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Natural Anxiolithics and Antidepressants in the Treatment of Irritable Bowel Syndrome

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Abstract

The aim this study was to assess how much could modulation of neural reactivity by natural herbal anxiolithics and antidpressants interfere with pathological nociception and subsequent life's quality of these patients. Material and Methds: 15 patients 7 men and 8 women, age between 35-80 years, diagnosed with IBS and treated with trimebutine with no satisfactory control of symptoms undertook this trial after obtaining of informal consent.Patients were treated with usual same dosage trimebutine plus mebeverine and a mixture of natural anxiolithics and antidepressants as herbal extracts such as: Withania Somnifera 125 mg,Centella Asiatica 100 mg, Valeriana Valichii 50 mg,Hypericum Perforatum, 25 mg, by oral administration 2x1 capsules/day, for 3 months. Global wellbeing and pain scores have ben assessed(Mc Gill part A and B quesionnary from 0 - 10 points), before and after 3 months of treatment. Reults: Previous treatment assessmnent of the global scoring was=6,67±0,62 and abdominal pain score was=4,33±0,82.After 3 months of treatment reassessment of scoring found these new data: global scoring was improving =7,33±0,62(p=0,0069,statistic signifficant) and abdominal pain score=3,80±0,77(p=0,0787, no statistic signifficance improvement). Conclusions: Natural mixture of anxiolithics and antidepressants was very efficient on improving quality of life and wellbeing status but not so much with respect to abdominal pain in patients with IBS.These data suggests that these kind of remedies act mostly as modulators on central processing of information and less on the local nociception per se.

Keywords: irritable bowel syndrome , natural herbal reactivity modulation

1. Introduction

Irritable bowel syndrome (IBS), is a functional intestinal disorder often seen in current medical practice, being characterized by abdominal recurrent pain associated to bowel habit disturbances and other various complaints affecting the life's quality of these patients.

Due to the complexity of the underlying pathogenic pathways resulting in pain and other forms of disconfort, till now no specific treatment is yet available.

A lot of studies tried to undestand what are the mechanisms responsible for the pain in patients with IBS.Some scientists claimed that chronic pain is a" disease" and that the underlying mechanisms of pain in IBS patients may be similar to those of fibromyalgia, regardless of whether pain is present throughout the body or localized to a specific area, being likely more as a product of central nervous system dysfunction [1,2].

Experimental pain testing studies in fibromyalgia and IBS revealed that pain thresholds correlated with distress, expectancy, and hypervigilance [3,4]. Other studies using sophisticated experimental paradigms demonstrated that: (1) unlike tender-point and dolorimetry exams, the random measures of pressure pain threshold were not influenced by levels of distress of the individual; (2) patients were much more sensitive to pressure, even when these more sophisticated paradigms were used; (3)

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patients were not more "expectant" or "hypervigilant" than controls [5];

In addition to heightened sensitivity to pressure, individuals with IBS also display decreased somatic thresholds to heat, cold, electrical, and sensory information other than somatic stimuli, such as auditory tones that might represent biological amplification of all sensory stimuli [6].

Besides the common observance of diffuse hyperalgesia/allodynia, attenuated activity of descending analgesic pathways may contribute to pain sensitivity. and appears to be one of the mechanisms of central pain augmentation and may eventually serve to help characterize subgroups of patients who might be differentially responsive to various treatment modalities.

In this view diagnosis, evaluation, and effective management of individuals with chronic pain is a complex and often difficult process so that the appropriate pharmacologic, procedural, and psychological therapies can be administered [7]. The treatment strategies for IBS are more effective at treating motility than pain.

2. Materials and Method

15 Patients, 7 men (46,66%) and 8 women (53,33%), age between 35-80 years, mean age= diagnosed with IBS, 11 (73,33%) with IBS-C (constipation) dominant form, 2 with IBS-D (diarrhea) (18,18%) and 1 (6,6%) with IBS-M (mixture of diarrhea/constipation), according to ROME III crietria, previously treated with trimebutine at standard dose: 3x100mg/day, 30 minutes before meals and mebeverine2x200mg/day with no satisfactory control of symptoms, undertook this trial after obtaining of each patient informal consent.

Beside the usual treatment with trimebutine and mebeverine at the same level of dosage patients received additionally a mixture of natural anxiolithics and antidepressants, as herbal extracts such as: Withania Somnifera 125 mg,Centella Asiatica 100 mg, Valeriana Valichii 50 mg,Hypericum Perforatum, 25 mg, by oral administration 2x1 capsules/day, for 3 months.

Global wellbeing and abdominal pain scores have been assessed, asking patients to answer as accurate as possible , after a clear explanation of the meaning of scoring points ,if necessary giving assistance with the questionnaire completing (Mc Gill part A and B quesionnary from 0 - 10 points), as showed below, before and after 3 months of treatment.

3. Results and Discussion

General data of patients with IBS included in this study are depicted in Table 1.

Previous treatment assessmnent of the global scoring was=6,67±0,62 and abdominal pain score was=4,33±0,82.

After 3 months of treatment reassessment of scoring found these new data: global scoring was improving =7,33±0,62 and also abdominal pain score=3,80±0,77.

Statistical analyze of data showed that between the two groups of global scoring , before and after treatment p=0,0069, respective very statistic signifficant.

The other group regarding the abdominal pain before and after therapy p=0,0787, that means no statistic signifficance improvement.No side effects were reported.

PART A

Considering all parts of your life: physical, spiritual, emotional in the past few days, the quality of your life have been:

Very bad 0 1 2 3 4 5 6 7 8 9 10 Excellent

PART B

Over the past days one troublesome symptom was……..(write the symptom)

No problem 0 1 2 3 4 5 6 7 8 9 10 Tremendous problem

Figure 1. Mc Gill questionnaire part A and B [8]

Table 1. General data of patients with IBS

Current number	Age	Gender	Clinical form	Scoring before treatment		Scoring after treatment	
				GS	PS	GS	PS
1	49	M	IBS-C	7	5	8	5
2	53	M	IBS -C	8	4	8	3
3	53	F	IBS -C	7	4	7	4
4	55	M	IBS -D	6	5	7	4
5	62	M	IBS -C	7	4	7	4
6	72	M	IBS -C	7	3	8	3
7	74	F	IBS -C	6	3	7	2
8	76	F	IBS -C	7	4	7	4
9	35	M	IBS -C	6	4	7	4
10	50	F	IBS -D	6	5	7	4
11	42	F	IBS -D	6	5	6	4
12	80	F	IBS -M	7	6	8	5
13	61	M	IBS -C	7	5	8	4
14	80	F	IBS -C	6	4	7	3
15	65	F	IBS -C	7	4	8	4

M= male, F=female, IBS-C=constipation, IBS-D=diarrhea, IBS-M =mixed pattern, GS=global scoring, PS= pain scoring

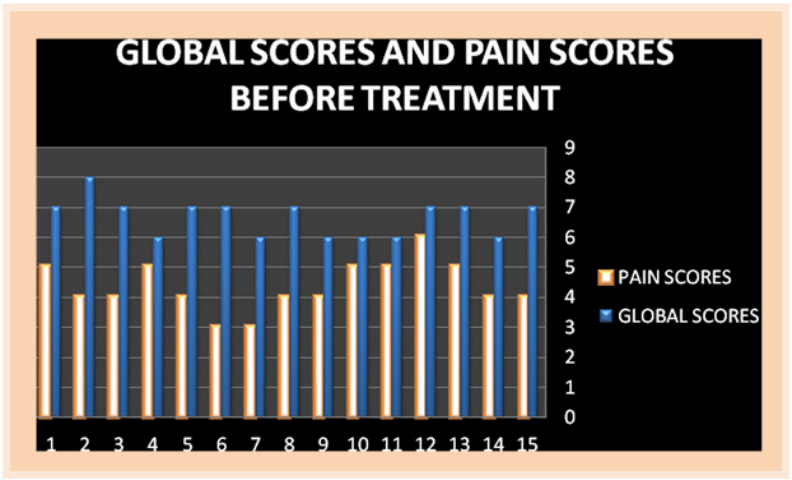

Figure 1. Global wellbeing and pain scores before treatment

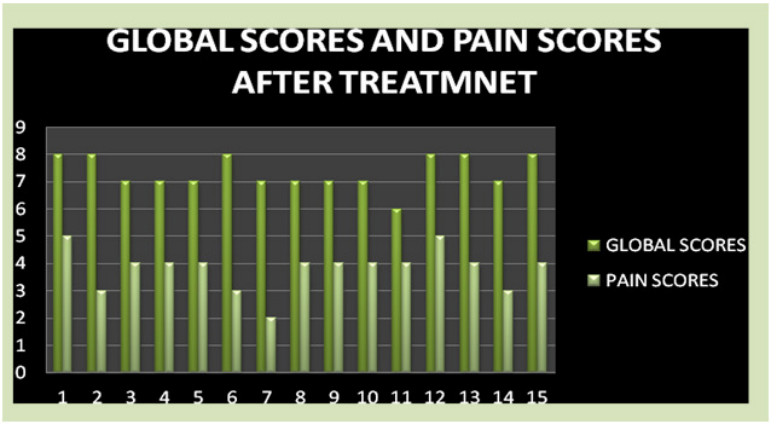

Figure 2. Global wellbeing and pain scores after treatment

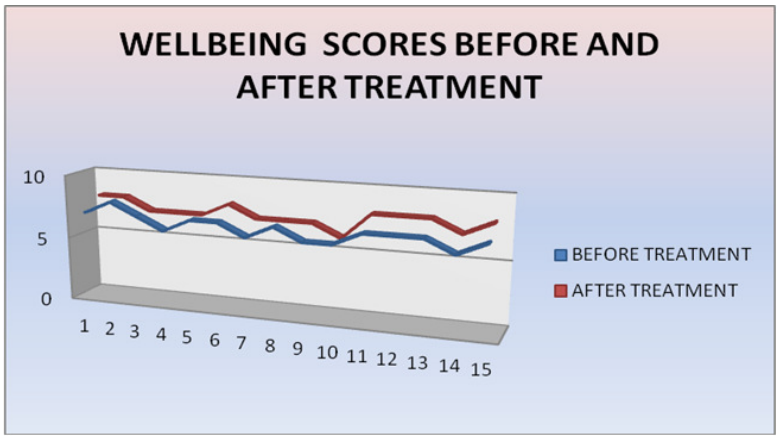

Figure 3. Wellbeing scores before and after treatment

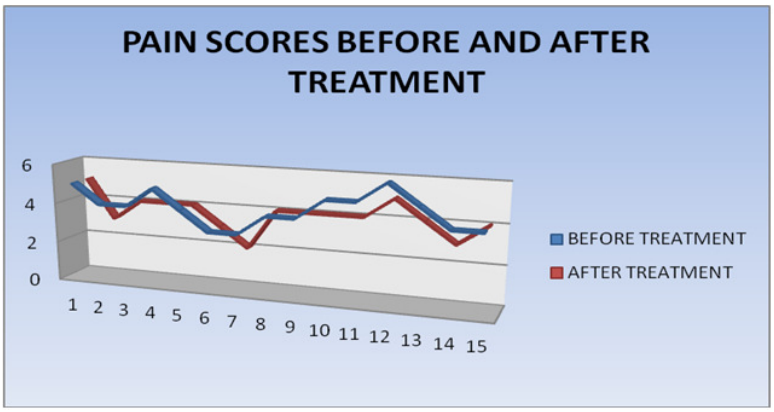

Figure 4. Pain scores before and after treatment

Treatment of patients with IBS is often challenging requiring a multimodal approach, but none of them is so far the 'magic" formula. As general guideline in the management of IBS very important is patient –doctor relationship with recognizing stressors or other inciting factors[9], as much as diet, for up to 65% of patients report that their IBS symptoms are triggered by food; however, studies to support the relationship between diet, specifically, food allergies or food intolerances, and IBS symptoms are limited [10].

Treatment based on predominant symptoms relief is another large possibility of treatment as seen in Table 2, with various results, many with no clear evidence for IBS.

Treatment against pain in IBS with tricyclic antidepressants (TCAs) - a class of antidepressants that function by inhibiting the reuptake of the neurotransmitters norepinephrine and serotonin, but also have varying degrees of anticholinergic and antihistamine receptor activity may help reduce pain. This kind of action was assessed in a brain imaging study by Morgan and colleagues [12,13]. Selective serotonin-reuptake inhibitors (SSRIs) are another class of medication to fight pain in IBS patients [14]. Recent studies demonstrate some results with anticonvulsivants as pain killers in these patients [15,16].

Other possibilities of treatment are nonpharmacological treatments as cognitive behavioral therapy (CBT),a form of psychotherapy based on cognitions, assumptions, beliefs and behaviors that identifies maladaptive thoughts and beliefs and replaces them with more realistic and self-helping alternatives [17,18].

Complementary and alternative medicine (CAM) provide patients with acupuncture alone or associated to other therapies.

Not many studies are dedicated to assess how much we can rely on herbal therapy in IBS. A Cochrane systematic review of herbal medicine treatment was recently conducted to evaluate its effectiveness in treatment of IBS. The study consisted of 75 randomized clinical trials, including 7957 participants with IBS. The study concluded that herbal medicines might be effective in improving the symptoms of IBS; however, future high-quality studies are needed [19].

Table 2 Treatment based on patient symptoms

Drug class	Generic name	Dose	Evidence for IBS
Bulking agent	Psyllium Methylcellulose Polycarbophil	1–3 tbsp q.d. 1–3 tbsp q.d. 2–4 tablets q.d.	– – –
5-HT_4 agonist	Tegaserod*#	6 mg b.i.d.	‡
Osmotic laxative	Lactulose Milk of magnesia Polyethylene glycol	1–2 tbsp q.d.–b.i.d. 1–2 tspn q.d.–b.i.d. 17 g in 8 oz fluid	– – –
Stimulant laxative	Cascara sagrada Senna	325 mg or 1 tspn qhs 187 mg tablets; 1–2 tablets qhs	– –
Prostone (type-2 chloride-channel activator)	Lubiprostone*	8 µg b.i.d.	‡
Antidiarrheal	Loperamide	1–2 tablets q.d.–q.i.d.¶	–
5-HT_3 antagonist	Alosetron*	0.5 mg to 1 mg q.d.–b.i.d.	‡
Antibiotic	Rifaximin	400 mg t.i.d.	‡
Antispasmodic	Hyoscyamine + scopolamine + atropine + phenobarbital Hyoscyamine sulfate	1–2 tablets t.i.d.–q.i.d. 0.125 mg q.i.d. prn, 0.375 mg b.i.d.	§ –
Tricyclic antidepressant	Amitriptyline Desipramine Nortriptyline	10–150 mg qhs 10–150 mg qhs 10–150 mg qhs	‡ ‡ –
SSRI	Fluoxetine Paroxetine Citalopram	10–40 mg q.d. 20–50 mg q.d. 20–40 mg q.d.	‡ ‡ ‡
SNRI	Duloxetine	30 mg b.i.d.	–
Probiotic	*Bifidobacterium infantis* VSL#3®	1 tablet q.d. 1 packet b.i.d.	‡ ‡

5-HT: 5-hydroxytryptamine; a.c.: Before meals; b.i.d.: Twice daily; IBS: Irritable bowel syndrome; prn: Whenever necessary; q.d.: Daily; qhs: At night; q.i.d.: Four-times daily; SNRI: Serotonin–norepinephrine-reuptake inhibitor; SSRI: Selective serotonin-reuptake inhibitor; tbsp: Tablespoon; t.i.d.: Three-times daily; tspn: Teaspoon [11].

Present study suggested that associated herbal therapy acting as agents that regulate general reactivity had good results by improving wellbeing state and subsequently the life quality of patients with IBS.

Abdominal pain had also better scores after receiving this therapy but not in the range of statistic significance. It is very possible that response regarding abdominal nociception to be more related to dose range.

Further study could use bigger dosage with careful taking account of the safety profile of this product.
It is obvious that there are many doors that should be opened in the next years in order to find out a better treatment for IBS patients. One of them could be herbal therapy but there are many formula that we should consider either of particular association of substances or specific dosage.

4. Conclusion

The natural herbal mixture of anxiolithics and antidepressants used in this study was very efficient on improving quality of life and global wellbeing patients status.

With respect to abdominal disconfort, response of the patients with IBS to this specific association of remedies was slightly efficient but statistically insignificant, possibly dose related.

Our data suggest that these substances prescribed at this dosage act mostly as modulators on central processing of information and less on the local nociception, making them very usefull, at least as adjuvant therapies.

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