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Mebeverine alleviates lower urinary tract symptoms in patients with irritable bowel syndrome

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ABSTRACT

Introduction: Lower urinary tract symptoms (LUTS) are common in patients suffering from irritable bowel syndrome (IBS). LUTS are categorized into storage, voiding and post-micturition symptoms. Mebeverine, a voltage-gated sodium channel blocker, can alleviate IBS symptoms via inducing smooth muscle relaxation. The effect of mebeverine on LUTS is not cleared yet. Consequently, we aimed to evaluate the effect of mebeverine on LUTS in IBS patients.

Materials and Methods: Seventy-five IBS patients were included in the present study. IBS was diagnosed according to the Rome IV criteria. International prostate symptom score (I-PSS) questionnaire was used to evaluate LUTS and quality of life in IBS patient. Patients were treated with 200 mg mebeverine per day. All patients were assessed once before the treatment and then one, three and six months after the treatment with mebeverine.

Results: The prevalence and severity of voiding symptoms were significantly higher in males than females ($P < 0.05$). One-month treatment with mebeverine reduced storage and voiding urinary symptoms in IBS patients ($P < 0.01$ and $P < 0.0001$, respectively). The beneficial effects of mebeverine increased over the time and the maximum effect were found following six-months treatment ($P < 0.0001$). Furthermore, using mebeverine in IBS patients improved the quality of life both in men and women ($P < 0.0001$).

Conclusion: Mebeverine could obviously ameliorate both gastrointestinal and urinary symptoms in IBS patients. These findings may propose that smooth muscle relaxants including mebeverine might be proper therapeutic agents for IBS patients with LUTS.

Keywords: Irritable bowel syndrome, Lower Urinary Tract Symptoms, Mebeverine, Smooth muscle

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Introduction

Irritable bowel syndrome (IBS) is a common disorder which is presented by abdominal pain and discomfort in defecation while, there is not any morphological abnormality in gastrointestinal (GI) system (1). IBS impairs patient's quality of life and is associated with increased health care costs (2, 3). The pathophysiology of IBS is not completely understood. Several mechanisms have been proposed in the pathogenesis of IBS disorder including altered brain-gut interactions, visceral hyperalgesia, perturbation of the gut microbiota, intestinal inflammation, altered sympathetic nervous activity and altered hypothalamic-pituitary-adrenal (HPA) axis responses (4).

Lower urinary tract symptoms (LUTS) are common in IBS patients and their prevalence are the same between men and women (5-7). LUTS are divided into three categories; 1. Storage symptoms which include increased micturition frequency, nocturia, urgency and urinary incontinence, 2. voiding symptoms including slow or weak stream, hesitancy, and terminal dribble, 3. post-micturition symptoms including the sensation of incomplete emptying and post-micturition dribbling (7). Presence of LUTS in accompany with IBS symptoms induces more negative impact on patient's quality of life (8).

Mebeverine is a beta-phenyletylamine derivative of reserpine, which is used to alleviate IBS symptoms (9, 10). It blocks voltage-operated sodium channels and inhibits calcium accumulation in the smooth muscle cell (11, 12). This compound induces relaxation in smooth muscle cells without atropine-like side effects in humans (11).

The effect of mebeverine on LUTS is not clear. Consequently, in the present study we aimed to investigate the effect of mebeverine on LUTS in IBS patients.

Materials and Methods

Forty-seven women (aged 16-64 years) and 28 men (aged 14-62 years) were evaluated in the present study. Before starting the project, the research protocol was described for participants and written consent was signed by them. All the patients referring to GI clinic diagnosed with IBS were included in the study. Those patients with urinary tract infection (UTI), abnormal prostate-specific antigen (PSA), ureteral stones and post-void residual urine (PVR) were excluded from the experiment. The study protocol was approved by the Ethics Committee of Ilam University of Medical Sciences (IR. MEDILAM.REC.1397.100).

The IBS was diagnosed according to the Rome IV criteria (1). The patients that suffering from recurrent abdominal pain or discomfort for more than two days in a week which presenting two or more of the followings were diagnosed as IBS; 1. Symptoms relief with defecation, 2. Symptom onset is associated with change in frequency of stool production, 3. Symptom onset is associated with change in stool consistency. International prostate symptom score (I-PSS) questionnaire was used as a tool to determine the level of LUTS and their effects on participant's quality of life. All patients received 200 mg /day mebeverine for six months. Notably, the symptoms were assessed before treatment and one, three and six months after the treatment with mebeverine.

Statistical Analysis

Chi-square test was used to compare incidence of symptoms between the groups. Nonparametric statistical tests, Friedman and Wilcoxon tests, were used to compare the symptom level between the groups. $P < 0.05$ was considered as a significant difference.

Results

Seventy-five IBS patient (47 women and 28 men) ware evaluated in the present study.

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35 women and 22 men expressed both LUTS and IBS symptoms. Table 1 shows the general characteristics of participants. Prevalence of storage symptoms was the same between the groups. However voiding symptoms was more prevalent in men than women.

Table 1. The general characteristics of the participants in the current study.

General characteristics	Male	Female	P value
Age (year)	38.82 ± 2.21	36.34 ± 1.80	0.39
(kg/m^2)	24.39 ± 0.50	26.07 ± 0.71	0.04
IBS	28	28	-
IBS + LUTS	22	22	0.40
IBS + Storage symptoms	22	35	-
IBS + Voiding symptoms	15	9	<0.0001

BMI: Body mass index. IBS: Irritable bowel syndrome. LUTS: Lower urinary tract symptoms.

Figure 1 shows the effect of mebeverine (200 mg/day) on storage urinary symptoms in IBS patients. The mean of I-PSS of the participant was 3.09 ± 0.30 before the treatment. After one, three and six-months' treatment with mebeverine, I-PSS changed to 0.95 ± 0.19, 0.60 ± 0.15 and 0.40 ± 0.13, respectively, which were significantly lower than this value before starting the treatment. What's more, six-month treatment with mebeverine induced greater reduction in the scores compared to the one-month treatment and three-month. Similarly, the I-PSS score after three-month treatment with mebeverine was significantly lower than this parameter after one-month treatment.

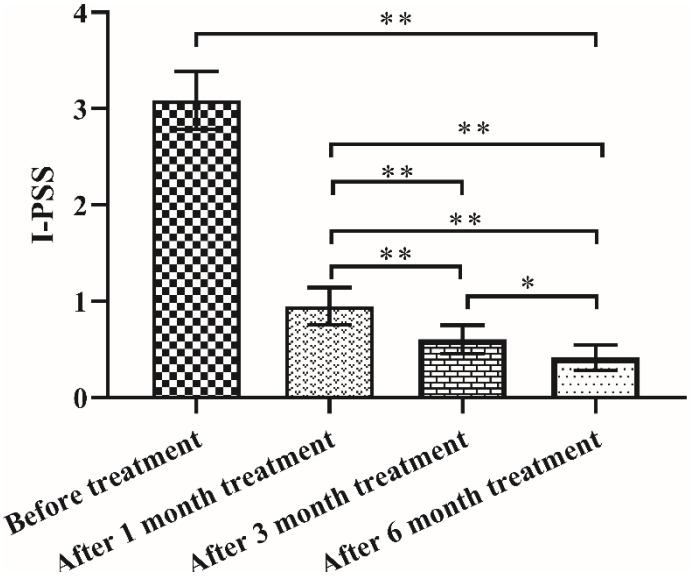


Figure 1. Effect of mebeverine (200 mg) on storage urinary symptoms in irritable bowel syndrome (IBS) patients. The graph represents Mean ± SEM in the different groups. Mebeverine administration significantly decreased international prostate symptom scores (I-PSS) in the patients. The maximum therapeutic effect was observed after six-month treatment. * and ** Indicate significant differences between the groups ($^{*}P < 0.05$ and $^{**}P < 0.0001$).

Figure 2 shows the influence of gender on mebeverine effect on storage urinary symptoms in IBS patient. There was no significant difference in storage urinary symptoms between men and women before treatment. In addition, effect of mebeverine on storage urinary symptoms was almost the same between men and women suffering from IBS disorder.

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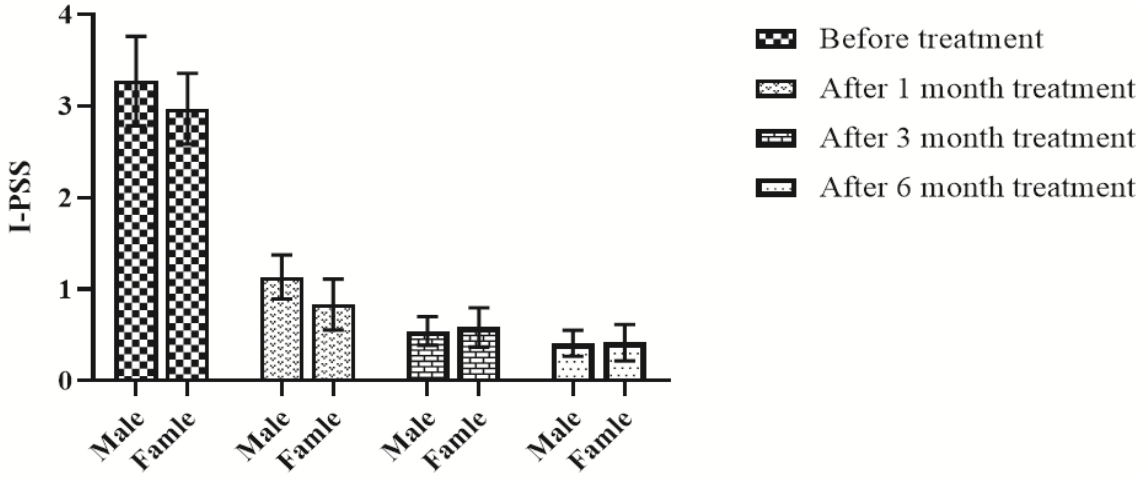


Figure 2. Influence of gender on mebeverine effect on storage urinary symptoms in symptoms in irritable bowel syndrome (IBS) patients. I-PSS: International prostate symptom score. The graph represents Mean ± SEM in the different groups. The was no significant difference in storage urinary symptoms between men and women before treatment. The effect of mebeverine on storage urinary symptoms was the same in men and women suffering IBS.

Figure 3 shows the effect of mebeverine (200 mg/day) on voiding urinary symptoms in IBS patients. The mean of I-PSS of the participants was 2.80 ± 0.36 before treatment. The scores changed to 1.33 ± 0.33, 0. 50 ± 0.17 and 0.33 ± 0.44 one, three and six-months after the treatment respectively, which were significantly lower than the score before treatment. Interestingly, three and six-months treatment with mebeverine induced more reduction in I-PSS compared to one-month treatment ($P < 0.01$, $P < 0.001$, respectively).

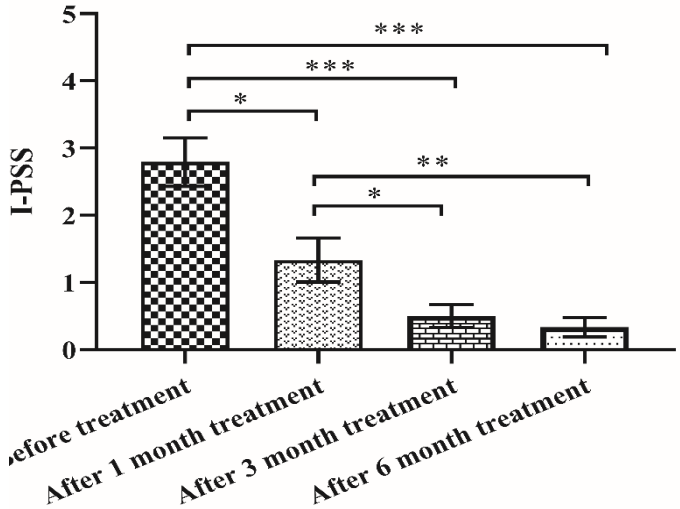


Figure 3. Effect of mebeverine (200 mg) on voiding urinary symptoms in irritable bowel syndrome (IBS) patients. The graph represents Mean ± SEM in the different groups. Mebeverine administration significantly decreased international prostate symptom scores (I-PSS) in the patients. The maximum therapeutic effect was observed after six-month treatment. *, ** and *** Indicate significant differences between the groups ($^{*}P < 0.01$, $^{**}P < 0.001$ and $^{***}P < 0.0001$).

Figure 4 shows the influence of gender on mebeverine effect on voiding urinary symptoms in IBS patient. Before treatment, voiding urinary symptoms was more severe in male than females ($P < 0.05$). Mebeverine could reduce voiding symptoms in both men and women suffering from IBS disorder. There was no significant difference in voiding symptoms between men and women after treatment with mebeverine.

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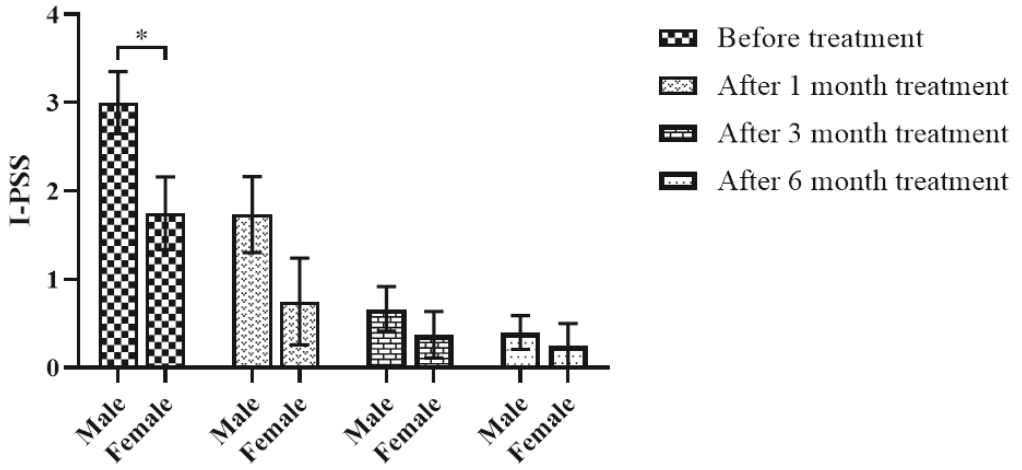


Figure 4: Influence of gender on mebeverine effect on voiding urinary symptoms in irritable bowel syndrome (IBS) patients. The graph represents Mean ± SEM in the different groups. *Indicates a significant difference between the groups ($P < 0.05$).

Figure 5 shows the effect of mebeverine (200 mg/day) on the quality of life in IBS patients suffering from LUTS. The mean of the men's score was 2.35 ± 0.35 before treatment, which decreased to 0.40 ± 0.1.8 following 6-month treatment with mebeverine ($P < 0.0001$). The mean of women's score was 1.06 ± 0.21 before treatment, which was significantly lower than men's score before treatment ($P < 0.05$). Similarly, six-month treatment with mebeverine significantly increased the quality of life in women (0.21 ± 0.11; $P < 0.0001$). There was no significant difference in quality of life between men and women after six-month treatment with mebeverine.

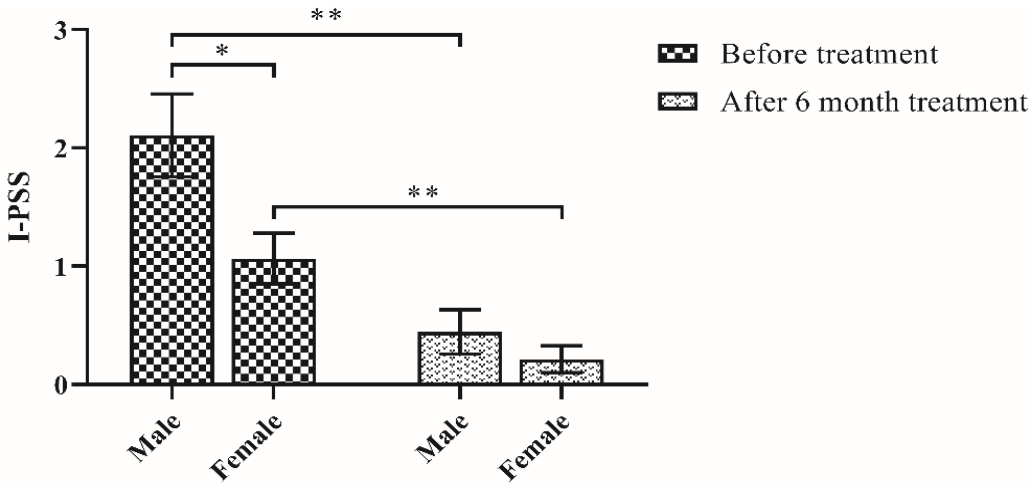


Figure 5. Effect of mebeverine (200 mg) on the quality of life in irritable bowel syndrome (IBS) patients suffering Lower urinary tract symptoms (LUTS). The graph represents Mean ± SEM in the different groups. Before treatment, international prostate symptom scores (I-PSS) were significantly higher in men than women. Six-month mebeverine administration significantly decreased the scores in the male/female patients. *and **Indicate significant differences between the groups (*$P < 0.05$, **$P < 0.0001$).

Discussion

For the first time, our results showed that mebeverine not only can alleviate gastrointestinal symptoms in IBS disorder, but also is able to relieve urinary symptoms in the patients. Moreover, it improves quality of life in both men and women.

IBS is a GI disorder manifested by abdominal pain and defecation disorder in the absence of organ abnormality (1). In addition to GI problems, IBS patients make

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complaint about LUTS which are expressed as storage, voiding and post-micturition symptoms (5-7). Prevalence and severity of storage symptoms were almost similar between male and female prior to the treatment with mebeverine, however; voiding symptoms were more prevalent and severe in men with IBS disorder than women. Compatible with our findings, previous studies have shown that prevalence of storage symptoms is the same between male and female. However, men are more susceptible to voiding symptoms than women due to anatomical differences in urinary system of men and women (14-16).

In addition, our results showed that mebeverine reduced storage and voiding urinary symptoms in IBS patients. Visceral hypersensitivity to mechanical stimulus is one of the hallmark features of IBS. This hypersensitivity causes an increased perception of bowel distension and discomfort during normal bowel activity (17). Exaggerated smooth muscle contraction is also reported in patients suffering from LUTS (18). Smooth muscle relaxants are commonly used to alleviate symptoms in patient with IBS disorder or suffering from LUTS. α_1-adrenergic blockers are the first choice of medical treatment to alleviate LUTS symptoms. These compounds induce smooth relaxation in both bladder and prostate and might relieve storage and voiding symptoms (19). Although, α_1-adrenergic receptor antagonists could decrease IBS symptoms in rat IBS model, however; there is no data regarding their effect on humans (20). Meanwhile, α_1-adrenergic receptor antagonists induce hypotension and increase the incidence of hip fracture in patient suffering from LUTS (21).

Mebeverine can decrease smooth muscle contraction without affecting normal gut motility. It inhibits voltage-gated sodium channels and prevents calcium accumulation in the smooth muscle cells (11, 12). Tolerability to mebeverine is excellent and no remarkable side-effects have been reported in IBS patients treated with mebeverine (22). It has been shown that six-weeks treatment with mebeverine can alleviate GI symptoms in patients with IBS disorder (23). Our results showed that even four-weeks treatment with mebeverine might decrease storage and voiding urinary symptoms in IBS patients. However, to get the maximum effect we need to continue the treatment for six-months.

Although, IBS has no influence on the patient's mortality rate, however; it induces negative impact on patient's quality of life. Incidence of LUTS in IBS patient make the situation even worse (10, 24). Prior to treatment, quality of life was lower in men than women which may resulted from higher severity of voiding urinary symptoms in the men in compare with the women (14, 16). Our results showed that six-months treatment with mebeverine can improve quality of life in IBS patient suffering from LUTS. Compatible with our results, four to six weeks treatment with mebeverine has increased quality of life in IBS patients (10). The improvement in quality of life may resulted from alleviation in both LUTS and GI symptoms in IBS patients.

Conclusion

Our results for the first time showed that mebeverine, a smooth muscle relaxant, can ameliorate both GI and urinary symptoms in IBS patients. This finding may propose smooth muscle relaxants as proper therapeutic agents for IBS patients with LUTS disorder.

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Disclosure

The authors have nothing to disclose.

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