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Original Article

Expression of transient receptor potential vanilloid type 1 (TRPV1) in colonic mucosa of patients with irritable bowel syndrome

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Abstract: Objective: To investigate the expression pattern of the transient potential vanilloid type 1 (TRPV1) in the colonic mucosa of patients with irritable bowel syndrome (IBS), its clinical manifestations, and possible pathways of action. Methods: This study included 80 IBS patients (IBS group) diagnosed at The Second Affiliated Hospital of Soochow University from 2013 to 2017, and 60 healthy examinees as controls (N group). All participants underwent colonoscopy and the results were normal. Colonic mucosal tissue was obtained through biopsy and paraffin sectioned for routine pathologic evaluation. Immunohistochemistry was used to detect the expression of TRPV1, and its correlation with IBS symptoms was analyzed. Results: The expression of TRPV1 in the IBS group (0.8, 0-8.4) was significantly higher than that of the control group (0.4, 0-1) (P=0.023). Spearman correlation analysis revealed a significant positive correlation between TRPV1 expression and IBS symptoms (r=0.772, P<0.001). There were no significant differences in the expression of TRPV1 among IBS patients in each subgroup (Kruskal Wallis test, P=0.938>0.050). Comparing genders, the TRPV1 expression levels in male (1.0, 0-7.2) and female (0.8, 0-8.4) IBS patients were similar (P=0.871). Similarly, no significant gender differences were observed in symptom scores between male (4.0, 2-9.5) and female (3.75, 2.0-11.5) IBS patients. Additionally, there was no significant difference in TRPV1 expression in the mucosa of the ascending and descending colon among different subgroups (P>0.050). Conclusion: TRPV1 expression in the colonic mucosa of IBS patients is elevated and positively correlated with symptom severity. However, no significant differences were found in TRPV1 expression among patients with different IBS subtypes or between genders. The expression of TRPV1 was abnormal in the mucosa of ascending and descending colon, but the difference was not statistically significant.

Keywords: Irritable bowel syndrome, colonic mucosa, transient receptor potential vanilloid type

Introduction

Capsaicin receptor, also known as Vanilloid receptor subtype 1, belongs to the transient receptor potential (TRP) ion channel protein family. It is considered the most significant member of this family and is often referred to as transient receptor potential vanilloid type 1 (TRPV1) [1, 2].

Irritable bowel syndrome (IBS) is a prevalent gastrointestinal dysfunction, characterized by abdominal pain or discomfort, accompanied by changes in bowel pattern and stool properties, without significant morphologic or biochemical abnormalities [3, 4]. IBS is classified into four subtypes: constipation-predominant (IBS-C), diarrhea-predominant (IBS-D), mixed-diarrhea-and-constipation (IBS-M), and unspecified type (IBS-U). IBS is common in developed countries and is the most frequently diagnosed disease by gastroenterologists worldwide. A 2020 meta-analysis indicated that the global prevalence of IBS is about 9.2%, according to the Rome III diagnostic criteria [5]. While IBS affects women more frequently, most female patients are diagnosed before the age of 50, with prevalence decreasing after 50 [6].

IBS significantly affects patients' quality of life, contributing to increased somatization symptoms and the development of serious psycho-

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logical problems [7]. It is a condition that not only affects patients' well-being but also consumes substantial healthcare resources. Its remains incompletely understood [8, 9]. Furthermore, diagnosing and treating IBS presents considerable challenges to clinical practice [10]. Visceral hypersensitivity, a well-established pathophysiological mechanism of IBS, may result from factors such as psychological stress, immune dysfunction, gastrointestinal secretion disorder, and infections. Visceral hypersensitivity serves as a key target for researching the pathogenesis and treatment of IBS [11].

Previous studies have indicated that TRPV1 is associated with gastrointestinal visceral hypersensitivity and the pathogenesis of IBS. This study employs immunohistochemical techniques to investigate the precise expression pattern of TRPV1 in the colonic mucosa of both healthy individuals and IBS patients. The aim is to uncover a possible link between TRPV1-distribution characteristics and IBS, and to explore the underlying pathological mechanisms, thereby offering new insight into a therapeutic strategy for IBS. Studying the expression differences of TRPV1 in IBS patients may lay the foundation for future drug intervention research.

Materials and methods

Subjects

This study was approved by the Ethics Committee of The Second Affiliated Hospital of Soochow University (approval number: JD-LK-2017-012-01). Patients from the Department of Gastroenterology at The Second Affiliated Hospital of Soochow University, who were treated between July 2013 and November 2017, were selected as study participants.

Inclusion criteria

IBS group: The IBS group included 80 patients who were diagnosed with IBS for the first time. The inclusion criteria for IBS patients were as follows: 1. Persistent abdominal pain or discomfort occurring at least 3 days per month for the past 3 months. 2. Meeting at least two of the following three additional characteristics: (1) Symptoms were relieved after defecation; (2) Symptoms occurred with changes in bowel habits; (3) The appearance of stool changed during the onset of symptoms. 3. All symptoms must have been present for at least 6 months prior to diagnosis, and the above criteria must have been met in the last 3 months. 4. Supporting characteristics for diagnosis: (1) Changes in bowel patterns (e.g., fewer than three bowel movements per week or more than three bowel movements per day); (2) Abnormal stool texture (e.g., hard balls, paste-like, or watery stools); (3) Difficulty defecating; (4) Urgent defecation, a sense of incomplete evacuation, mucous stool, or abdominal bloating. 5. Exclusion of other systemic organic diseases through endoscopy, abdominal ultrasound, barium meal of the digestive tract, X-ray examination, blood biochemical indicators, and other related auxiliary examinations.

Control group: The control group (N group) consisted of 60 healthy individuals who underwent routine physical examinations and colonoscopy. All participants in this group had no gastrointestinal symptoms and no history of diseases affecting the respiratory, circulatory, digestive, or endocrine systems. They also had no known allergies, recent medication use, or abnormal colonoscopy results.

Exclusion criteria

Participants were excluded from the study if they met any of the following criteria: 1. History of abdominal surgical trauma, intestinal vascular disease, or use of antibiotics or gastrointestinal motility drugs within the last month. 2. Organic intestinal mucosal lesions identified by colonoscopy. 3. Pregnancy. 4. Severe heart, lung, or kidney disease.

Main experimental reagents

Citrate solution, peroxidase blocking solution, phosphate buffer saline (PBS) buffer, 3,3'-etrahydrochloride (DAB), hematoxylin dye, biotin-labeled secondary antibody kit, and antigen repair solution were purchased from Suzhou Cancer-cell medical laboratory Co., LTD. (Suzhou, China). Xylene solution and alcohol were purchased from Boster Biological Technology Co., LTD. (Wuhan, China). Rabbit anti-human TRPV1 polyclonal antibody (1:200 dilution) was purchased from Sinopharm Chemical Reagent Co., LTD. (Shanghai, China).

Classification of IBS

IBS can be categorized into four types: IBS-C (constipation-predominant), IBS-D (diarrhea-predominant), IBS-M (mixed type), and IBS-U (unspecified type). For IBS-D, at least 25% of bowel movements are soft (mushy) or watery, while hard or dry stools constitute less than 25%. For IBS-C, hard or dry stools account for at least 25% of defecation, while soft (paste-like) or watery stools are less than 25%. IBS-M involves both soft and hard stools, each accounting for at least 25% of bowel movements. If stool morphology does not fit into any of these categories, it is classified as IBS-U.

Scoring criteria for gastrointestinal symptoms of IBS

Bowel discomfort assessment: The assessment covers defecation effort, sensation, urgency, and anal obstruction. The scoring system is as follows: none, 0 point; mild, 1 point; moderate, 2 points; and severe, 3 points.

Abdominal discomfort assessment: The score was based on both frequency and intensity (frequency + degree). 1. Frequency score: no symptoms, 0 point; less than once a month, 0.5 points; once a month, 1 point; three times a month, 1.5 points; once a week, 2 points; more than once a week, 2.5 points; every day, 3 points. 2 Degree score: mild pain (does not affect daily life), 1 point); moderate pain (slightly affects activity), 2 points; severe pain (limits movement), 3 points. 3. Abdominal distension degree: mild (occasional, short remission), 1 point; moderate (frequent, long duration), 2 points; severe (persistent, requiring drug remission), 3 points. 4. The final score was determined by discussing the symptoms with the patient and doctor, combining the bowel discomfort score with the abdominal pain and distention scores.

Specimen collection

Participants from both the IBS and control (N) groups followed a standardized preparation protocol: The day before the colonoscopy, participants used colon cleansing fluid for bowel preparation. On the day of the colonoscopy, participants fasted to ensure an empty stomach. A painless colonoscopy was performed by an experienced physician, starting from the anus and continuing to the ileocecal junction for a thorough intestinal examination. A sample of 0.3*0.3 cm mucosal tissue was obtained from both the ascending and descending colon using electronic enteroscopy. The samples were processed through fixation, paraffin embedding, sectioning, and staining. Two optimal sections were selected: one for use as a negative control and the other for subsequent TRPV1 testing.

Detection procedure

The S-P immunohistochemical staining technique was used to determine the location and expression of TRPV1 in the colon mucosa. The procedure followed these steps: (1) The paraffin sections were preheated in the oven, followed by dewaxing and hydration. The sections were washed three times with PBS for 3 minutes each for antigen retrieval. (2) A peroxidase inhibitor was applied to each slice and incubated at room temperature for 10 minutes to block endogenous peroxidase activity. The slides were then washed three times with PBS for 3 minutes each. (3) PBS was removed, and normal non-immune animal serum was added into each slide for 10 minutes at room temperature to block non-specific binding. (4) After removing the serum, the primary antibody was added to each slide and incubated at 4°C overnight. The slides were then washed three times with PBS for 3 minutes each. (5) PBS was removed, and a biotinylated secondary antibody was applied to the slides. The slides were incubated at room temperature for 10 minutes and then washed with PBS three times for 3 minutes each. (6) PBS was removed, and a streptavidin-peroxidase complex was added to each slide. The slides were incubated at room temperature for 10 minutes and then washed three times with PBS for 3 minutes each. (7) PBS was removed, and freshly prepared DAB solution was applied to each slide. The slides were observed under a microscope for 3 to 10 minutes to assess the staining. (8) The sections were washed with running water, counterstained with hematoxylin, and rinsed with running water to achieve blue coloration. After dehydration through graded alcohols, the slides were cleared in xylene and mounted with neutral gum. The slides were then observed under a microscope, and images were recorded.

Outcome evaluation

The staining results for TRPV1 were evaluated using the following criteria and image analysis methods:

Table 1. General information on all subjects

Group	Case (%)	Gender (%) Male/Female	Age (range, years)	Age (mean ± SD, years)
N	60 (42.9)	32 (53.3)/28 (46.7)	50 (34-69)	52 (IQR: 42-62)
IBS	80 (57.1)	29 (36.3)/51 (63.7)	48 (27-67)	47 (IQR: 36-58)
IBS-D	46 (57.5)	23 (50.0)/23 (50.0)	51 (31-67)	49 (IQR: 39-59)
IBS-C	15 (18.8)	0 (0)/15 (100)	35 (27-50)	39 (IQR: 32-46)
IBS-M	19 (23.7)	6 (31.6)/13 (68.4)	52 (32-63)	48 (IQR: 39-56)

N, number; IBS, irritable bowel syndrome; IBS-C, constipation-predominant; IBS-D, diarrhea-predominant IBS; IBS-M, mixed-diarrhea-and-constipation IBS.

(a) Staining intensity: no staining, 0 point; weak staining, 1 point; medium staining, 2 points; and strong staining, 3 points. If the TRPV1 positive product had the same color as the background, it was rated as negative ("-") with 0 point. Light brown staining was rated as weak positive ("+") with 1 point, brown as positive ("++") with 2 points, and dark brown as strongly positive ("+++") with 3 points.

(b) Cell positive rate score: No positive cells, 0 point; Positive rate ≤10%, 1 point; Positive rate 10% to 50%, 2 points; Positive rate 50% to 80%, 3 points; Positive rate >80%, 4 points.

The final score for each field was calculated as the product of staining intensity and cell positive rate (a×b). The average score from five non-overlapping fields (top, bottom, left, right, and middle) under a high-power lens (40×) was taken as the final score for each slice.

Statistical analysis

The experimental data were expressed as medians. The Mann-Whitney U test (rank sum test) was used for comparing two independent groups, with a significance level set at α=0.05. A *p*-value less than 0.05 was considered significant.

Non-parametric tests (Kruskal-Wallis tests) were used to compare different subtypes of IBS. To explore the association between TRPV1 expression and IBS symptom scores, Spearman's rank correlation analysis was performed, with the correlation coefficient (r) used to express the strength and direction of the relationship. A *p*-value of less than 0.05 was considered a significant relationship. All data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25.0. Sample size calculations were conducted using G*Power software, with an effect size of 0.5, α=0.05, and power =0.8. Based on these criteria, the required sample size was determined to be 80 for the IBS group and 60 for the N group to detect significant differences in TRPV1 expression.

Results

Comparison of baseline data between the two groups

Group N comprised 32 males and 28 females, with age ranging from 34 to 69 years (mean age of 50 years). IBS group consisted of 29 males and 51 females, with age ranging from 27 to 67 years (average age of 48 years). IBS group was further subdivided into the following groups: IBS-D group (n=46), with an age ranging from 31 to 67 years (mean age of 51 years); IBS-C group (n=15), all female, aged 27 to 50 years; IBS-M group (19 patients, 6 male and 13 females), aged 32 to 63 years. No significant differences were found in age or gender between the IBS and control groups (**Table 1**).

Location of TRPV1 in colon mucosa

In both the IBS and control groups, TRPV1 expression was primarily positive in the cytoplasm and nucleus of colon adenocytes, with some sporadic distribution in the interstitial region. In the IBS group, the average TRPV1 expression was 0.8 (range 0-8.4), which was significantly higher than that of the control group (0.4, range 0-1) ($P<0.05$) (**Table 2** and **Figure 1**).

Correlation analysis of TRPV1 expression and IBS symptoms

IBS patients had an average irritable bowel symptom score of 4 (range 2-11.5). Rank cor-

Table 2. Expression of TRPV1 in the colonic mucosa

Group	Case (%)	TRPV1	TRPV1	*P* value
N	60 (42.9)	0.4 (0-1)	0.5 (IQR: 0.39-0.77)	0.023
IBS	80 (57.1)	0.8 (0-8.4)	4.4 (IQR: 2.9-5.7)	

TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome.

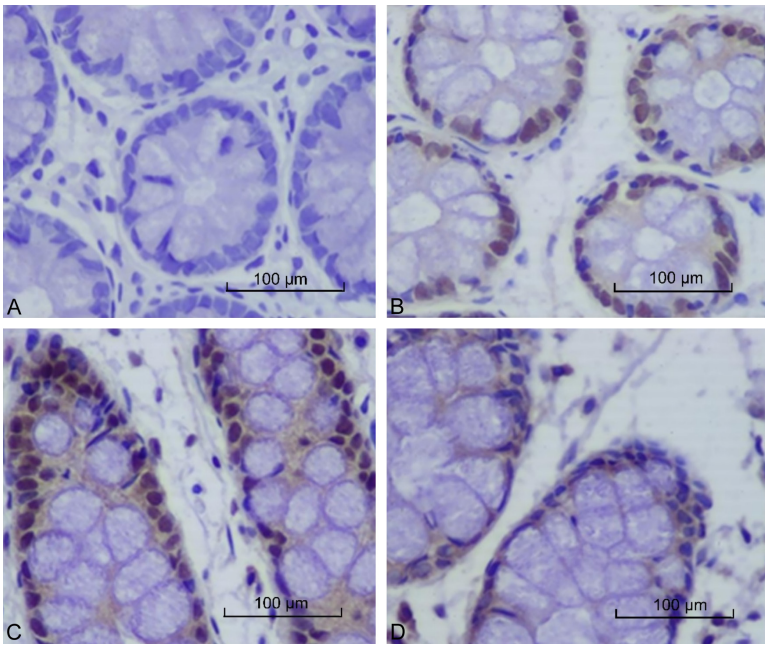

Figure 1. Electron microscopy of TRPV1 expression in colonic mucosal cells of N group (A), IBS-C group (B), IBS-D group (C), and IBS-M group (D) (40×). TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome; IBS-C, constipation-predominant; IBS-D, diarrhea-predominant IBS; IBS-M, mixed-diarrhea-and-constipation IBS.

Table 3. Correlation analysis of TRPV1 expression and IBS symptom scores in the IBS group

Data			*r* value	*P* value
TRPV1	0.8 (0-8.4)	4.6 (IQR: 2.78-5.56)	*r*=0.772	0.002
IBS symptom scores	4 (2-11.5)	7.33 (IQR: 4.74-8.99)		

TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome.

Table 4. Expression of TRPV1 in IBS subgroups

Subgroup	Case (%)	TRPV1		*P* value
IBS-D	46 (57.5)	1.1 (0-8.4)	4.33 (IQR: 2.69-5.36)	0.938
IBS-C	15 (18.8)	0.6 (0.2-6.2)	3.35 (IQR: 2.32-4.19)	
IBS-M	19 (23.7)	0.8 (0-7.8)	4.52 (IQR: 3.17-5.88)	

TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome; IBS-C, constipation-predominant; IBS-D, diarrhea-predominant IBS; IBS-M, mixed-diarrhea-and-constipation IBS

relation analysis (Spearman), revealed a positive correlation between TRPV1 expression and symptom severity, with a correlation coefficient of r=0.772 (P<0.05) (**Table 3**).

Comparison of TRPV1 among various IBS subgroups

The average TRPV1 expression in IBS-D, IBS-C, and IBS-M subgroups were 1.1 (0-8.4), 0.6 (0.2-6.2), and 0.8 (0-7.8), respectively. However, a non-parametric test (Kruskal-Wallis) showed no significant differences in TRPV1 expression among the IBS subgroups (*P*>0.050) (**Table 4** and **Figure 1B-D**).

Comparison of TRPV1 between male and female IBS patients

TRPV1 expression was 1.0 (0-7.2) in male patients and 0.8 (0-8.4) in female patients. No significant difference was observed between the genders (*P*=0.871, *P*>0.050) (**Table 5**).

Comparison of symptom scores between male and female IBS patients

The average symptom score was 4.0 (2-9.5) in male IBS patients and 3.75 (2.0-11.5) in female IBS patients. The rank sum test revealed no significant difference between genders in symptom scores (*P*=0.835) (**Table 6**).

Comparison of TRPV1 expression in ascending and descending colon mucosa among different groups

There was no significant differences in TRPV1 expression between the ascending and descending colon mucosa across the different groups (N, IBS-D, IBS-C, IBS-M) (*P*>0.050) (**Table 7** and **Figure 2**).

Table 5. TRPV1 expression in male and female groups of IBS

Group	Case (%)	TRPV1		*P* value
Male	29 (36.3)	1.0 (0-7.2)	3.35 (IQR: 2.26-4.35)	0.871
Female	51 (63.7)	0.8 (0-8.4)	4.10 (IQR: 2.41-5.69)	

TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome.

Table 6. IBS symptom scores of males and females

Group	Case (%)	IBS symptom scores	*P* value
Male	29 (36.3)	4.0 (2-9.5)	0.835
Female	51 (63.7)	3.75 (2.0-11.5)	

IBS, irritable bowel syndrome.

Table 7. Comparison of TRPV1 expression among different groups

Group	Case (%)	TRPV1	
		Ascending colon	Descending colon
N	60 (42.9)	0.4 (0-1)	0.5 (0-1)
IBS-D	46 (57.5)	1.1 (0-8.4)*	1.3 (0-8.4)*
IBS-C	15 (18.8)	0.8 (0.2-6.2)*	1.1 (0.2-6.2)*
IBS-M	19 (23.7)	1.0 (0-7.8)*	1.3 (0-7.8)*

N, number; TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome; IBS-C, constipation-predominant; IBS-D, diarrhea-predominant IBS; IBS-M, mixed-diarrhea-and-constipation IBS. Compared to N group, *$P<0.05$.

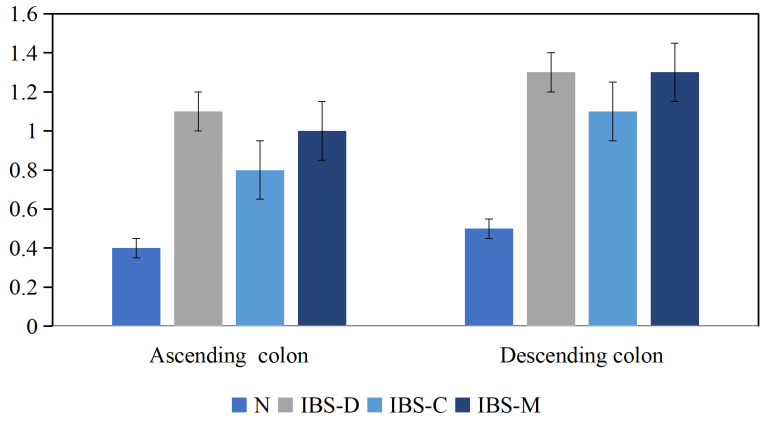

Figure 2. Comparison of TRPV1 expression in ascending and descending colon among different groups. TRPV1, transient receptor potential vanilloid type 1; IBS, irritable bowel syndrome; N, number; IBS-C, constipation-predominant; IBS-D, diarrhea-predominant IBS; IBS-M, mixed-diarrhea-and-constipation IBS.

Discussion

TRPV1 is a multifunctional, non-selective, ligand-triggered cation channel that plays a key role in sensory neurons, particularly those involved in pain perception. This channel integrates various signals and is activated by a range of environmental and physiologic stimuli, including high temperature (over 43°C), acidic environment (pH below 6.0), capsaicin, bradykinin, substance P, adenosine triphosphate (ATP), and nerve growth factor, all of which enhance its sensitivity [12, 13]. Upon activation, TRPV1 channels open, allowing calcium ions to enter the cell, while small amounts of sodium and potassium ions are exchanged, and chloride ions help maintain the intracellular charge balance [14]. This ion influx leads to electrical changes in nerve endings, which trigger the release of neuropeptides, such as substance P, calcitonin gene-related peptides, and excitatory amino acids. These molecules act as messengers, transmitting pain signals to secondary neurons and initiating the pain response [15].

TRPV1 is primarily located in the non-myelinated C fibers responsible for pain perception, and some Aδ fibers, which are involved in pain sensation. It is also present in the dorsal root ganglion, trigeminal nerve, and small neurons in the autonomic nervous system, playing a significant role in the nervous system's recognition of noxious stimuli. Beyond the nervous system, TRPV1 is also widely expressed in the sensory nerve fibers of the gastrointestinal tract, including the mucosal, submucosal, and muscular layers, suggesting its involvement in the gut's sensory functions [16]. Increasing evidence points to TR-PV1's critical role in the development of visceral pain [17].

Akar et al. showed that the expression of TRPV1 receptor neurons in the colonic mucosa of IBS patients was 3.5 times higher than that in the

normal control group [18]. These findings support the notion that TRPV1 expression is significantly enhanced in IBS patients. Animal model studies have suggested that TRPV1 mediates visceral hypersensitivity in humans, and elevated numbers of TRPV1-positive nerve fibers have been identified in colonic biopsies from IBS patients compared to healthy controls [19]. Additionally, Keszthely et al. revealed that the increased TRPV1 expression in the colonic mucosa of IBS patients correlated with the severity of symptoms [20]. Similarly, our study also confirmed that higher TRPV1 expression in the colon mucosa was positively correlated with the improvement of IBS symptom score, and this association was statistically significant.

While a clear link exists between TRPV1 overexpression in the colonic mucosa and the severity of IBS symptoms, the role of gender remains unclear. Our study observed a significantly higher proportion of women than men in the IBS group, which is consistent with a previous study [21]. Some studies report a sex ratio of 1:2.12, while a study in China found a ratio of 1:1.78 for male to female IBS prevalence [22]. Such differences may be attributed to gender-related factors such as hormone levels, stress coping mechanisms, pain perception, bowel habits, psychological states, socio-cultural differences, access to medical resources, and women's social roles and status [23]. Despite the expectation that this sex difference would correlate with increased TRPV1 expression in women with IBS, our results did not show such an association, possibly due to insufficient sample size. As current research on this topic is limited, this presents a promising area for future exploration regarding TRPV1 expression in IBS.

This study delved into the effect of gender differences on IBS symptom severity, but the results showed no significant difference. While the incidence of IBS is clearly higher in women, and physiological factors such as estrogen levels, along with social roles and status, suggest that IBS symptoms could be more severe in women, our findings did not support this hypothesis. Possible explanations for this include: (1) No inherent difference in symptom severity between genders; (2) Insufficient sample size, and variations in how patients perceive and report their symptoms, with some possibly underestimating or excessively worrying about their condition, which could lead to discrepancies between reported scores and actual severity.

Regarding TRPV1 expression across different IBS subtypes, our study found no significant differences among subtypes. Literature on this topic remains limited. Given the small sample size, the uneven distribution of IBS subtypes, and possible inaccuracies in symptom descriptions by some patients leading to classification errors, these factors may have influenced the study's accuracy. Therefore, further validation in larger studies is needed. Additionally, we observed no statistical significance in TRPV1 expression between the ascending and descending colon mucosa in the IBS-D, IBS-C, and IBS-M groups, suggesting that TRPV1 distribution in the colon mucosa does not vary significantly across different IBS subtypes.

The pathogenesis of IBS is multifactorial, with visceral hypersensitivity playing a central role in its development. Therefore, targeting this feature has emerged as a promising approach to treatment. The upregulation and phosphorylation of TRPV1 receptors are key drivers in the development of visceral hypersensitivity [24]. By focusing on TRPV1 receptors, understanding their associated factors and signaling pathways, and regulating the upstream mechanisms responsible for their upregulation and phosphorylation, we can gain deeper insight into the pathogenesis of IBS and foster the development of innovative therapy.

While significant progress has been made in studying TRPV1 expression in the digestive system and its connection to gastrointestinal diseases, much remains to be explored - particularly the physiologic characteristics of TRPV1, the relationship between its structure and function, and its changes under pathological conditions. With the advancements in biotechnology and omics research, we are poised to gain a clearer understanding of the exact role TRPV1 receptors play in both physiologic and pathologic processes. This progress will not only advance the development of novel drugs targeting TRPV1 channels, but also further our understanding of the link between TRPV1 and gastrointestinal diseases.

Disclosure of conflict of interest

None.

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References

[1] Oz M, Lorke DE and Howarth FC. Transient receptor potential vanilloid 1 (TRPV1)-independent actions of capsaicin on cellular excitability and ion transport. Med Res Rev 2023; 43: 1038-1067.

[2] Szymaszkiewicz A, Włodarczyk J, Wasilewski A, Di Marzo V, Storr M, Fichna J and Zielińska M. Desensitization of transient receptor potential vanilloid type-1 (TRPV1) channel as promising therapy of irritable bowel syndrome: characterization of the action of palvanil in the mouse gastrointestinal tract. Naunyn Schmiedebergs Arch Pharmacol 2020; 393: 1357-1364.

[3] Aguilera-Lizarraga J, Hussein H and Boeckxstaens GE. Immune activation in irritable bowel syndrome: what is the evidence? Nat Rev Immunol 2022; 22: 674-686.

[4] Aboubakr A and Cohen MS. Functional bowel disease. Clin Geriatr Med 2021; 37: 119-129.

[5] Oka P, Parr H, Barberio B, Black CJ, Savarino EV and Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2020; 5: 908-917.

[6] Lovell RM and Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. Clin Gastroenterol Hepatol 2012; 10: 712-721, e714.

[7] Horn A, Stangl S, Parisi S, Bauer N, Roll J, Löffler C, Gágyor I, Haas K, Heuschmann PU, Langhorst J and Keil T. Systematic review with meta-analysis: Stress-management interventions for patients with irritable bowel syndrome. Stress Health 2023; 39: 694-707.

[8] Flacco ME, Manzoli L, De Giorgio R, Gasbarrini A, Cicchetti A, Bravi F, Altini M, Caio GP and Ursini F. Costs of irritable bowel syndrome in European countries with universal healthcare coverage: a meta-analysis. Eur Rev Med Pharmacol Sci 2019; 23: 2986-3000.

[9] Sebastián Domingo JJ. Irritable bowel syndrome. Med Clin (Barc) 2022; 158: 76-81.

[10] Liu GC and Liu TJ. Research progress of Chinese and Western medicine in the treatment of diarrheal irritable bowel syndrome. Med Recapitulate 2023; 29: 5453-5457.

[11] Cheng F, Fan Z, Lin C, Zhu Y, He H, Dai N and Du L. Effect of altered gut microbiota on visceral hypersensitivity of postinfectious irritable bowel syndrome mice. Eur J Gastroenterol Hepatol 2022; 34: 1220-1230.

[12] Cui LK, Li HN, Lu Y, Hai XH, Wang XY and Sun Q. Research progress of intestinal microbiota and intestinal mucosal immunity in the pathogenesis of irritable bowel syndrome. Med Recapitulate 2024; 30: 108-112.

[13] Lian J, Sun LX and Yin WL. Research progress of intestinal microecological imbalance in the pathogenesis of irritable bowel syndrome. Shanxi Med J 2021; 50: 739-742.

[14] Gao M, Wang Y, Liu L, Qiao Z and Yan L. A patent review of transient receptor potential vanilloid type 1 modulators (2014-present). Expert Opin Ther Pat 2021; 31: 169-187.

[15] Liu XY, Li Z, Zhou XY and Guo XH. Biological function of transient receptor potential vanillin subfamily 1 (TRPV1). Prog Biochem Biophys 2023; 50: 437-447.

[16] Xu ZC, Nian YY and Meng XM. The mechanism of TRPV1 in the pathogenesis of gastroesophageal reflux disease. Mod Dig Interventional Diagn Treat 2021; 26: 697-701.

[17] Matos R, Santos-Leite L, Cruz F and Charrua A. Early in life stressful events induce chronic visceral pain and changes in bladder function in adult female mice through a mechanism involving TRPV1 and alpha 1A adrenoceptors. Neurourol Urodyn 2024; 43: 533-541.

[18] Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ and Müller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut 1999; 45 Suppl 2: II43-47.

[19] Singh P, Sayuk GS, Rosenbaum DP, Edelstein S, Kozuka K and Chang L. An overview of the effects of tenapanor on visceral hypersensitivity in the treatment of irritable bowel syndrome with constipation. Clin Exp Gastroenterol 2024; 17: 87-96.

[20] Keszthelyi D, Troost FJ, Jonkers DM, Helyes Z, Hamer HM, Ludidi S, Vanhoutvin S, Venema K, Dekker J, Szolcsányi J and Masclee AA. Alterations in mucosal neuropeptides in patients with irritable bowel syndrome and ulcerative colitis in remission: a role in pain symptom generation? Eur J Pain 2013; 17: 1299-1306.

[21] Zhao EY, Zhou JW, Chu HY, Lv SJ and Yang YJ. Epidemiology and pathogenic factors of irritable bowel syndrome: a review on research progress. Chin J Publ Heal 2021; 37: 764-768.

[22] Qin HY, Luo JL, Qi SD, Xu HX, Sung JJ and Bian ZX. Visceral hypersensitivity induced by activation of transient receptor potential vanilloid type 1 is mediated through the serotonin pathway in rat colon. Eur J Pharmacol 2010; 647: 75-83.

[23] Ford AC, Sperber AD, Corsetti M and Camilleri M. Irritable bowel syndrome. Lancet 2020; 396: 1675-1688.

[24] Cortright DN and Szallasi A. Biochemical pharmacology of the vanilloid receptor TRPV1. An update. Eur J Biochem 2004; 271: 1814-1819.