported lack of improvement, 4 reported worsening of the SUI symptoms, 2 reported worsening of urgency, and 7 referred partial improvement, not relevant enough to repeat. A total of 27 women (40%) decided not to repeat the injection because they considered their symptoms remained controlled after one procedure – either with general measures or pharmacological therapy. Nine women were lost to follow-up, though 4 of them had reported clinical improvement in immediate post-operatory evaluation. Three are waiting for a new procedure (Table 3).

Twenty-seven women reported a sustained improvement of the symptoms, without the need to repeat the procedure, and 55 who improved decided to repeat the procedure due to the loss of the effect over time.

Discontinuation of the therapy at the first injection was not dependent on the presence of incontinence at baseline (p=0.73) nor it was related to age (p =0.6).

On univariate analyses, several parameters, such as age, presence of OAB wet, MUI, number of deliveries, previous hysterectomy and recurrent ITU, were not useful for prediction of clinical outcome after the first BTX-A injection. Although not statistically significant, there was a trend in women who had had a previous MUS surgery for SUI, to have a lower chance of having a positive response in the first injection (OR=0.45 95%;

CI:0.195-1.034; p=0.06). In multivariate analysis, no factor was associated with positive treatment response (Table 4).

Of those 70 women who were submitted to a second injection, 42 (60%) reported to feel clinically better, 25 (35.8%) experienced no symptomatic improvement or had even a symptomatic worsening and 3 (4.3%) were lost to follow-up without a post-injection evaluation. Of the 42 patients with symptomatic improvement, a total of 20 discontinued BTX-A treatment: 18 after a sustained positive clinical response, 1 after the loss of effect over time and one was lost to follow-up. Globally, 31 patients underwent a third injection: 22 women had improved after the second injection, and 9 of them decided to undergo a third treatment although their expectations were not met after the second one.

From patients submitted to a second injection (n=70), 55 had had a positive response in the first treatment. Regarding this 55, thirteen did not respond to the second treatment or the partial improvement did not meet their expectations and 2 worsened. Nevertheless, 38 reported again a clinical improvement. In conclusion, women who had a positive response after the first treatment had 7.5 times more chances to improve after the second (OR=7.46 95%CI 2.038-27.337; p=0.01)

Safety

The total number of AE was 39 (28.7%), all of the grades I and II according to Clavien-Dindo classification. Considering all the injections given, 39 (28.7%) women had at least one adverse event of any kind, 27 (19.9%) presented a UTI after the procedure, 14 (10.3%) had straining to void and 8 (5.9%) required clean intermittent catheterization (CIC) post-operation.

On univariate analyses, considering all the injections given, we tried to identify potential predictors of complications, such as age, presence of OAB wet, previous MUS, and history of recurrent UTI, but no association was found. Addressing post-op UTI, older age (≥65 years) was the only predictor associated with less risk (OR=0.38; p=0.039). Further, none of the predictors was associated with the need for CIC. Multivariate analyses revealed that age was an independent predictor of the occurrence of UTI after the procedure (Table 5).

After the first intravesical injection, 29 (21.3%) patients experienced at least one AE. The two most prevalent were UTI (n= 11; 8.1%) and straining to void (n=8; 5.9%), which was present with UTI in 3 more women, 4 women (2.9%) needed clean intermittent catheterization (CIC), and 3 of them had UTI as well.

Of the 70 women who had a second intravesical injection, only 7 (%) had an AE, even though 3 (%) needed CIC. None of these women had previously required it. Of the 31 women who went to the third injection, 4 (12.9%) had an AE.

Discussion

This study was conducted to evaluate the clinical efficacy and safety of BTX-A therapy in the real clinical practice in a tertiary centre, in opposition to a trial-controlled situation.

Some of our results were not in line with data within the literature. In our study, we found that age was not a predictor of treatment response, unlike other authors such as Richter *et. al* that found that the treatment in older women with refractory iOAB had less efficacy compared with younger women (20). Like in our study, Liao *et. al* found no difference in treatment response during the first 12 months post-BTX-A, when comparing younger patients and elderly patients without frailty (21). When analyzing the characteristics of our patients by their age (<65 or >65-year-old, the cut off age used by most scientific papers

in OAB), we identified some significate differences in features like the presence of incontinence or MUI, both more frequent in older patients. Despite these important differences, the results were similar in two groups, which lead us to think of BTX-A more like an inclusive treatment.

Miotla *et. al* showed that the efficacy of BTX-A injection in women who had or had not a previous midurethral sling surgery was comparable (22), while in our study there seems to be a trend to worse clinical outcome in patients with a history of previous sling procedure (p=0.06).

As to the interval between injections, we found that it was longer than the usually reported in the literature, 6 to 9 months' interval. Maybe, one of the main causes for delaying a second treatment is the fact that in our department the treatment is performed in the operating room under sedation and, some patients tend to avoid such procedure.

Concerning side effects, in our clinical practice bladder, BTX-A injection is well tolerated, with most of the AE being limited to the urinary tract. AE after the BTX-A injection affects 20-43% of the patients according to the literature (23), which is in line with our results. Our figures might be underrated due to multiple factors: on one hand, AE are usually mild and amenable to treat by a general practitioner and end up not being reported in the clinical diaries. On the other hand, we believe that patients with good health literacy in real clinical practice do not report minor AE that they were aware of and resolve spontaneously (e.g. abdominal straining). The need for clean intermittent catheterization in our patients was in line with other studies (1.3-42.2%), as well as the prevalence of UTI reported (1.3-64%) (24).

In our study, age was not a predictor for any kind of complications, except for UTI. Despite not being consistent with other studies (21, 25), in our study younger patients had a higher rate of UTIs. This might be due to a less active sexual life in older patients. A more

detailed comprehensive study involving sexual activity, and possibly with post-voiding residual (PVR) evaluation, would be interesting. We believe this shows the generalized application of BTX-A injections as a treatment for OAB regardless of patients' age, as already mentioned above. Elderly women can be proposed for this treatment, always with the needed precaution.

In our department, it is recommended a postoperative evaluation after 2 weeks to rule out elevated bladder residual volumes. We assume that the cases with the highest PVR, probably higher than 150-200cc, correspond to the 8 patients who needed to perform CIC – a rate below the incidence reported in other studies. The women who needed this procedure after the second and third procedures didn´t need it before.

Our results show that most patients who underwent a second procedure, 55 out of 70, did it because they had a positive response to the first treatment. We also found that age has no influence on requesting to repeat the treatment. In some patients, with a negative response in the first treatment, a second treatment was offered since technical issues could have been the cause of the failure. Patients who responded positively to the first treatment were more prone to respond favourably to a second one (p=0.01). This could lead us to suspect that a favourable clinical response to the first treatment can be used as a good predictor of a successful response to a second treatment.

One limitation of our study was its retrospective nature and the different type of clinical registers between urologists diaries, namely the absence of a questionnaire/score or bladder diary in the pre-injection attendance, making it harder to objectively quantify the patient improvement which makes it likely to have an interviewer bias (19). On the other hand, iOAB syndrome treatment results might be very subjective and highly individual,

influenced by the patient lifestyle and treatment expectations(19). The patients' perception of the treatment result more important than incontinence scores to decide whether or not advance to another treatment.

Since it is not mandatory to have a pre-treatment urodynamic study in every patient with OAB, only a few numbers of patients made the study or had the result registered in clinical diaries, preventing the evaluation of the treatment effect on urodynamic parameters.

Due to its inherent characteristics, this was an exploratory study more than a confirmatory one. Although we could not identify any clinical predictor of positive response to the first BTX-A injection, we can considerer that the response to the first injection can be itself a predictive factor to the response to the second treatment.

Conclusion

We conclude that in the real clinical practice BTX-A intravesical injection (either a unique or repeated treatment) is an effective and safe treatment. Moreover, the response to the first injection indicates a predictor of good clinical outcomes in a second treatment.

Acknowledgements

Assistance with the study: none

Financial support and sponsorship: none

Conflicts of interest: none

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Table 1: Demographic characteristics of the patients

Variable	
Age at first injection (years)	60.7±15.3
Parity	2±1.5
Previous hysterectomy	23 (16.9%)
Recurrent urinary tract infection	28 (22.1%)
Overactive Bladder wet	121 (89%)
Mixed urinary incontinence	99 (72.8%)
Previous midurethral sling in Mixed urinary incontinence	33 (24.3%)

Continuous variables are mean±standard deviation; categorical variables are n (%).

Table 2: Characteristics of patients urologic history by age groups

Variable	< 65 years	≥65 years	*p** value
Age at first injection	71 52.2%	65 47.8%	0.6
Overactive Bladder dry	12 8.8%	4 2.9%	0.052
Absence of Mixed urinary incontinence	27 19.9%	7 7.4%	0.003
Recurrent Urinary tract infection	17 12.5%	13 9.6%	0.5
Discontinuation after the first injection	33 24.3%	33 24.3%	0.62

Table 3: Breakdown of repeated Onanbotulinumtoxin injections and reasons for discontinuation, number of patients

Number of injections	**1**	**2**	**3**	**4**	**5**	**6**	**8**
Patients	136	70	31	16	6	3	2
Decided not to have further injection	63	39	14	10	3	1	2
Reasons given for no further injection, no							
Symptoms controlled	27	18	9	5	2	1	1
Worsening of stress urinary incontinence	4	0	0	0	0	0	0
Worsening of overactive bladder	2	1	1	0	0	0	0
Lost of effect over time	0	5	3	5	1	0	1
Not significant improvement	7	0	0	0	0	0	0
Lost to follow-up	9	4	0	0	0	0	0
Waiting for a new injection	3	0	1	0	0	0	0

Table 4: Univariate and multivariate analysis of first injection response according to patient demographics

	Outcome after the first injection			
	Univariate analyses		**Multivariate analyses**	
	OR (95%CI)	*p** value	OR(95%CI)	p*value
Age ≥65 years	1.51 (0.721-3.18)	0.27	-	>0.05
Parity	1.25 (0.912-1.714)	0.17	-	>0.05
Previous Hysterectomy	0.7 (0.264-1.838)	0.46	-	>0.05
Recurrent UTI	0.87 (0.371-2.112)	0.78	-	>0.05
Presence of MUI	0.9 (0.394-2.065)	0.8	-	>0.05
Previous MUS in MUI	0.45 (0-195-1.034)	0.06	-	>0.05
OAB Wet	1.1 (0.354-3.486)	0.86	-	>0.05

OR= Odds Ratio; CI= Confidence Interval; OAB= Overactive Bladder; MUI= Mixed urinary incontinence; UTI= Urinary tract infection; MUS= Midurethral Sling

Table 5: Univariate and multivariate analyses of all adverse events and separately according to patient demographics

	AEs		**UTI**		**Straining to void**		**CIC**	
	OR (95%CI)	p* value	OR (95%CI)	p* value	OR (95%CI)	P* value	OR (95%CI)	P* value
Univariate analyses								
Age ≥65 years	0.5(0.23-1.08)	0.08	0.38(0.15-9.5)	0.039	0.57(0.18-1.81)	0.34	0.14(0.02-1.19)	0.07
Recurrent UTI	0.62(0.26-1.46)	0.27	0.6(0.23-1.55)	0.29	0.68(0.19-2.33)	0.54	0.25(0.06-1.1)	0.065
Previous MUS	1.1(0.46-2.63)	0.84	0.89(0.34-2.35)	0.82	1.1(0.31-4.57)	0.79	0.51(0.11-2.26)	0.38
OAB Wet	2.1(0.73-6.22)	0.16	1.4(0.41-4.76)	0.58	3.67(1.01-13.5)	0.05	1.1(0.12-9.36)	0.95
Multivariate analyses								
Age ≥65 years	-	>0.05	0.39(0.15-0.98)	0.04	-	>0.05	-	>0.05
Recurrent UTI	-	>0.05	-	>0.05	-	>0.05	-	>0.05
Previous MUS	-	>0.05	-	>0.05	-	>0.05	-	>0.05
OAB Wet	-	>0.05	-	>0.05	-	>0.05	-	>0.05

AE= Adverse Events UTI= Urinary tract infection; CIC= Clean intermittent catherization; OR= Odds Ratio; CI= Confidence Interval; OAB= Overactive Bladder; MUS= Midurethral Sling

Anexos

1) Normas para a submissão de artigos segundo a revista Porto Biomedical Journal;
2) Autorização pela Comissão de Ética para Saúde do CHUSJ para a realização da investigação e da reutilização dos registos clínicos para investigação e desenvolvimento

Porto Biomedical Journal

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29 de Julho de 2019

A Coordenadora da Unidade de Investigação

(Prof.ª Doutora Ana Azevedo)

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PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Exmo. Senhor Presidente do Conselho de Administração
do Centro Hospitalar de São João

AUTORIZADO

CONSELHO DE ADMINISTRAÇÃO | REUNIÃO DE
Presidente do Conselho de Administração
2019-08-01
(Prof. Doutor Fernando Araújo)
Diretora Clínica | Enfermeira Diretora | Vogal Executivo | Vogal Executivo
(Profª Doutora Maria João Baptista) (Enfª Florena Cardoso) (Dr. Luís Pinto Gomes) (Drª Sofia Leal)

Nome do Investigador Principal:

Pedro Filipe Pinto de Abreu Mendes

Título da Investigação:

Evaluating the effect of intravesical botulinum neurotoxin-A injection in women with idiopathic overactive bladder

Pretendendo realizar no(s) Serviço(s) de:

Serviço de Urologia do CHUSJ

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar de São João/ Faculdade de Medicina da Universidade do Porto respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/ Promotor

Porto, 30 *de* junho *de* 2019 .

assinatura

•Centro Hospitalar São João•
Centro de Epidemiologia Hospitalar
24/7/2019

CES-IM005-0

Parecer da Comissão de Ética para a Saúde do
Centro Hospitalar Universitário de São João / Faculdade de Medicina da Universidade do Porto

Título do Projecto: Evaluating the effect of intravesical botulinum neurotoxin-A injection in women with idiopathic overactive bladder

Nome do Investigador Principal: Dr. Pedro Filipe Pinto de Abreu Mendes, interna de formação específica em Urologia no CHUSJ

Onde decorre o Estudo: No Serviço de Urologia. *Falta apresentar declaração da Direcção de Serviço.*

Objectivos do Estudo:
Perceber qual a eficácia da terapia intravesical com toxina botulínica, feita no Serviço de Urologia, como 3ª linha de tratamento em mulheres com idades compreendidas entre os 18 e os 90 anos com bexiga hiperactiva idiopática.

Perceber quais as características das pacientes em que a terapêutica com toxina botulínica é bem sucedida ou mal sucedida.

Concepção e Pertinência do estudo:
Identificação de fenótipos que poderão permitir reconhecer as doentes que mais beneficiam da escalada terapêutica para a toxina botulínica.
Identificação de sinais precoces da falência da terapêutica intravesical.
Implementação de medicina personalizada no tratamento da bexiga hiperactiva.
Avaliar se a técnica cirúrgica no Serviço de Urologia é uniforme.
Análise retrospectiva das doentes do sexo feminino, entre 18 e 90 anos, com bexiga hiperactiva idiopática submetidas a injecções de toxina botulínica intravesical no CHUSJ durante um período de 14 anos (Janeiro de 2005 a Janeiro de 2019).

Benefício/risco: Não aplicável

Confidencialidade dos dados: Está garantido a confidencialidade dos dados.

Incluiu um pedido de reutilização de registos clínicos para investigação e desenvolvimento ao RAI.

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável

***Curriculum* do investigador**: Adequado à investigação.

Data previsível da conclusão do estudo: Março de 2020

Conclusão: Proponho um parecer favorável à realização deste projecto de investigação, após resposta à questão em itálico.

Porto, 19 de Julho de 2019

O Relator da CES, Dr. John Preto

Foi entregue a declaração da Direcção de Serviço

19/07/19

Pedro Brito

SÃO JOÃO

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

Questionário para submissão de Investigação

Exmo. Sr. Presidente da Comissão de Ética do Centro Hospitalar de São João/ Faculdade de Medicina da Universidade do Porto,

Pretendendo realizar a investigação infracitada, solicito a V. Exa., na qualidade de Investigador, a sua apreciação e a elaboração do respetivo parecer. Para o efeito, anexo toda a documentação requerida.

IDENTIFICAÇÃO DO ESTUDO

Título da investigação: Evaluating the effect of intravesical botulinum neurotoxin-A injection in women with idiopathic overactive blac

Nome do investigador: Pedro Filipe Pinto de Abreu Mendes

Endereço eletrónico: pedromendes.uc@gmail.com **Contacto telefónico:** 917923110

Caracterização da investigação:

☒ Estudo retrospetivo ☐ Estudo observacional ☐ Estudo prospetivo

☐ Inquérito ☐ Outro. Qual? ____

Tipo de investigação:

☐ Com intervenção ☒ Sem intervenção

Formação do investigador em boas práticas clínicas (GCP): ☒ Sim ☐ Não

Promotor *(se aplicável)*: ____

Nome do orientador de dissertação/tese *(se aplicável)*: Pedro Filipe Pinto de Abreu Mendes

Endereço eletrónico: pedromendes.uc@gmail.com

Local/locais onde se realiza a investigação: Serviço de Urologia CHUSJ

Data prevista para início: 10 / 07 / 2019 Data prevista para o término: 31 / 03 / 2020

PROTOCOLO DO ESTUDO

Síntese dos objetivos:

- Perceber qual a eficácia da terapia intravesical com a toxina botulínica, feita no serviço de urologia, como 3ª linha de tratamento em mulheres com idades compreendidas entre 18 e 90 anos com bexiga hiperativa idiopática (Overactive Bladder - OAB);
- Perceber quais as características das pacientes em que a terapêutica com toxina botulínica é bem sucedida ou mal sucedida;

Fundamentação ética (ganhos em conhecimento/inovação; ponderação benefícios/riscos):

- Identificação de fenótipos que poderão permitir reconhecer as doentes que mais beneficiam da escalada terapêutica para a toxina botulínica;
- Identificação de sinais precoces da falência da terapêutica intravesical;
- Implementação de medicina personalizada no tratamento de bexiga hiperativa.
- Avaliar se a técnica cirúrgica no serviço é uniforme

LISTA DE DOCUMENTOS ANEXOS

- [x] Pedido de autorização ao Presidente do Conselho de Administração do Centro Hospitalar de São João *(se aplicável)*
- [ ] Pedido de autorização à Diretora da Faculdade de Medicina da Universidade do Porto *(se aplicável)*
- [x] Protocolo do estudo
- [x] Declaração do Diretor de Serviço onde decorre o estudo

  (sendo um estudo na área de enfermagem deve anexar também a concordância da chefia de enfermagem)
- [ ] Profissional de ligação
- [ ] Informação dos orientadores
- [ ] Informação ao participante
- [ ] Modelo de consentimento
- [ ] Instrumentos a utilizar *(inquéritos, questionários, escalas, p.ex.)*: _____
- [x] Curriculum Vitae abreviado *(máx. 3 páginas)*
- [ ] Protocolo financeiro
- [ ] Outros:

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (1960 e respetivas emendas), e da Organização Mundial da Saúde, Convenção de Oviedo e das "Boas Práticas Clínicas" (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CES o relatório final da investigação, assim que concluído.

Porto, 2 *de* Julho *de* 2019

Nome legível: Pedro Filipe Pinto de Abreu Mendes

assinatura

Parecer da Comissão de Ética do Centro Hospitalar de São João/ FMUP Emitido na reunião plenária da CE de 19 / 07 / 19

A Comissão de Ética para a Saúde [redacted] APROVA a realização deste projecto de investigação na sua actual conformidade.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

224-19

RESPONSÁVEL PELO ACESSO À INFORMAÇÃO

SÃO JOÃO

Pedido de Reutilização de Registos Clínicos para Investigação e Desenvolvimento (I&D)

Número do Pedido
1 1 5 0 0 0 9 6 1 6
(A preencher pelo Gabinete de Apoio ao RAI)

Exmo. Senhor
Responsável pelo Acesso à Informação
(Artigo 9.º da Lei n.º 26/2016, de 22 de agosto)
Dr. Rui de Vasconcellos Guimarães

SÃO JOÃO

AUTORIZADO
RAI - Responsável pelo Acesso
[illegible] 22/8)
23/02/19

1. Identificação do(s) Investigador(es) Preenchimento Obrigatório

1.1. Investigador Principal

Nome Pedro Filipe Pinto de Abreu Mendes
Contacto telefónico 9 1 7 9 2 3 1 1 0
Endereço eletrónico pedromendes.uc @ gmail.com

1.2. Investigador(es) Associado(s)

Número Total: 3

Nome Maria Inês Portugal Rodrigues
Contacto telefónico 9 1 3 8 0 1 3 6 1
Endereço eletrónico inesp_rodrigues @ hotmail.com

Nome Luís Manuel Pedrosa do Vale
Contacto telefónico 9 1 9 9 6 9 5 8 7
Endereço eletrónico luismpvale @ gmail.com

Nome Carlos Manuel Pires Martins da Silva
Contacto telefónico 9 6 3 2 7 1 7 6 2
Endereço eletrónico carsil @ med.up.pt

1.3. Afiliação Institucional do Investigador Principal

1.3.1. Grupo Profissional

☒ Médico(a) ☐ Enfermeiro(a) ☐ Docente ☐ Estudante
☐ Outro. Qual? _____

1.3.2. Documento de identificação pessoal ou profissional

☒ Cartão de Cidadão ☐ Bilhete de Identidade ☐ Célula Profissional
☐ Cartão de Docente ☐ Cartão de Estudante ☐ Outro. Qual? _____

Número de Documento 1 4 1 7 5 9 7 2

2. Enquadramento e Identificação do Trabalho de Investigação e Desenvolvimento Preenchimento Obrigatório

2.1. Enquadramento da investigação

☒ Trabalho académico de investigação e desenvolvimento:
- ☐ Não conferidor de grau
- ☐ Conferidor de grau: ☐ Licenciatura ☒ Mestrado ☐ Doutoramento

☐ Projeto de investigação e desenvolvimento

RAI-IM002-0

3. Observações *Preenchimento Facultativo*

4. Aceitação dos Termos e Condições da Reutilização

Cumulativamente com as obrigações decorrentes da lei já citada *(n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12, ambos da Lei n.º 26/2016, de 22 de agosto)* ao submeter o presente pedido concordo e fico ainda vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Não vou elaborar registos, susceptíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Não vou elaborar, nem ficar na posse, de cópias de bases de dados utilizadas na recolha de informação;
- Comprometo-me a obter junto da Comissão Nacional de Proteção de Dados (CNPD) as necessárias autorizações, para eventuais bases de dados que venha a conceber e utilizar no âmbito da presente investigação;
- Comprometo-me a devolver ao Centro Hospitalar de São João, na pessoa do seu Diretor Clínico, as bases de dados e o resultado da investigação;
- Comprometo-me a ocultar os elementos de identificação da(s) pessoa(s) a quem os registos digam respeito, em futuras e eventuais publicações de resultados;
- Comprometo-me a consultar os processos clínicos nas instalações que me forem indicadas para o efeito;
- Comprometo-me a obter os necessários pareceres, quer da Comissão de Ética do Hospital, quer do Centro de Epidemiologia Hospitalar, sempre que necessário;
- Comprometo-me a citar as fontes sempre que publicitar o trabalho de investigação independentemente de requerer a Certidão de Reutilização (DAta REuse Certificate for Research – DARE);
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, resultará no apuramento de responsabilidades disciplinares, civis e penais e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.

5. Decisão do investigador sobre requerer a DAta REuse Certificate for Research – DARE *Preenchimento Obrigatório*

☒ Pretendo desde já requerer a Certidão de Reutilização (DARE) cujo sentido, valor e significado consultei em *http://portal-chsj.min-saude.pt/pages/710.*

☐ Não pretendo requerer a Certidão de Reutilização (DARE) cujo sentido, valor e significado consultei em *http://portal-chsj.min-saude.pt/pages/710.*

6. Assinatura

Nota 1: Se o presente pedido for submetido eletronicamente ou faz assinatura digital qualificada; ou posteriormente vem ao Centro Hospitalar de São João exibir o seu documento de identificação pessoal; ou no âmbito do seu espaço de liberdade e como manifestação expressa do seu consentimento envia cópia do referido documento, neste caso, concluído o processo ser-lhe-á devolvida ou eliminada a cópia do documento de identificação pessoal, conforme as indicações que dê.
Nota 2: Se o presente pedido for entregue presencialmente, assina e exibe o documento de identificação a quem recebe o pedido.

Data 2019-07-02

Investigador Principal

Em caso de dúvida no preenchimento contacte através dos endereços eletrónicos
rai.reutilizacao.id@chsj.min-saude.pt **ou** ruiguimaraes@chsj.min-saude.pt
ou pelos números de telemóvel 962 204 194 **ou** 918 880 299

SUBMETER