The use of citalopram in Irritable Bowel Syndrome: A prospective study

İrritabl Barsak Sendromu'nda Sitalopram Kullanımı"

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Abstract

Background: Irritable Bowel Syndrome (IBS) is a commonly seen condition. Medications used in its treatment include anti-depressants and anti-spasmotics. This study aimed to examine the effect of citalopram, a selective serotonin reuptake inhibitor groupped antidepressant on IBS symptoms and depression-anxiety scores.

Materaial and Methods: 103 patients diagnosed with IBS according to the Rome 3 diagnostic criteria were included in the study. Patientswith IBS were divided into three groups:those with minimal-mild Beck Depression Score (BDS) and Beck Anxiety Score (BAS) were only given otilonium bromide 120 mg/day (group 1, n=29), those with moderate- severe scores were given otilonium bromide120 mg/day and citalopram20 mg/day (group 2, n=41) and those with moderate- severe scores were only given otilonium bromide 120 mg/day (group 3, n=33). At the end of 3 months treatment, the responses to treatment were evaluated with the IBS severity scoring system and BDS-BAS.

Results:.While a significant improvement was detected in the BDS and BAS of first and second groups ($p<0,001$), there was no improvement in the questionnaire scores ofthird group ($p>0,05$).Statistically significant improvementwas found in IBS severity score of three groups($p<0,001$), this improvement was more pronounced in the first group.There was no statistically significant difference between IBS severity score of second and third groups ($p>0,05$).

Conclusion: According to our findings, if depression and anxiety in IBS patients are not so severe, a treatment regime with only anti-spasmotics may be an appropriate choice.

Key words: Irritable Bowel Syndrome, citalopram, anxiety, depression

Özet

Amaç: İrritabl Barsak Sendromu (İBS) yaygın görülen bir durumdur. Medikal tedavisinde antidepresanlar ve antispazmotikler kullanılır. Çalışmamızda, selektif serotonin reuptake inhibitörü (SSRI) grubundan bir antidepresan olan sitalopramın, İBS semptomları ve depresyon- anksiyete skorları üzerine etkisini

araştırmayı amaçladık.

Materyal ve Metot: Çalışmaya, Roma 3 tanı kriterlerine göre İBS tanısı konan 103 hasta alındı. İBS'li hastalar, 3 gruba bölündü: 1. grupta (n=29) Beck Depresyon Skoru (BDS) ve Beck Anksiyete Skoru (BAS) minimal- hafif derecede olan hastalara, bir antispazmotik olan otilonyum bromide 120 mg/gün verildi. 2. grupta (n=41) BDS ve BAS orta- ciddi olanlara, otilonyum bromid 120 mg/gün ve sitalopram 20 mg/gün verildi. 3. grupta (n=33) ise yine BDS ve BAS orta- ciddi olanlara, sadece otilonyum bromid 120 mg/gün verildi. 3 aylık tedavinin sonunda, tedavi cevapları İBS şiddeti skorlama sistemi ve BDS- BAS ile değerlendirildi.

Bulgular: Tedavi sonunda 1. ve 2. gruplarda BDS ve BAS'larda anlamlı düzelmeler olurken ($p<0,001$), 3. grupta bu skorlarda belirgin bir düzelme saptanmadı ($p>0,05$). İBS şiddet skorlarında ise, 1. grupta daha belirgin olmak üzere, her üç grupta da istatistiksel olarak anlamlı azalmalar oldu ($p<0,001$). 2. ve 3. gruplar arasında İBS şiddet skorları açısından anlamlı farklılık saptanmadı ($p>0,05$).

Sonuç: Bulgularımıza göre, İBS'li hastalardaki depresyon ve anksiyete şiddetli değilse, bu hastaların tedavisinde tek başına antipazmotik verilmesi, uygun bir seçenek olabilir.

Anahtar kelimeler: İrritabl Barsak Sendromu, sitalopram, anksiyete, depresyon

Introduction

Irritable Bowel Syndrome (IBS) is characterized by chronic abdominal pain and changes in bowel habits, which has not been shown to be caused by other organic diseases (1,2). This definition and the close relationship of the digestive tract with emotions has caused IBS to be accepted as a functional gastroenterological disease (3,4). The physiopathology has not as yet been fully elucidated (5).

Among the factors suggested to have a role in IBS etiology are genetic, bowel infections, excessive production of bacteria in the bowel, increased cytokine response and inflammation, irregularity of serotoninergic processes and psychosocial factors (3,6,7). The role of various neurotransmitters, such as serotonin, has been examined in the pathogenesis as well as abnormalities in the autonomous nervous system (8-10).

The relationship between psychiatric disorders and IBS has been known for a long time and there continue to be studies on this subject (11). It has been reported that there is frequently an increase in major depressive disorders (MDD) and anxiety disorders in patients with IBS (12). In addition, it has been determined that IBS is often seen as an additional diagnosis in patients diagnosed with MDD (2). Despite the epidemiological evidence related to IBS and depression often being seen together, the exact nature of the relationship between them has not been able to be clarified. The comorbidity has been attempted to be explained by an increase in sympathetic factors (12,13).

Several previous studies have shown the effective use of anti-depressants in IBS treatment (14-18). There are also studies showing the benefits of anti-spasmotics as well (18,19).

This study aimed to examine the effect on IBS and depression- anxiety symptoms in patients diagnosed with IBS, of citalopram as an anti-depressant of the selective serotonin reuptake inhibitor (SSRI) group, by comparison with the anti-spasmotic otilonium bromide.

Materials and Methods:

At the beginning, the study protocol was reviewed and approved by the local ethics committee, in accordance with the ethical principles for human

investigations, as outlined by the Second Declaration of Helsinki, and written informed consent was obtained from all the patients. The local Ethics Committee approved the study protocol (01/25/2012).

This prospective study was started with 119adult patients who applied at the gastroenterology outpatient clinic consecutively and were diagnosed with IBS according to the Rome 3 diagnostic criteria (20). The patients were given the Turkish version of Beck Depression and Anxiety Rating scales at the beginning of the study and after three months (21-24). Turkish version of the both scales were made before and they are available under general public license (25). Baseline and post-treatment scores were recorded.

In the Beck Depression Scale (BDS), patients were asked 21 questions. The response to each question was scored between 0 and 3 according to the severity. According to the total score, 0-9 points was evaluated as minimal, 10-16 points as mild, 17-29 points as moderate and 30-63 points as severe depression. In the Beck Anxiety Scale (BAS), patients were asked 21 questions. The response to each question was scored between 0 and 3 according to the severity. According to the total score, 0-7 points was evaluated as minimal, 8-15 points as mild, 16-25 points as moderate and 26-63 points as severe anxiety.

Patientswith IBS were divided into three groups:Group 1 comprises of patients with minimal or mild the BDS and BAS were only given the antispasmotic (otilonium bromide 40 mg three times a day (t.i.d.)), group 2 comprises of patients with moderate or severe BDS and BAS were given both the antispasmotic and the antidepressant (otilonium bromide 40 mg t.i.d. and citalopram 20 mg/day) and group 3 comprises of patients with moderate or severe the BDS and BAS were only giventhe antispasmotic (otilonium bromide 40 mg t.i.d.). The treatment period for all groups was 3 months.

Patients with history of malignancy, diabetes mellitus, hypertension, any chronic disease, previous gastrointestinal system surgery, severe haemotological, renal, hepatic, cardiovascular or neurological disease or regular use of medication were excluded from the study. Pregnant or lactating female patients were not included in the study as well.

At the end of the 3-month treatment period, the depression and anxiety scores of the patients were again evaluated with the Beck Depression and Anxiety Scales. Baseline and after the treatment, the severity of the IBS symptoms of the patients was evaluated according to the IBS Severity Scoring System (26). In this scoring system, the maximum points were 500. Cases were classified as below 75 points in remission, 75-175 points mild, 175 -300 points moderate, and over 300 points severe.

Venous blood samples after fasting for 12 hours were collected from all subjects for biochemical analyses during the baseline evaluation only. TSH (Thyroid stimulating hormone) levels were analyzed using an electrochemiluminescence immunometric assay (ECLIA) method with a Roche Elecsys E170 immuno-analyzer (Roche Diagnostics, Burgess Hill, UK), and HbA1c by high performance liquid chromatography assay. Serum urea, creatinine, fasting blood glucose, aspartate aminotransferase, alanine aminotransferase, triglycerides, total cholesterol, and high-density and low-density lipoprotein cholesterol levels were determined using commercially available assay kits (Abbott®, Abbott Park, North Chicago, Illinois, USA) with an auto-analyzer (Abbott®, Abbott Park, North Chicago, Illinois, USA).

Statistical evaluation was made by SPSS for Windows 15.0 (Illinois, Chicago, USA) program. Independent sample t-test was used for continious

data and Chi-square test for categorical variables. Results were given as mean ± standard deviation. A value of $p<0.05$ was accepted as statistically significant.

Results:

At the end of the 3-month treatment, 16 patients didn't not come to the follow up visits therefore they were excluded from the study. The data of the remaining 103patients (60 (58.3%) female, 43 (41.7%) male) were used in this study. Group 1 comprised 29 patients with minimal or mild depression and anxiety scores. First group of patients were only given the antispasmotic (otilonium bromide 40 mg t.i.d.). Group 2 comprised 41 patients with moderate or severe depression and anxiety scores. The patients insecond group were given the antispasmotic and an SSRIantidepressant(otilonium bromide 40mg t.i.d. and citalopram 20 mg/day).Group 3 comprised 33 patients with moderate or severe depression and anxiety scores. Third group of patients were only given the antispasmotic (otilonium bromide 40 mg t.i.d.).

There were no significant differences in baseline demographic featuresamong threegroups ($p>0,05$). The patients in group 1 were 17 females and 12 males and no statistically significant difference was found in respect of gender. In group 2, the patients were 24 females and 17 males and no statistically significant difference was found.In group 3, the patients were 19 females and 14 males and no statistically significant difference was found ($p>0,05$) (table 1).

BDS and BAS were significantly higher in group 2and group 3 than in group 1 at the beginning of the study design.While there was no significant improvement in the BDS and BAS of third group after the treatment of patients,BDS and BAS were significantly decreased with the treatments in first and second groups ($p<0,001$) (Table 2).

Statistically significant improvement in IBS severity scoring was observed after 3 months of treatment in all three study groups ($p<0,001$) (table 2). Statistically significant improvement in the IBS severity scoring of group 1was greater than that of group 2($p=0,017$).There wasno significant differencebetweenIBS severity scoring of group 1 and group 3. Also, no significant difference observed between IBS severity scoring of group 2 and group 3 ($p>0,05$) (table 2).

Discussion:

The results of this study determined a reduction in depression and anxiety scores in the patients who had taken citalopram. Similarly, previous studies have reported that anti-depressants have reduced the symptoms of comorbid depression and anxiety in IBS patients (17,27).

Depending on the local effects on the gastrointestinal tract, anti-depressants may increase the motor functions of the colon (28). There is more evidence of the use of tricyclic antidepressants (TCA) than SSRI in the treatment of IBS. However, due to the tolerability profile of TCAs, they are accepted as second stage agents. When compared to SSRI, TCA have more anticholinergic and antihistaminergic side effects and a much higher potential for overdose (29). The higher rate of females to males (58.6%, 41.4%, respectively) of IBS patients in the our study conforms with findings in literature (3,30).

Although there was an improvement inthe IBS symptom severityofall threegroups, this improvement was greater in the groupwith low BAS and BDSwhich had not received citalopram. These findings conform with the results of a study by Frederich et al. Which investigated whether any effect could be seen on IBS symptoms when antidepressants were given to patients with depression. The conclusion was reached that the beneficial effects of antidepressants on IBS symptoms were limited and controversial (31). In

another placebo-controlled study published in 2010, which used a rectal barostat technique, citalopram make very little or no contribution to the improvement of IBS symptoms, which is parallel to the results of the our study (32).

In contrast to the results of the our study, J Tack et al determined a significant improvement in IBS symptoms including abdominal pain, in patients given citalopram in a placebo-controlled study[33]. That study also concluded that the therapeutic effect of citalopram was independent of the effects on anxiety, depression and colon sensorimotor function. However, in a later, similarly designed, more extensive study, citalopram was found to have made no improvement to IBS symptoms including the severity and frequency of abdominal pain[34]. In the J Tack's study, patients were given 20 mg citalopram for 3 weeks followed by a further 3 weeks of a 40 mg dose of the same medication. The differences in the results between that study and the our study may be due to the difference in the dosage of citalopram given.

Two studies which used fluoxetine as another SSRI group anti-depressant, revealed different results regarding the improvement of IBS symptoms. In a placebo-controlled study by Kuiken et al using rectal barostat measurements, fluoxetine was found no improvement in IBS symptoms and rectal sensitivity. In a study by Vahedi et al of constipation-dominant IBS, short-term use of fluoxetine was concluded to be effective in the improvement of abdominal pain and was well-tolerated by patients (35,36). When these studies using fluoxetine are evaluated together with studies using citalopram and the findings of the present study, it can be said that SSRI group medications do not show any significant differences from each other in terms of efficacy in the treatment of IBS symptoms.

In the previous 2 studies, anti-depressants were selected only for IBS patients with resistant symptoms (19,37).

Our study differs from other studies in that in the treatment of IBS, most of the previous studies using antidepressants were placebo-controlled. Whereas in this study, rather than giving a placebo, antispasmotic medication was given either alone or together with anti-depressants for the relief of IBS symptoms.

The results of this study led to the conclusion that antispasmotic treatment relieved the symptoms of IBS and this conforms with the results of another recently published study which also showed antispasmotics to be effective in the treatment of IBS (19).

In addition, a lesser improvement in IBS symptoms of the patients with high depression and anxiety scores compared to those with low scores may be due to the temperament, character and personal characteristics of the patients (38). To understand how temperament, character and personal characteristics affect the response to treatment, it would be necessary to conduct questionnaires evaluating those characteristics.

Conclusion:

It can be concluded that, according to the results of this study, a more selective path should be taken when prescribing citalopram for IBS patients if there is no psychiatric comorbidity and intestinal complaints are the priority, so that rather than giving citalopram, starting a treatment regime including antispasmotics could be a more appropriate choice.

Conflict of interest:

The authors declare no conflict of interest.

Table 1. Baseline characteristics of the study population

Parameters	Group 1 (n=29)	Group 2 (n=41)	Group 3 (n=33)	p
Age (years)	38,1±12,1	40,5±12,0	39,2±11,7	>0,05
Sex				>0,05
Male	12 (41,4%)	17 (41,5%)	14 (42,4%)	
Female	17 (58,6%)	24 (58,5%)	19 (57,6%)	
Hematocrit (%)	40,9±4,8	41,9±4,4	42,7±4,6	>0,05
Glucose (mg/dL)	107,2±7,3	97,7±4,1	102,3±4,5	>0,05
Urea (mmol/L)	28,5±8,7	26,5±9,1	27,2±11,2	>0,05
Creatinine (mg/dL)	0,7±0,1	0,6±0,1	0,7±0,2	>0,05
AST (U/L)	23,3±8,5	25,6±16,2	26,2±13,1	>0,05
ALT (U/L)	28,6±19,7	29,7±26,5	25,5±14,2	>0,05
TSH (mIU/L)	2,9±0,5	3,0±0,4	2,7±0,5	>0,05

Abbreviations: AST: aspartate aminotransferase, ALT: alanine aminotransferase, TSH: Thyroid stimulating hormone

Table 2: The effects of two treatment regimens on the clinical symptoms

	Group 1 (n=29)			Group 2 (n=41)			Group 3 (n=33)			*P**
	B	AT	*P*	B	AT	*P*	B	AT	*P*	
BDS	9,3±3,0	8,6±2,7	<0,001	36,3±7,2	24,7±9,2	<0,001	37,1±7,5	36,6±7,3	>0,05	<0,001[a] <0,001[b] <0,001[c]
BAS	9,0±2,2	8,3±2,1	<0,001	36,1±6,6	24,5±9,0	<0,001	36,7±6,8	36,1±6,9	>0,05	<0,001[a] <0,001[b] <0,001[c]
SS	324,1±90,3	172,4±114,0	<0,001	329,5±77,4	227,8±82,4	<0,001	331,2±57,8	218,4±37,7	<0,001	0,017[a] >0,05[b] >0,05[c]

P* values of comparison of groups after treatment
[a] Group 1 vs. 2, [b] Group 1 vs. 3, [c] Group 2 vs. 3

Abbreviations: BDS: Beck Depression Inventory score, BAS: Beck Anxiety Inventory score, SS: IBS Severity Scoring, B: Baseline, AT: After Treatment

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