CHRONIC PELVIC COMPLAINTS IN FEMALES WITH IRRITABLE BOWEL SYNDROME: ANOTHER BURDEN TO DEAL WITH

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Abstract

Introduction: Pain is ubiquitariur in patients with irritable bowel syndrome (IBS) being associated with diminished quality of life.

Aim: comparing effectiveness of gabapentin high dose versus gabapentin half dose plus probiotics and dimeticone in mitigating the pelvic complaints in female patients with IBS.

Methods: Open label random clinical study of 30 female patients, mean age = 38,76±15,51 years, diagnosed with predominant constipation IBS, according to Rome III criteria, suffering from chronic pelvic complaints were enrolled after ruling out other causes of pelvic symptoms. Intensity of dyspareunia, cystalgia, urinary urge were scored according to Likert scale from 0 = no symptoms to 6 = very severe. Patients were randomly devised in 2 groups, each of 15 patients. First group received gabapentinum in dose of 1200 mg/day, the second group received Gabapentin 600mg/day associated with probiotics (1 billion strains/ capsule Lactobacillus acidophilus 50% and Bifidobacterium bifidus 50% ).3 capsules/day plus dimeticone 80 mg, 3x2 chewing pills/day for 3 months.

Results: First group had the following scoring : prior therapy dyspareunia =2,93±0,88, cystalgia =3±1,31, urinary urge =2,58±1,25; after therapy: dyspareunia= 2,20±0,77 (p=0,0022),cystalgia =2,2±0,86 (p=0,058),urinary urge =2,07±0,73 (p=0,26).Second group had the following scoring prior therapy: dyspareunia =3,13±1,06, cystalgia =2,73±1,16.urinary urge =1,87±1,13; after treatment: dyspareunia =1,6±0,63 (p<0,0001), cystalgia =1,40±0,50 (p=0,0003), urinary urge =0,66±0,61 (p=0,0011).

Conclusions: Gabapentin in high dose monotherapy was significantly efficient only for mitigating dyspareunia. Association with probiotics and dimeticone to gabapentin half doses resulted in an increased response and all the assessed complaints were significantly alleviated.
Keywords: Chronic pelvic complaints, IBS, gabapentin, probiotics, dimeticone

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology, very often seen in modern and active women [Chang, 2002].

Pain, either abdominal or extra-abdominal, is ubiquitariun in patients with IBS and in many cases associated to diminished quality of life. It was traditionally explained, by theories regarding pathophysiology, as a three part complex: altered GI motility, visceral hyperalgesia, and/or the abnormal processing of information by the central nervous system (CNS) [Camilleri, 2002].

Altered GI motility includes distinct aberrations in small and large bowel motility and is probably associated to a generalized smooth muscle hyperresponsiveness. Visceral hyperalgesia characterizes IBS secondary to an enhanced perception of normal motility and rectosigmoid balloon inflation produces more pain at lower volumes in patients than in controls.

Sensitization of the intestinal afferent nociceptive pathways, that synapse in the dorsal horn of the spinal cord, could provide a unifying mechanism for abdominal pain.

It is by now well known that IBS is characterized not only by digestive issues but also by a lot of other complaints of great diversity, like: fibromyalgia, chronic fatigue syndrome, temporomandibular joint disorder and chronic pelvic pain (CPP). The overlap of gynecologic conditions and IBS was noted in a study in which patients in a gynecologist's office had, in 50% of cases, symptoms compatible with diagnosis of IBS. CPP as a chronic condition, defined as pelvic pain of at least 6 months duration is estimated to affect approximately 15% of women and may be related, at least in part, to visceral hypersensitivity and is thought to involve multiple systems including the neurologic, musculoskeletal, and endocrine systems [Gunter, 2003]. Despite a lot of research IBS remains a poorly understood condition and yet treatments of IBS are very heterogenous, none of them being quite satisfactory.

Much more difficult is the situation with IBS patients having concurrent conditions like CPP. A comprehensive treatment plan for women who have multiple concurrent conditions such as CPP and IBS has not yet been developed and tested.
Objectives

The aim of this study was comparing efficiency of gabapentin alone, high dose versus gabapentin half dose plus probiotics and dimeticone in mitigating the pelvic complaints in IBS patients, based on the observation that gabapentin was reported useful in the treatment of fibromyalgia, condition very often associated with IBS, which has many common pathophysiologic pathways of pain. The rationale of including probiotics and dimeticone to therapy schedule was based on the fact that one of the major factor triggering the pelvic pain process in IBS is distension of the colon.

Patients and methods

Study design: open label, random clinical study. 30 female patients, mean age= 38,76±15,51 years, diagnosed with IBS predominant constipation form, according to Rome III criteria [Spiller,2010] and suffering from chronic pelvic complaints were enrolled in this study after ruling out other causes of pelvic pain. An accurate disease history was taken, each patient being thoroughly examined. The intensities of every symptom were scored by using a 7-graded Likert-like scale from 0 = no symptoms to 6 = very severe symptom, according to Gastrointestinal Symptom Rating Scale (GSRS), considering that this one is more accurate and reliable than the previously 5 graded scale [Junghard,1998]. The following symptoms were assessed prior and after 3 months of treatment: dyspareunia, cystalgia and urinary urge.

Patients undertook biochemical tests (blood, urine, stool), bacteriological examination of urine and stools, parasitological stool exams, colonoscopy, abdominal and pelvic ultrasound with concurrent transvaginal examination, interdisciplinary consultations: gynecological and urological ones, in order to rule out other conditions and causes of their symptoms.

Patients were randomly devised in 2 groups, each of 15 patients. First group received gabapentin in gradually increasing amount up to the dose of 1200mg/day, the second group received 2x300mg/day of gabapentin associated with probiotics (1 billion strains/ capsule Lactobacillus acidophilus 50% and Bifidobacterium bifidus 50%), 3 capsules/day plus dimeticone 80 mg, 3x2 chewing pills/day for 3 months long.

The study was approved by the local ethical comitee and patients provided written informed consent.

Statistical analysis was made using GraphPad software with the panel for continuous data, with calculation of mean values and standard deviation, unpaired t test, p values with CI= 95%.
Results

Our patients baseline clinical data, depicted in table I, showed no statistically significant difference between the two groups of patients.

<table>
<thead>
<tr>
<th>Baseline clinical data</th>
<th>First group</th>
<th>Second group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb(11.7-16.1g/dl)</td>
<td>12.19±0.43</td>
<td>12.29±0.40</td>
<td>P=0.48</td>
</tr>
<tr>
<td>RBC(3.8-5.2x1000,000/microL)</td>
<td>4.16±0.21</td>
<td>4.10±0.22</td>
<td>P=0.44</td>
</tr>
<tr>
<td>WBC(4-10x1000/microL)</td>
<td>4.84±0.52</td>
<td>4.81±0.62</td>
<td>P=0.87</td>
</tr>
<tr>
<td>CRP(&lt;0.5/dl)</td>
<td>0.20±0.08</td>
<td>0.23±0.07</td>
<td>P=0.36</td>
</tr>
<tr>
<td>ALAT(&lt;31U/L)</td>
<td>24.27±4.37</td>
<td>23.33±3.15</td>
<td>P=0.50</td>
</tr>
<tr>
<td>Creatininemia(0.5-0.9 mg/dl)</td>
<td>0.74±0.10</td>
<td>0.72±0.77</td>
<td>P=0.43</td>
</tr>
<tr>
<td>Fasting blood sugar level(60-99 mg/dl)</td>
<td>77.32±8.11</td>
<td>76.40±7.62</td>
<td>P=0.80</td>
</tr>
<tr>
<td>Urine bacteriology(&lt;1000 CFU/mL)</td>
<td>&lt;1000</td>
<td>&lt;1000</td>
<td>-</td>
</tr>
<tr>
<td>Stool exams parasitology and bacteriology</td>
<td>Negative</td>
<td>Negative</td>
<td>-</td>
</tr>
</tbody>
</table>

Legend: Hb= hemoglobin, RBC = red blood count, WBC = white blood count, ALAT = alanin-aminotranspherase, CRP = C reactive protein, CFU= colonies forming units

As seen in table II and figure 1, the first group that was treated with gabapentin alone, high dose, had a statistically significant difference of scoring only for dyspareunia (p=0.0022).The other two symptoms, respectively cystalgia and urinary urge didn’t show any statistically significant difference of scoring after this treatment (p=0.056 and p=0.26).

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Prior therapy scoring</th>
<th>After therapy scoring</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td>Dyspareunia</td>
<td>2.93±0.88</td>
<td>2.20±0.77</td>
<td>(p=0.0022)</td>
</tr>
<tr>
<td>Cystalgia</td>
<td>3±1.31</td>
<td>2.2±0.86</td>
<td>(p=0.058)</td>
</tr>
<tr>
<td>Urinary urge</td>
<td>2.58±1.25</td>
<td>2.07±0.73</td>
<td>(p=0.26)</td>
</tr>
</tbody>
</table>

Figure 1. First group treated with gabapentinum alone, therapy results
Results recorded from the second group of patients, those that have associated probiotics and dimeticone to gabapentin half dose, are depicted in the table III and figure 2, showing a much better outcome, with statistically significant difference of scoring for all the symptoms that have been assessed:

<table>
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</table>

Figure 2. Results in second group treated with associated probiotics and dimeticone

Discussions

Fighting pain in IBS is not such an easy task due to the complexity of involved pathogenic pathways.

It is well described that people with IBS report worse quality of life, compared with the general public and with those with chronic disease conditions, such as lung disease, heart failure and diabetes, fibromyalgia, chronic fatigue syndrome [Gralnek,2000].

While altered bowel habits and pain may be the major factors that affect daily functioning, lifestyle, and hence quality of life, other factors associated with IBS may also affect quality of life, especially in women.

Pelvic floor disorders, such as pelvic organ prolapse, urinary urgency and incontinence,[Monga 1997, Jelovsek, 2005] and sexual dysfunction[Guthrie 1987,Fass,1998] have been associated with IBS in women and can all influence overall quality of life.

Several studies have described that women with IBS have a higher likelihood of a co-diagnosis of other somatic conditions.

One study found that women with interstitial cystitis or painful bladder syndrome had a greater likelihood of an antecedent diagnosis of fibromyalgia, chronic fatigue syndrome and IBS.[Warren, 2009]
A systematic review of the comorbidities associated with IBS described a high prevalence of somatic syndromes such as fibromyalgia (33%), chronic pelvic pain (50%), dysuria (50%) and interstitial cystitis (30%). It is not clear whether these other diagnoses were initially misdiagnoses or whether these conditions coexist, but it is suggested that there is a subgroup of IBS patients who have these other coexisting somatic disorders and often have higher levels of anxiety or depression. Whether these disorders are related because of underlying psychological factors or a common pathophysiological mechanism remains unknown. [Riedl, 2008, Mikocka-Walus, 2008, Wang, 2010]

Other studies observed the relationship between bladder and bowel function. There is a clear statement of a “complex physiology of urologic and gastrointestinal function”, practically an interrelation, which “has implications for the management of disorders affecting both organ systems”. This complexity is based on the convergence of dorsal root ganglia neurons, “receiving sensory input from multiple pelvic organs, that have been identified in the colon, bladder and reproductive organs”. It’s about a process of “cross-sensitization, or 'crosstalk', between neural pathways in the pelvic organs, necessary for the routine mediation of bladder, bowel and sexual function” which also mediates some functional changes in pelvic organs close related to dysfunctions of others located in proximity. Consequently, crosstalk between the bladder and bowel may play a role in pelvic disorders, including chronic pelvic pain syndromes and overactive bladder symptoms [Kaplan, 2013]. In fact there is still a lot of overlap among pelvic pain conditions " [Heitkemper, 2005]

The notion of dysfunction of central nervous system may be present in IBS is supported by studies using both PET and functional MRI. The perception of acute rectal stimulation is associated with anterior cingulate cortex activation in controls while patients with IBS showed an aberrant brain activation pattern both during noxious rectal stimulation and in anticipation of rectal pain [Silverman, 1997]. Gender-related differences in brain activation patterns in response to colonic distention have also been noted [Naliboff, 2003].

Taking all these neurological tribulations into account we considered that the treatment with gabapentin currently used for controlling pain in various conditions including fibromyalgia seemed quite reasonable. In this view, with pain in IBS having many different pathways, treatment with Gabapentin may interfere one or more of them [Moore, 2011].

The "visceral hyperalgesia" may explain the role of specific dietary substances in IBS symptoms, like sorbitol, fructose, and lactose intolerance, associated with increased gas production that may subsequently trigger abdominal discomfort secondary to bowel lumen distention. Therefore
treatment with probiotics and gas absorbent are currently used in IBS in order to relief some abdominal complaints: cramps, bloating, flatulence [Wilhelm,2008], but there are not consistent available data about their efficiency in the management of pelvic floor syndrome symptoms.

From currently available data we’ve found, there is no record neither of another study using gabapentin alone, in CPP, nor in association with probiotics and dimeticone.

Our experience showed a consistent therapeutical response in the second group of patients, regarding all symptoms assessed.

However, we should also consider the fact that all patients that joined this study had only mild to moderate severity symptoms.

Further observation should be taken in larger cohorts of patients with more severe complaints.

Conclusion

This study revealed that despite high dose, gabapentin as single therapy had a significant response only in mitigating dyspareunia.

Gabapentin in lower doses, but associated with probiotics and dimeticone resulted in a satisfactory response for all the assessed complaints, which were significantly alleviated.

References:


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Silverman DH, Munakata JA, Ennes H, Mandelkern MA, Hoh CK, Mayer EA. Regional cerebral activity in normal and pathological perception of visceral pain. Gastroenterology 1997;112 (1), 64-72

