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A eficácia do tratamento psicofarmacológico e psicoterapia nas Doenças Inflamatórias Intestinais

The effectiveness of psychopharmacologic treatment and psychotherapy in Inflammatory Bowel Diseases

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The effectiveness of psychopharmacologic treatment and psychotherapy in Inflammatory Bowel Diseases

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Abstract

Objectives: The aim of this revision article is to re-examine what we currently know about the efficacy of psychological therapies and psychotropic drugs in inflammatory bowel diseases(IBD), with particular emphasis on disease activity and psychological well-being. *Methods*: A literature review was performed using MEDLINE with the following keywords: "Psychotropic Drugs" , "Psychotherapy" and "Inflammatory Bowel Diseases". *Results*: Psychotherapy as an intervention for pain, fatigue, co-op mechanisms, medication adherence and reduction of healthcare utilization has shown early promise. For other variables such as anxiety, depression, quality of life, disease symptoms and disease course, results are mixed and differ from the type of psychotherapy applied. Moreover, the patients involved in psychotherapies report, in their own view, describe positive changes in their psychological state, their behavior and their ability to cope with their disease. The therapists had similar clinical feedback as well. Psychotropic drugs seem to decrease clinical IBD relapses, steroid treatment, endoscopies while improving both mental and somatic status of patients All in all, psychiatric interventions have tendency towards fewer surgical interventions, fewer relapses and reduction of psychological comorbidities was noted. *Discussion/Conclusion:* There isn't still a general consensus about the effectiveness of psychiatric interventions in IBD. It is currently not known the exact mechanisms of how or why psychopharmacologic and psychotherapies work and how to optimize them so that they render more robust outcomes. Nevertheless, these results indicate the possibility of an effect that needs experimental verification and given the high desire for and positive experiences of psychologic care and psychotropic drugs. Psychiatric interventions, supported by validated scientific evidence, will surely play an important role in the treatment of IBD.

Introduction

In the last decades, the incidence of IBD(Inflammatory Bowel Diseases) has increased worldwide[1, 2].

IBD include Ulcerative colitis (UC) and Crohn's disease (CD). Both diseases are chronic, with remissions and relapses over the years. Symptoms include diarrhea, abdominal cramps, pain, weight loss, and bleeding from intestines[3]. There is also an higher prevalence of psychiatric conditions (such as anxiety, depression, somatization, perceived stress) among these group of patients, that are associated not only with active disease but also with ongoing symptoms in the absence of inflammation/active disease.

Even though a temporal relationship between the presence of psychological comorbidity and the onset of inflammatory bowel disease activity has been established, a casual relationship remains to be proven. Nevertheless, there is a possibility that the coexistence of mood disorders might influence the natural history of the disease and worsen prognosis[2, 4, 5] and therefore psychiatric intervention may be relevant in the treatment of IBD.

Psychiatric intervention of patients with IBD normally involves two types of approaches: 1. Psychotropic medication and 2. Psychotherapy

Pharmacological agents such as antidepressants, are some of the most widely used interventions for anxiety and depression and have been extensively evaluated [6]. About a third of patients with IBD already take these medications, more than the general population [1, 7].

Although their role in the management of IBD still remains uncertain[2, 8], given that psychological factors play an important role in IBD activity and have been reported to have anti-inflammatory properties [2, 6, 8], psychotropic drugs may be worth to consider as an adjuvant treatment for IBD.

Moreover, a systematic review and meta-analysis looking at the effect of antidepressants on irritable bowel syndrome, found antidepressants to have efficacy over placebo in the improvement of somatic bowel symptoms, with similar effects for both serotonin reuptake inhibitors and tricyclic antidepressants[8].

In addition to psychotropic drugs due to the chronic nature and frequently reported poor quality of life for many patients with IBD, psychotherapy may be a crucial component in the treatment of IBD[6]. Some studies already report statically significant success of psychological interventions in other gastrointestinal diseases such as Irritable Bowel Syndrome aswell as most IBD mental health concerns [4, 9].

Furthermore, in a study done with 631 inflammatory bowel disease patients, using a web based questionnaire , about the need of psychotherapy as additional therapy in IBD. Half of the patients clearly expressed the need for psychotherapy especially those with previous experience with the treatment(p 0.001) fear of progression(p0.001), lower quality of life(0.001), smoking(p 0.003) and no previous surgery(p0.001)[10].

So given that there is no cure for IBD, psychological interventions are increasingly being recommended as a component of a multidisciplinary treatment approach[11, 12].

The aim of this revision article is therefore, to re-examine what we currently know about the efficacy of psychological therapies and psychotropic drugs in inflammatory bowel diseases, with particular emphasis on disease activity and psychological well-being.

Methods

A systematic revision was made from the literature published since 2009, utilizing Medline's electronic database, with the last research being made on the 10th of October of 2019.

The following keywords were used: (("Psychotropic Drugs"[Mesh]) OR "Psychotherapy"[Mesh]) AND "Inflammatory Bowel Diseases"[Mesh]

In a first phase, articles were excluded by the reading of their titles and abstracts. Out of 112 articles obtained, 61 articles were chosen.

In a second phase, the articles were read in their full and selected according to their relevance as well as published in the last 10 years(from 09/10/2009 to 09/10/2019, with clinical trials in humans and/or animals, published in Portuguese or English. Any publication such as case report, historical article, narration, letters to the Editor and with full article not available, were excluded. During this phase, from the 61 articles, 14 were further excluded, remaining with a total of 47 articles.

For each included study, the following information was obtained: title; author, year of publication, country, study type, studied population, methods used and main results/conclusions

Results

Psychotherapies

Psychologic distress over the course of IBD is consistent and can be independent from disease activity therefore, solely treating IBD symptoms is insufficient in its alleviation and mental health treatment may be relevant in this group of patients[11]

Should be noted that the most explored psychological treatments include cognitive behavioral therapy(CBT), gut-directed hypnotherapy and mindfulness[12-14] while others such as acceptance and commitment therapy, relaxation training/solution focused therapy are not so well studied, especially in IBD and therefore they lack sufficient evidence to make proper recommendations at this time

On one hand, some studies, especially systematic reviews, found the evidence supporting psychotherapy in IBD patients, inconclusive especially whether it improves anxiety, depression, quality of life, symptoms or disease course[6, 9, 15]

On the other hand, psychotherapy as an intervention for pain, fatigue, medication adherence and reduction of healthcare utilization has shown early promise. Furthermore, many studies which used a psychologist, psychotherapist, counsellor, or unspecified therapist reported significant effects in terms of at least one outcome variable[9, 16, 17]

Also, there wasn't found any benefit of psychological therapy relatively to the type of inflammatory bowel disease[4]

The specific results gathered in this article for the use of psychotherapeutic approaches in IBD is presented below:

Cognitive behavioral therapy (CBT) :

Is an intervention limited in time, problem focused, structured and with prescriptive therapy based on two main principles: 1. Symptoms are learned and reflect skill deficits in domains of cognitive and behavioral functioning. 2. Teaching new skills for modifying maladaptive thoughts and behavior patterns which can remediate these deficits and, in turn, relieve symptoms[3].

CBT is already been found to be effective in the treatment of both anxiety and depression but this intervention on IBD patients has had has mixed results[15]

While some studies, especially systematic reviews, found the evidence supporting CBT intervention in patients, inconclusive or not statistically significant in all relevant parameters[6, 15]. For instances:

In 2017 RCT, CBT did not significantly influence disease activity nor did CBT significantly affect mental health, coping or quality of life in adult patients [18] And also,

in 2015, a pilot randomized controlled trial, shown CBT does not seem to improve disease activity, anxiety, depression or coping measures at 12 months but improves individual's quality of life [19]

Other studies, show therapeutic gains in the treatment of patients, especially with higher degrees of distress[12, 20], with improvement on depression, anxiety, stress levels, somatic symptoms[21], quality of life[22], medication adherence[23] and disease course[24-26]. One day Behavioral therapy workshop with 20 adult patients has shown to improve anxiety statistically significantly at 3 months, concluding that effective behavioral intervention that can be completed in one day should be considered as an alternative to the regularly prescribed weekly treatments[27]. In a 2018, nonrandomized uncontrolled trial of CBT suggests that this intervention may have benefits for those with moderate-severe disturbances of mood and that effect sizes can be improved by targeting groups with higher distress levels. [20]

Furthermore, most studies with pediatric patients report very positive results[28] [29]. A trial done on 185 children with IBD and their parents suggests that a brief cognitive-behavioral intervention with children and their respective parents may result in improved child functioning and quality of life, and for some children may even decrease disease activity[25]. In a 2019, a CBT pilot study, done in Pediatric patients with IBD and integrating illness concerns, concluded: 88% of adolescents were treatment responders and 50% no longer met criteria for their principal anxiety disorder[30]. And in the largest randomized controlled trial of two psychotherapies for youth with comorbid IBD and depression, decreases were shown in anxiety, pain and disease severity[26].

Mindfulness-based therapies(MBT) :

Can be defined as free of judgement mentality, willingness to accept current circumstances and attention towards the present-moment experiences.

Furthermore, mindfulness interventions have already been integrated into a number of psychotherapies supported by the American Psychological Association including Acceptance and Commitment Therapy[12]

In a 2019 randomized controlled trial with 79 IBD patients, acceptance and commitment therapy improved stress, increasing overall psychological health in this group of patients[31].

Evidence supporting the treatment of anxiety, depression as well as disease activity in IBD patients is limited[12]. However, in a 2015 controlled study, mindfulness group reported significantly greater improvements in anxiety, quality of life after intervention, with reduction in depression and improvements in quality of life maintained at 6 months after intervention[32].

Moreover, mindfulness therapies seem to foster adaptive coping and maintain quality of life during flare ups, particularly among individuals with higher distress levels or abdominal symptoms[12, 32, 33] and the post hoc analysis suggest that this type of intervention may be effective in decreasing the rate of flare-ups in patients with heightened state of stress[12, 33] Despite these findings, mindfulness seems to not decrease inflammation markers and also time, severity or proportion of participants who flared [33]

Hypnosis

May be defined as "an ability to sustain a state of attentive, receptive, intense focal concentration with diminished peripheral awareness in response to a signal"[12]. As a

psychotherapy intervention for IBD, the clinician delivers hypnotic suggestions in order to improve patient's psychological and gastrointestinal well-being[12].

In a 2013 prospective study, it was found that patients receiving hypnotherapy were able to prolong clinical remission by 78 days, with 68% of HYP patients and 40% of CON patients maintaining remission for 1 year[34]

These results are also been seen in more recent studies[12, 35, 36] and Hypnotherapy may also have a have corticoids sparing effect, requiring less medication for the management of the disease[35, 36]

In a 2015 study, patients with severe psychosomatic IBD refractory to corticosteroids, reported an 80% improvement in quality of life after 12 sessions of hypnotherapy. Such benefits likely come from its ability to control emotional symptoms and possibly improve pain[15]

Recent Pediatric studies suggest that medical Hypnotherapy may be an effective way of treating functional abdominal pain and IBS. In IBD, data is more limited (small sample sizes) but findings show reduced rectal mucosal inflammatory responses and prolonged/maintenance of clinical remission[11]

A systematic revision concludes that evidence is building up towards the belief that gut-directed hypnotherapy has durable efficacy in patients with IBS and possibly IBD without apparent safety issues, improving psychological and physiological outcomes such as motility, visceral sensitivity, immune function and central processing pain. It should be pointed out though that not everyone is equally susceptible to hypnosis[14]

Stress management interventions:
Provide education on stress, coping while also teaching relaxation techniques.

In a 2012, prospective randomized control trial, 39 subjects submitted to a relaxation-training intervention, showed statically significant improvement versus control group. Their anxiety level decreased, quality of life and mood improved while levels of pain and stress decreased concluding that IBD patients may benefit from relaxation training in their treatment[37]. An intervention of behavioral stress management in 45 patients with non-active CD shown reduced abdominal pain($P<.05$) with improvement maintained up to 12 months [21]

This type of intervention appear then to have some results in reducing stress, anxiety and pain while also improving quality of life in IBD although no significant results for patients with lower disease activity. There is also limited support for the use of stress management for IBD patients with comorbid depression[12].

Supportive/expressive psychotherapy:
The main objective of this therapy is to encourage self-expression, reduce feelings of isolation while also increasing one's support.

In a prospective, uncontrolled pilot study with supportive/expressive group psychotherapy as an intervention, no significant changes were found in quality of life, anxiety, depression. Also, no significant changes occurred in IBD symptoms despite apparent reduction. However, changes in coping were observed: patients reported less use of maladaptive coping styles, including denial, suppression and self-blame[12].

Nevertheless, a different study, focused on individual supportive psychotherapy to an IBD counselor showed positive results in psychological well-being, stress reduction and disease activity.

Solution focused therapy:
Aims to improve one's coping abilities through a short psychotherapy. In a randomize controlled trial with 98 patients with IBD submitted to solution-focused therapy, had their fatigue levels reduced and thereby their quality of life improved[38].

In a more recent study of highly fatigued patients, authors found short/term therapeutic effects on quality of life and depression but no significant results in anxiety or fatigue. However, a latter study with the same patients shown significantly greater improvement of fatigue levels on the treatment group when compared to control group. This effect was only sustained until 6 months of follow up[12].

Multi-component behavioral treatment (MCBT) :
Is an intervention that combines different psychological approaches such as muscle relaxation techniques, thermal biofeedback, training in coping, and education in IBD.

A study using a multi-component intervention which included one-hour sessions of relaxation, biofeedback, cognitive coping strategies and education or symptom-monitoring control succeeded in improving abdominal pain. Also, people with CD had more pain at baseline when compared to those with UC and improved more than participants with UC, which indicates a better response to treatment by patients with CD [21]

In a RCT with 21 patients using MCBT stress reduction was the only psychological measure to significantly decrease out of 5 other variables, including psychosomatic symptoms. In contrast, results from a self-report of IBD symptoms, a greater number of controls reported symptom reductions than treatment group(82% vs 65%, $P<0.01$)[12].

Telemental health:
Can be defined as a psychotherapy treatment delivered through the internet. One could argue that psychotherapies such as CBT are less readily available, costlier and more labor/ time intensive than pharmacologic treatment[15] plus there is a barrier to the psychotherapy interventions and its acceptability, especially by "nonpsychiatric" population[3].

In this scenario, web based treatment is an inexpensive alternative, effective in treating depression, anxiety, insomnia and Irritable bowel syndrome[11]. In a randomized controlled study, a CBT online program shown improvements in quality of life scores at 12 weeks after baseline, but these were not maintained at 6 months. Even though there was a high drop-rate, this online intervention, according with the patients involved helped to better understand their IBD [39].

A summary table with the most relevant results(see Table 1) is presented down below

Table 1: Summary of the most relevant psychotherapies covered by the study

Psychological Intervention	Potential usefulness on IBD patients	Potential inapplicability
Cognitive behavioural therapy	• Reduces anxiety and depression[21] • Develop adaptive coping skills[12] • Reduce IBD/related stress[12, 21] • Improves quality of life[12, 19, 22] • Improves disease course[24-26] • Reduces somatic symptoms[21] • Medication adherence[23] • More significant therapeutic gains in individuals with higher degrees of distress[12, 20] and pediatric patients[28, 29]	• The outcomes mentioned are inconsistent[6, 12, 15, 18, 19]
Mindfulness based therapies	• Improves stress • Could foster adaptive coping[12] [32, 33] • Maintain quality of life during flare ups[12, 32, 33], especially in individuals with moderate/severe distress or abdominal symptoms[12, 33]	• Evidence supporting the treatment of anxiety, depression as well as disease activity in IBD patients is limited[12] • Does not decrease inflammation markers and also time, severity or proportion of participants who flared[12, 33]
Hypnosis	• Prolongs clinical remission[11, 12, 34-36] • Corticoids sparing effect[35, 36] • Improves quality of life[15] • Reduces pain [14]	• Not everyone is equally responsive[14] • Needs further and better designed research[14]

	• Most promise for managing disease activity[11, 12, 14] • Indicated for patients with severe psychosomatic IBD [15]	
Stress Management	• Reduces Anxiety[12, 37] • Reduce IBD-related stress[12, 37] • Improves quality of life[12, 37] • Some support for pain management[12, 21, 37]	• No significant results for patients with lower disease activity[12] • Limited support for IBD patients with comorbid depression[12]
Supportive expressive therapy	• May improve coping mechanisms[12], psychological well-being, stress levels and disease activity[17]	• At this point in time there is not enough evidence to make recommendations
Solution focused therapy	• May improve fatigue levels and quality of life[12, 38]	
Multi-component behavioural treatment	• May improve pain levels, reduce stress and improve symptoms[21]	
Telemental Health	• Proved results in diseases other than IBD[11] • May improve quality of life[39] • Cheaper and more accessible alternative to the common psychotherapies [3]	

Psychotropic drugs

Recent studies have shown adults with IBD are more likely to develop anxiety and depression before IBD onset. Moreover, the use of antidepressants appears to be more frequent among IBD patients than controls, and also the length of use or doses significantly exceeds those of controls[8, 40]

In addition to this, patients with active disease, used antidepressants and anxiolytics more frequently than those with quiescent disease, reflecting the burden of IBD on an individual's psychological well-being [1, 2].

In humans, it has been observed that anti-depressants improve both mental and somatic status of patients with IBD although due to the low quality of available research, there is still significant barriers in order to make definitive statement on their efficacy or lack thereof[6, 8]. Nevertheless, some studies, have found a statistically significant positive impact of antidepressants (desipramine and fluoxetine) on inflammation in animal models of IBD, reducing the risk of colitis and improving inflammatory markers, with little evidence of adverse effects[5, 8].

Studies have also have shown that amitriptyline acts on alpha1- adrenoreceptors to produce anti-inflammatory effects. Therefore, investigators have hypothesized that the antidepressant like effects of amitriptyline, via modulation of this pathway, may be more effective for treating and suppressing the development of IBD through its anti-inflammatory actions[6]

There is also been studies which showed that patients on psychotropic drugs such antidepressants reported fewer relapses [15] less need for steroid treatments[8] and endoscopies[40]

Selective serotonin reuptake inhibitors such as citalopram, fluoxetine and sertraline are effective in controlling symptoms of anxiety and depression as well has to decrease pain, gut irritability and defecation urgency. [15]. Tricyclic antidepressants have also been found to be effective for pain and other residual symptoms of IBD in adults, but findings are more mixed for children [40]. On the other hand, serotonin reuptake inhibitors used concomitantly with psychotherapy in youth patients have shown positive effects for depression and anxiety[40]. The use of selective serotonin reuptake inhibitors and tricyclic antidepressants protects against Crohn's disease. Mirtazapine, serotonin norepinephrine reuptake inhibitors, serotonin modulators and tricyclic antidepressants protect against Ulcerative Colitis [2]. Another study states patients with ulcerative colitis had significantly better response to tricyclic antidepressants therapy than Crohn's disease.[41] Same study also refers that tricyclic antidepressants could be used by clinicians irrespective of whether these residual symptoms are functional in etiology or related to occult inflammation due to tricyclic antidepressants being effective in producing symptom response in IBD even in the presence of mild inflammatory disease activity.[41]

Should be pointed out though, that like psychotherapy studies on IBD, psychiatric drugs studies on IBD have also presented some contradictory results. In a 2017 small randomized controlled trial of 24 patients with IBD, fluoxetine was not superior to placebo in maintaining remission or improving quality of life[42]. Also, even though a longitudinal follow-up study from 2013 demonstrated a trend of lower disease activity among patients receiving antidepressants and SSRIs, at baseline, particularly among those with abnormal anxiety or depression scores at baseline, results weren't statistically significant[5]. A brief table summary of the most important results for each drug and it's class is presented below.

Table 2: Summary of most relevant drug results covered by this study

Classes	Drugs	Advantages	Disadvantages
Dopaminergic reuptake blockers	Bupropion	• Improve depression, fatigue and inflammation [40] • Have shown results in inducing long-lasting remission	-
Tricyclic antidepressants	Overall	• Effective for pain and other residual symptoms [15, 40, 41] • Reduce risk of developing IBD[2]	• Mixed results in children[40] • More effective on UC than CD[41]
	Desipramine	• In animal models, reduces the risk of colitis and improves inflammatory marker with little evidence of adverse effects[8]	-
	Amitriptyline	• Anti-inflammatory effects[6]	-
	Mirtazapine	-	• May increase inflammation, needs experimental confirmation[6]
Serotonin reuptake inhibitors	Overall	• Improve of pain and somatic bowel symptoms such as gut irritability and urgency of defecation[8, 15] • Reduce risk of developing IBD[2] • Positive effects youth patients for anxiety and depression[40]	• Increased risk of gastrointestinal side effects such as nausea, pain, diarrhea and risk of gastrointestinal bleeding(1:2000)
	Fluoxetine	• In animal models, reduced the risk of	-

		colitis and improves inflammatory marker with little evidence of adverse effects[8]	
Serotonin norepinephrine reuptake inhibitors(SNRI)	Overall	• Protective of UC[6]	• Cause more frequently nausea and vomit when compared to SSRI[6] • Not protective of CD
	Venlafaxine	-	• Increased risk of gastrointestinal bleeding(1:2000)

Discussion

Psychiatric comorbidity and Inflammatory Bowel Disease:
As mentioned before, the relationship between psychiatric disorders and IBD is not clear. Some authors suggest a possible vulnerability of certain patients with IBD to develop a psychiatric disorder due to experiences that are independent of the disease process (e.g. childhood victimization and abuse). Other investigators report psychiatric disorder only in close relationship with increased disease activity, implying that the former may be a consequence of disease activity and not its cause[3]. Also, psychotherapy is more effective in changing psychological symptoms than physical ones which may further imply psychological distress is a factor for greater disease activity rather than a cause of it. [43]

Despite this, it is commonly accepted that changes in disease activity and presence of additional gastrointestinal symptoms seem to lead to changes in anxiety, depression and also quality of life of patients with IBD[3].
Psychotherapies: psychotherapies intervention studies have shown greater impact in FGID when compared to IBD. These results are likely related to the increased importance of psychopathology in the genesis and maintenance of FGID[28]

Moreover, there have been few adequate psychological treatment trials in IBD and these achieved mostly lower demands for health care rather than a reduction of anxiety or depression. This has been especially evident in youth patients, highlighting the importance of screening for depression in a pediatric population with IBD.[15, 16] And it is feasible to conclude that initiating psychological interventions such as CBT as an adjunct therapy may equip adolescents with necessary coping skills to better manage pain and symptoms associated with their medical illness. It may also help adolescents identify somatic symptoms associated with anxiety, which in turn may reduce misinterpretation of physical symptoms as signs of disease severity and therefore requiring less medical attention.[30]

Nevertheless, many studies, especially randomized controlled trials(RCT) using CBT, which is thought to have the best evidence for efficacy in management of anxiety and depression[4], appear to help patients to cope with their illness while having a positive impact in quality of life and consequently, depression and anxiety levels. This effect, is most likely secondary to improvements in cooping mechanisms as well as treatment of coexisting anxiety and depression[15]. It can't be excluded the possibility that the increasing use of new drugs in the treatment and management of Inflammatory bowel diseases could have an effect on the findings of these studies[4].

However, despite the positive findings, psychological treatment is not indicated in every patient. Psychological intervention should be used only in "risk patients" with comorbid psychiatric conditions. Otherwise psychological therapies seem to not improve clinical disease indices or other psychological outcomes in "non risk" patients with Inflammatory bowel disease[4-6, 12] [20]

The limited evidence of psychotherapy benefits might have arisen from an absence of sensitivity or specificity of the instruments used to detect changes in mood, as well as failure by most of the trials to recruit only patients who had abnormal levels of psychological health when compared with the general population[4]. Another possible reason for the lack of effect may be that most participants in several studies were in remission at the time of the investigation and rates of stress and psychological concerns tend to be higher during flares[13]. Also, many of the interventions, even though, tailored to the needs of individuals with IBD, were not exclusively used to treat anxiety, depression or other specific psychological parameters. Thus, more symptom-specific interventions may be necessary to effectively treat anxiety and depression in this population, possibly creating more reliable results for CBT and MBT and explain why hypnosis has shown to be effective at reducing disease activity but not anxiety or depression[43], answering the question of how hypnotherapy doesn't lead to a reduction of psychological distress when this distress is a result from physical symptoms rather than the cause of them[13, 15, 43]. On the other hand, CBT and MBT seem very limited in their impact on disease activity and this could be due to follow up not being long enough for health benefits from stress reduction to appear[13].

Other psychological interventions such as stress management, supportive expressive therapy, solution focused therapy and multi-component behavioral treatment share the same mixed results as the other interventions and could also benefit from the prepositions mentioned above[15]. The difference being, at this point in time, they still lack enough studies to make proper recommendations[12].

Relatively to telemental health, in spite of the absence of significant evidence to demonstrate the effectiveness of online CBT to manage mental and physical outcomes in gastrointestinal diseases, this type of intervention could be of relevance, especially when it has been successfully used as supportive treatment in many other chronic illnesses [44] and future research should aim to improve adherence rates. It may also come to play an important role In reducing the gap between demand and supply of these treatments while also increasing the number of patients it can reach [3].

This systematic revision includes studies with several limitations, which arise mainly from the small number available for analysis and their risk of bias. Additionally, many of the trials identified were at high risk of bias because of the absence of adequate masking. Future research could apply modifications of evidence-based psychotherapies that specifically target depression and/or anxiety as well as other psychological parameters such as stress and fatigue. Research into other interventions such as mindfulness and hypnosis could also continue to be explored due to their interesting results especially in terms of disease activity. Also, longer-term, carefully designed

psychological intervention trials are urgently needed to determine the optimal treatment for the patient[15]

Psychotropic drugs:

Antidepressants are commonly prescribed in IBD and appear to be mostly used for functional symptoms and psychological distress[2]. They also seem to decrease clinical IBD relapses[6] while also being cheaper than psychotherapies[15]

Beside their use being increased among adult patients, recent study has shown that compared to peers, adolescents with IBD are being dispensed more prescription antidepressants within a few years of diagnosis, becoming then a proxy indicator for depression, as this type of medication is not used for other purposes such as the management of long-lasting pain in youth patients[45].This conclusion addresses the importance of considering mental health in all IBD patients, including pediatric.

The mechanism behind the efficacy of antidepressants in decreasing clinical relapses in IBD, on one hand can be explained by the fact that patients in better psychological health report fewer functional gastrointestinal symptoms[6, 15]. On the other hand, it may also indicate an inflammation-specific benefit from anti-depressants[6] or even their capability to treat depression which by itself also augments inflammatory responses[2].

In IBD patients, not all symptoms reflect IBD disease activity or failure of immunosuppressive therapy. There is a need for agents to address these symptoms in patients who do not require, or are not candidates for, further escalation of immunosuppression. Psychotropics drugs may well be those agents and have been proven to be effective in producing symptom response even in the presence of mild inflammatory disease activity, suggesting that psychotropic drugs like antidepressants could be used by clinicians irrespective of whether these residual symptoms are functional in etiology or related to occult inflammation.[41]

So judging by the success of psychotropic drugs intervention in functional gut disorders and particularly in bowel functions and abdominal pain, but also by its usage from a significant proportion of patients with IBD (between 10% and 30%)[8] ,these medications seem to have a role to play in IBD management. Whether this is because they influence the inflammatory processes or simply because they can improve mood is hard to decipher at present, and their role in IBD should be further investigated with properly conducted RCTs, validated measures, larger samples and adequate follow-up periods to accurately determine the efficacy of antidepressants on improving disease course

Conclusion

There isn't still a general consensus about the effectiveness of psychiatric interventions in IBD. Nevertheless, a tendency towards fewer surgical interventions, fewer relapses and reduction of psychological comorbidities was noted. Moreover, the patients involved in psychotherapies report, in their own view, that the therapy they received was helpful to them, and they describe positive changes in their psychological state, their behavior and their ability to cope with their disease. The therapists had similar clinical feedback as well [3, 40, 46, 47].These results indicate the possibility of an effect that needs experimental verification

Furthermore, even though IBD has little impact on mortality, the relapsing course of the disease leads to considerable morbidity and often requires extensive therapeutic

interventions over the course of patients lives, it causes considerable costs to society [1] plus it can lead to higher rates of missed school or work, medical costs, hospitalizations, surgery and even death[25]. Therefore, although it is not known how or why psychopharmacologic treatments work, when they work and how to optimize them so that they render more robust effect sizes but, there is an immediate need for more, alternative and safe treatment interventions in IBD, besides the ones already being used, of course. Nonetheless, given the high desire for and positive experiences of psychologic care and psychotropic drugs. psychiatric interventions, supported by validated scientific evidence, will surely play an important role in the treatment of IBD. However, whether it belongs to an adjunct to other conventional therapies or first line treatment, remains to be ascertained

Finally, according to the current international evidence-based guidelines, psychological distress should be screened for and treated in IBD patients, with psychotherapy/psychopharmacotherapy offered if required [6, 8]. With that in mind, in order to aid the reader, a bullet-point list of the most useful and prominent information gathered in this revision article has been created:

- Psychiatry interventions are already successful treatment option in other gastrointestinal diseases such IBS as well as most IBD mental health concerns[4, 9]
- From all the psychotherapies revised in this article, by far the most well studied are CBT, Hypnotherapy and Mindfulness and therefore, the ones presenting the most robust results[12-14]
- Evidence is building up towards the usefulness of psychotherapy on improving several outcomes in IBD such as anxiety, depression, stress, disease activity, quality of life, medication adherences well as reducing pain, fatigue, somatic symptoms and healthcare utilization.
- Psychotherapy interventions in pediatric populations[15, 16, 30] appear to show more promising results.
- Psychotherapy and psychotropic drugs seem to be more effective in IBD individuals with higher degrees of distress[5, 12, 20]
- Psychotropic drugs, besides their already known therapeutic effects and adverse reactions, at present time appear to have some advantages and disadvantages inherently to IBD patients such as :
    - Advantages: seem to Improve mental and somatic status of patients[6, 8]
    - Disadvantages: most IBD patients prefer psychotherapy as choice of treatment rather than psychotropic drugs[44]
- For more specific results of each psychiatric intervention, please see Tables 1 and 2.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Anexo

Normas de submissão da revista de referência:

Journal Title

Concise and Informative Article Title

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Abstract

The abstract should be a single, self-contained paragraph which summarises the manuscript. Ideally it will provide a brief context for the study, before describing the scientific approach and some key results in a qualitative manner. It should finish with a sentence to describe the implications for the field. The abstract must not include references, figures or tables.

Introduction

The introduction should be succinct, with no subheadings. Limited figures may be included only if they are truly introductory, and contain no new results.

Materials and Methods

The materials and methods section should contain sufficient detail so that all procedures can be repeated. It may be divided into headed subsections if several methods are described.

Results and Discussion

Subheadings

The results and discussion may be presented separately, or in one combined section, and may optionally be divided into headed subsections.

Advice on Equations

Equations should be provided in a text format, rather than as an image. Microsoft Word's equation tool is acceptable. Equations should be numbered consecutively, in round brackets, on the right-hand side of the page. They should be referred to as Equation 1, etc. in the main text.

$$x = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a} \quad (1)$$

Advice on Figures

At the point of submission, authors may provide all figures embedded within the manuscript at a convenient break near to where they are first referenced or, alternatively, they may be provided as separate files. All figures should be cited in the paper in a consecutive order. Where possible, figures should be displayed on a white background. When preparing figures, consider that they can occupy either a single column (half page width) or two columns (full page width), and should be sized accordingly. All figures must have an accompanying caption which includes a title and, preferably, a brief description (see Figure 1).

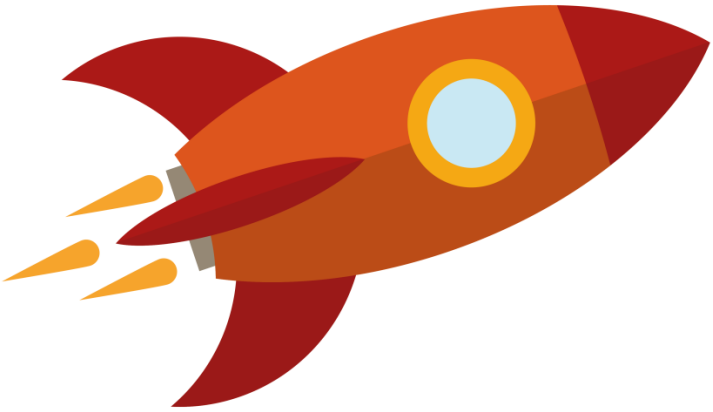

Figure 1: Basic rocket ship design. The rocket ship is propelled with three thrusters and features a single viewing window. The nose cone is detachable upon impact.

The caption can also be used to explain any acronyms used in the figure, as well as providing information on scale bar sizes or other information that cannot be included in the figure itself. Plots that show error bars should include in the caption a description of how the error was calculated and the sample size (see Figure 2).

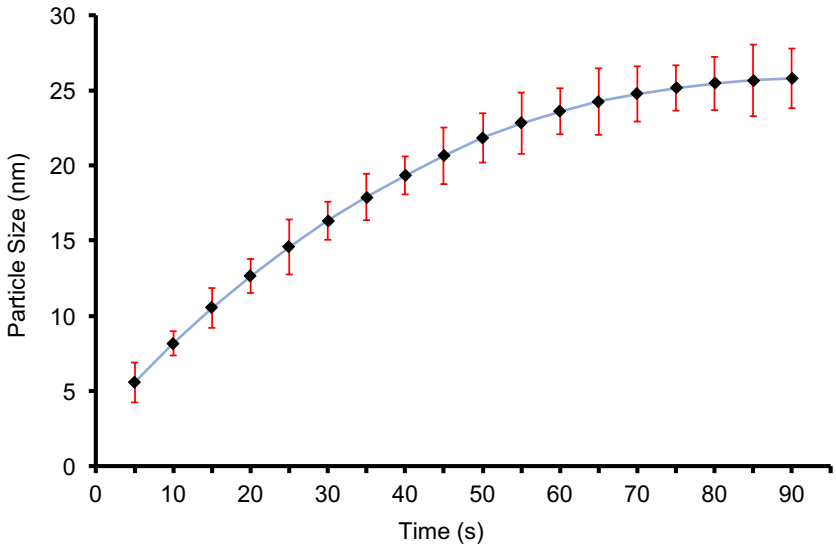

Figure 2: Plot of nanoparticle size with respect to time, recorded over a 90 s period. The error bars represent the standard deviation of measurements for 20 particles in five separate sample runs (n = 100).

If a figure consists of multiple panels, they should be ordered logically and labelled with lower case roman letters (i.e., a, b, c, etc.). If it is necessary to mark individual features within a panel (e.g., in Figure 3a), this may be done with lowercase Roman numerals, i, ii, iii, iv, etc. All labels should be explained in the caption. Panels should not be contained within boxes unless strictly necessary.

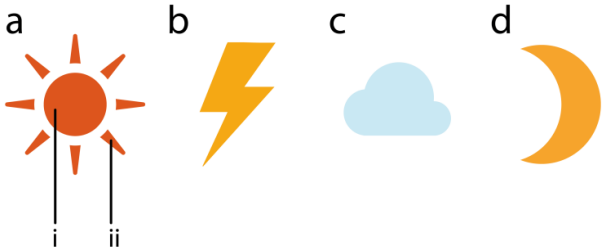

Figure 3: Representations of some common weather symbols. (a) The sun with (i) core, and (ii) rays. (b) Thunder bolt. (c) Cloud. (d) Moon.

Upon acceptance, authors will be asked to provide the figures as separate electronic files. At that stage, figures should be supplied in either vector art formats (Illustrator, EPS, WMF, FreeHand, CorelDraw, PowerPoint, Excel, etc.) or bitmap formats (Photoshop, TIFF, GIF, JPEG, etc.). Bitmap images should be of at least 300 dpi resolution, unless due to the limited resolution of a scientific instrument. If a bitmap image has labels, the image and labels should be embedded in separate layers.

Advice on Tables

Every table must have a descriptive title and, if numerical measurements are given, the units should be included in the column heading. Vertical rules should not be used (see Table 1). Tables should be cited consecutively in the text.

Table 1: Temperature and wildlife count in the three areas covered by the study.

Location	T [° C]	Turtles	Sharks	Octopuses	Starfish
Blue Lagoon	21.2	5	3	4	543
Regent's Canal	5.2	8	0	24	312
Shark Bay	12.8	4	7	9	122

Conclusions

The Conclusions section should clearly explain the main findings and implications of the work, highlighting its importance and relevance.

Data Availability

A data availability statement is compulsory for research articles and clinical trials. Here, authors must describe how readers can access the data underlying the findings of the study, giving links to online repositories and providing deposition codes where applicable. For more information on how to compose a data availability statement, including template examples, please visit: https://www.hindawi.com/research.data/#statement.

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This section is compulsory. A competing interest exists when professional judgment concerning the validity of research is influenced by a secondary interest, such as financial gain. We require that our authors reveal any possible conflict of interest in their submitted manuscripts. If there is no conflict of interest, authors should state that "The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper."

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Authors should state how the research and publication of their article was funded, by naming financially supporting bodies followed by any associated grant numbers in square brackets.

Acknowledgments

An Acknowledgements section is optional and may recognise those individuals who provided help during the research and preparation of the manuscript.

Supplementary Materials

If Supplementary Materials are provided (e.g., audio files, video clips or datasets) they should be described here. Note that authors are responsible for providing the final Supplementary Materials files that will be published along with the article, which are not modified by our production team. You should remember to reference the Supplementary Materials' contents at appropriate points within the manuscript. We recommend citing specific items, rather than referring to the Supplementary Materials in general, for example: "See Figures S1-S10 in the Supplementary Material for comprehensive image analysis."

References

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[22] Author initials and surname, "Title in sentence style," Journal title, vol. (volume number), no. (issue number), pp. (page numbers separated by an en-dash), Year.

For example:

[1] J. D. Watson and F. H. C. Crick, "A structure for deoxyribose nucleic acid," *Nature*, vol. 171, no. 4356, pp. 737–738, 1953.

For articles with six or more authors, the first three authors are listed followed by 'et al.'. When journals use only article numbers, no page numbers are necessary. For example:

[2] B. P. Abbott, R. Abbott, T. D. Abbott et al., "Observation of Gravitational Waves from a Binary Black Hole Merger," *Physical Review Letters*, vol. 116, no. 6, Article ID 061102, 2016.