International Journal of Pharmacology

ISSN 1811-7775

science alert

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Asian Network for Scientific Information

OPEN ACCESS International Journal of Pharmacology
ISSN 1811-7775
DOI: 10.3923/ijp.2025.443.452

Research Article
Effect of Electricity on the Expression of CGRP and its Receptor RAMP1 in Rat IBS-C Model and its Mechanism of Action

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Abstract
Background and Objective: Irritable Bowel Syndrome (IBS), a common chronic functional disorder, poses a severe risk of increasing physical and mental health concerns. The current animal study was carried out to investigate how electricity affects CGRP and RAMP1 expression and its mode of action. **Materials and Methods:** In this study, intragastric ice-water techniques were followed. Each group's rats' mental state, weight, faeces mass, auricle colour, hair colour and quality, activity level, water and food intake and bowel movement frequency were observed. The leftover small intestine and stomach propulsion of gavaged rats were investigated and ELISA and western blotting were conducted. **Results:** Rat behaviour before and after treatment was evaluated for each group. The rats in the model and electroacupuncture groups had considerably poorer general condition ratings ($p<0.05$) than the blank group. In comparison to the blank group, the model rats had a substantial increase ($p<0.05$) in stomach residual rate and a decrease ($p<0.05$) in small intestine propulsion rate. Electroacupuncture significantly increased intestinal propulsion rate ($p<0.05$) and decreased stomach residual rate compared to the model group. Electroacupuncture increased plasma CGRP and SP in both groups. Electroacupuncture significantly altered TRPV1, PAR4, CGRP, RAMP1 and SP mRNA and proteins in all groups. Compared to the blank group, model rats had substantially greater ($p<0.05$) mRNA and protein expressions of TRPV1, PAR4, CGRP, SP and RAMP1 in their colon tissues. **Conclusion:** Electroacupuncture regulates TRPV1, PAR4, CGRP, RAMP1 and SP expression, which may help IBS-C stomach pain patients.

Key words: Electroacupuncture, irritable bowel syndrome, CGRP, RAMP1, protein expressions, electricity

Citation: Mao, W., F. Xie, Q. Hu, M.M Zhang and X.L. Mao, 2025. Effect of electricity on the expression of CGRP and its receptor RAMP1 in rat IBS-C model and its mechanism of action. Int. J. Pharmacol., 21: 443-452.

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Funding: The research was funded by the Traditional Chinese Medicine Research Project of the Hubei Provincial Health Commission (No. ZY2021Q016).

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

With an annual increase in prevalence, Irritable Bowel Syndrome (IBS) is one of the most prevalent chronic functional disorders and poses a severe risk to patients' physical and emotional well-being. Individuals with IBS who satisfy the Rome diagnostic criteria make up 10-20% of the general population in Western affluent nations[1]. It is also quite common in China, with an incidence of about 10-15% and in some areas, IBS patients account for about 1/3 of digestive outpatients[2]. According to distinct stool characteristics, IBS can be classified clinically into three types: Diarrhea (IBS-D), constipation (IBS-C) and alternating diarrhea and constipation. At present, the treatment of IBS-C is mainly symptomatic, but the effect is not ideal, there are many clinical reports of acupuncture treatment and its curative effect is recognized by the majority of patients[2,3]. Investigating acupuncture's mechanism of action is crucial for both treating and preventing IBS-C because its exact mode of action is yet unknown.

Numerous investigations have proven that patients with IBS-C exhibit visceral hypersensitivity and studies have demonstrated that this is a critical link in the pathophysiology of IBS-C[3,4]. The visceral hypersensitivity associated with IBS is mostly caused by a range of cytokines, neurotransmitters, receptors and associated signal transduction pathways, all of which interact and influence one another[5].

Protease-Activated Receptor 4 (PAR4) belongs to the protease-activated receptor family. The PAR4-positive neurons are widely distributed in colon tissues. More and more studies have shown that activated PAR4 can cause hyperalgesia and increase pain response[5,6]. As a newly discovered receptor with potential endogenous analgesia, PAR4 has a regulatory effect on the transduction of peripheral nociceptive signals under normal and inflammatory conditions[7]. Although PAR4 is now known to be involved in the peripheral mechanism of pain regulation, the mechanism of PAR4's action in pain regulation is still unclear. One potential explanation is that intracellular signal transduction via Transient Receptor Potential Vanilloid type 1 (TRPV1) controls the transmission of pain signals[8]. Low concentrations of PAR4 agonist on cultured dorsal root ganglion (DRG) neurons have been shown in some studies to have no effect on intracellular Ca^{2+} but to have an effect on Ca^{2+} mobilization brought on by KCl and capsaicin[7-9]. Furthermore, the elevated levels of PAR4 agonists on cultured DRG sensory neurons caused increased sensitivity of TRPV1 via the PLCB/PKC pathway. These two experiments suggest that PAR4 may regulate neuronal activity by affecting the capsaicin receptor TRPV1[8,9].

In addition, PAR4 can sensitize TRPV1 receptors and act on primary afferent nerve fibers to release pain-related active substances P (SP) and Calcitonin Gene-Related Peptide (CGRP)[10]. Information about visceral pain is transmitted by SP and in addition to direct injury, CGRP can amplify the impact of SP. In this way, activation of PAR4 causes overexcitation of sensory neurons, releasing neurotransmitters, resulting in increased visceral sensitivity[10,11]. A neuropeptide of 37 amino acids, CGRP is released from sensory nerve endings and is extensively disseminated throughout the body's peripheral and central vascular tissues. It comes from the same gene as calcitonin (CT) and is another expression product of the calcitonin gene[9,10,12]. The functions of CGRP are diverse and include vasodilation, contraction of the heart, suppression of the proliferation and death of vascular smooth muscle cells and involvement in the control of the neurological and digestive systems. The functional diversity of CGRP may be related to the signal integration of receptor transmembrane signal transduction[12]. It has been discovered that the calcitonin receptor-like receptor (CRLR), Receptor Activity Modifying Protein 1 (RAMP1) and receptor component protein (RCP) make up the CGRP receptor. Among these, RAMP1 is important in IBS-C. The RAMP1's primary function is to chaperone (or glycosylate) CRLR and deliver it to the cell membrane[12,13].

Acupuncture has a demonstrable therapeutic impact when used to treat visceral disorders and numerous studies have documented how well it works to treat IBS-C[10,12]. For the function of the gastrointestinal tract, acupuncture has a bidirectional and benign adjustment effect, which can normalize the abnormal intestinal movement, that is, it can promote the recovery of peristalsis for those with low bowel movement function and slow down the movement for those with hyper bowel movement function[13,14]. At the same time, acupuncture also has an obvious effect on the adjustment of the nervous system and endocrine system, which can effectively correct the abnormal immune function of IBS-C individuals[14]. Nevertheless, a thorough examination of acupuncture's therapeutic benefits has revealed that its exact mechanism of action and regulatory function remains unknown.

The current study proposes that regulating TRPV1, PAR4, CGRP, RAMP1 and SP expression is the mechanism by which electricity treats IBS-C. Thus, the IBS-C model was created for this investigation using the ice-water intragastric approach, along with the use of other techniques such as enzyme-linked immunosorbent test, western blot and real-time fluorescence quantitative PCR. To elucidate the beneficial effect and mechanism of acupuncture and to establish a scientific foundation for the clinical treatment of IBS-C, it is important to observe the effects of electroacupuncture on CGRP and SP expression in the plasma of IBS-C model rats as well as the effects of electroacupuncture on TRPV1, PAR4, CGRP, RAMP1, as well as SP mRNA and protein expression in colon tissue.

MATERIALS AND METHODS

Study area: The research was conducted at the Wuhan Institute of Technology Hospital in Hongshan, Wuhan, Hubei, China from March, 2023 to June, 2023.

Experimental animals selection: Eighty adult male Sprague-Dawley rats (200±20 g) with SPF grade were donated by Hubei Academy of Medical Sciences Experimental Animal Center. The institutional ethics review board approved this study (Reg. No.: 83654/2023/IBS/10.01.2023). For a week, the animals in the SPF animal house were fed, with free eating and drinking. Keep indoor air circulation and natural day and night light and keep the indoor temperature of 22-25°C and the relative humidity of about 60%. Following seven days of adaptive feeding, individuals were split into three groups at random (20 animals each): The model group, the electroacupuncture treatment group and the blank control group.

Establishment of IBS-C rat model: The IBS-C animal model was prepared by ice water intragastric method. Each group of rats in the same cage was given 0.3 mL of ice water (4°C NaCl) once a day for 14 days. The signs of success in modeling were withered yellow hair, dry stool, significantly reduced diet, weakened activity, clumping or even sleepiness and abnormal mood.

Electroacupuncture therapy: Following acupuncture on both sides of Shangjiu Xu and Zusanli, the Korean acupuncture point nerve stimulator was attached to the electric acupuncture team following the formation of the IBS-C model. The frequency of the continuous wave was 2 Hz and the intensity was 1 m A. Rats' limbs showed no signs of rejection or evident discomfort. Tianshu Acupoint does not get blunt per time lasting 30 min, once per day for two weeks, spanning 14 days.

Specimen collection: All cages were weighed on the morning of the first day after electroacupuncture treatment and all cages were deprived of water for 24 hrs. All the animals were confiscated on the morning of the second day. For anesthesia and fixed perfusion of the stomach antrum and jejunum tissues, 10 rats per group were chosen at random and the remaining 10 rats in each group were given the intragastric infusion of nutritional confusion. After 30 min of nutrition rice paste intragastric administration, 10 rats in each group were anesthetized, abdominal aorta blood extraction, gastric emptying and small intestine propulsion tests and gastric antrum and jejunum tissue were extracted.

Gastrointestinal tissue samples involved ligating the stomach's pylorus and stomach cardia, swabbing the stomach using filter paper, weighing the entire stomach, cutting the appetizer body along the stomach's larger bend and then washing, drying and weighing the contents. After being taken out, the stomach antrum was put in the cryopreservation tube. The small intestine was simultaneously rapidly removed for measurement and cleaned with ice-salted water. After being removed, the colon was put into the cryopreservation tube. To be measured, immediately freeze in liquid nitrogen and place in a refrigerator set at 80°C.

Observational index

General situation score: During the treatment period, the hair activity and stool status of the rats were observed daily. The daily dietary and weight changes for every group of rats during the experiment were computed based on the experimental record and the relevant scores were given: Hair color moist 5 points, still moist 3 points, dry and dull 1 point: Sensitive activity 5 points more sensitive 3 points, tired 1 point. Food intake had no change of 5 points, decreased by 3 points and significantly decreased by 1 point; weight gain was 5 points, no significant change was 3 points and weight loss was 1 point. The scores of each rat were cumulatively added to the normal scores. The general condition score of each group was compared.

Gastric emptying rate: The residual weight of the stomach was the difference between the total and net stomach weights; the residual rate of the stomach was expressed as a percentage of the given paste weight. Every group's stomach emptying was contrasted.

Small intestine propulsion rate: Measurements were made of the entire length (L1) from the pylorus to the cecum and the distance (L2) from the pylorus to the black semi-solid paste front. The small intestine propulsion rate (%) = L2/L1×100 was then compared across each group.

ELISA: A CGRP detection kit (Shanghai Xinyu Biotechnology Co., Ltd., China) was used to detect the level of CGRP in rat serum. The SP detection kit (Beijing Equation Biology, China) was used to detect SP levels in the serum of rats.

Total RNA isolation and qRT-PCR (Quantitative Real-Time Polymerase Chain Reaction): Using the TRIzol® reagent (Ambion, USA), RNA was extracted from rat colon tissues following the manufacturer's instructions. Additionally, the PrimeScript RT reagent kit (Takara, China) was used to reverse transcribe cDNA. The ABI 7500 RT PCR equipment was used to perform qRT-PCR utilizing the SYBR Premix Ex TaqII Kit (Takara, China). Every quantification was adjusted based on the amount of β-actin present in the reaction. The relative fold changes in gene expression were calculated using the comparative threshold cycle (CT) approach, which examines variations in CT values between common reference RNA and target gene RNA. The $2^{-\Delta\Delta ct}$ technique was used to calculate the expressions. Every experiment was carried out three times in triplicate.

Western blot analysis: After lysing rat colon tissue and adding a protease inhibitor, the lysates were centrifuged at 12,000 rpm and 4°C. The Pierce bicinchoninic acid assay kit (Thermo Fisher) was used to measure the quantity of protein. Proteins were moved to PVDF membranes, separated using 10% SDS-PAGE and then probed with primary antibodies. After incubating the membranes in a secondary antibody (1:1,000, Abcam, USA) coupled with horseradish peroxidase, bands were identified utilizing an ECL chemiluminescence kit (Millipore, Burlington, Massachusetts, USA).

Statistical analysis: The software for statistical analysis was SPSS 25.0, while the software for analysis and mapping was GraphPad Prism 8.0. Every measurement result is presented as Mean±Standard Deviation (SD), based on data comparison between two and more groups using student t-tests and one-way ANOVA. The $p<0.05$ was regarded as a significant difference.

RESULTS

Comparison of general situation scores among each group of rats: The score is based on general condition, fur, activity, diet and weight change. (1) Comparing groupings within the same time frame: Before treatment: The model category and electroacupuncture category had significantly different scores ($p<0.05$) when compared to the blank group. Following treatment: Rats in the model category showed a statistically important ($p<0.05$) difference from the blank group, and the electroacupuncture group also showed a difference of statistical significance ($p<0.05$). The rats in the electroacupuncture group scored considerably ($p<0.05$) higher than those in the model group. (2) Pre- and post-treatment comparison: In the model group, there was no statistically significant difference between the general scores before and after therapy ($p>0.05$). Following treatment, there was a significant ($p<0.05$) increase in the electroacupuncture group's general score (Fig. 1 and Table 1).

Impact of electroacupuncture on gastrointestinal motility in rats: Rats in each group had their intestinal propulsion rate and gastric emptying rates assessed following electroacupuncture treatment to compare and evaluate the alterations in gastrointestinal dynamics. Rats in the model group had a statistically significant ($p<0.05$) rise in their gastric residual rate and a substantial decrease in their small intestine propulsion rate when compared to the blank category. Rats in the electroacupuncture treatment group had a statistically significant ($p<0.05$) increase in small intestine propulsion rate and a substantial decrease in gastric residual rate when compared to the model group (Fig. 2 and Table 2).

Effect of electroacupuncture on plasma CGRP and SP content in rats: Rats in the model group had significantly higher serum CGRP as well as SP contents than rats in the blank group, as shown in Table 3 and Fig. 3. This difference was considered statistically important ($p<0.05$), suggesting that rats' plasma CGRP and SP contents increased as a result of modeling. The levels of CGRP and SP in the serum of rats receiving electroacupuncture therapy were considerably lower ($p<0.05$) than those in the model category, suggesting that the treatment harmed the levels of CGRP and SP in the rats' plasma. Between the electroacupuncture therapy population as well as the blank category, there was no statistically significant distinction ($p>0.05$) in the levels of CGRP and SP in serum. This suggests that there was also no difference between the electroacupuncture therapy and control category in terms of CGRP as well as SP levels in plasma.

Effect of electroacupuncture on mRNA expression levels of TRPV1, PAR4, CGRP, SP and RAMP1 in rat colon tissue: The mRNA relative expression levels of TRPV1, PAR4, CGRP, SP and RAMP1 in the colon tissues of rats in the model category were statistically substantially ($p<0.05$) higher than those of the blank category. There was a statistically significant drop ($p<0.05$) in the mRNA relative expression levels of TRPV1, PAR4, CGRP, SP and RAMP1 in the colon tissues of rats in the electroacupuncture cohort as compared to the model cohort. Furthermore, as shown in Table 4 and Fig. 4, there was no statistically significant difference in the relative expression levels of TRPV1, PAR4, CGRP, SP and P1 in the colon tissues of the rats in the electroacupuncture category as compared to the blank category ($p>0.05$).

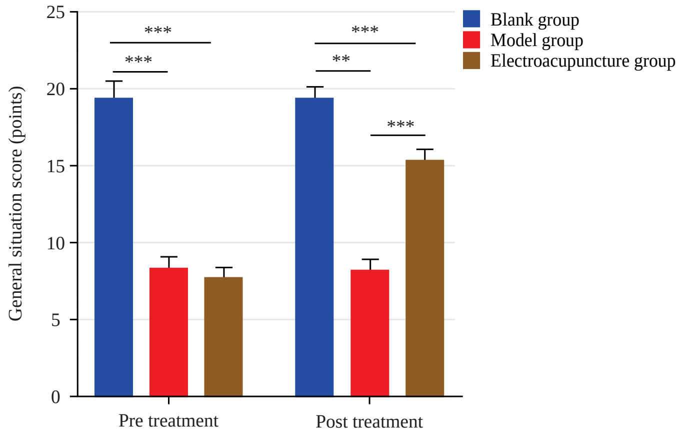

Fig. 1: Comparison of the score of the general situation before and after electroacupuncture treatment in each group

**p<0.01 and ***p<0.001

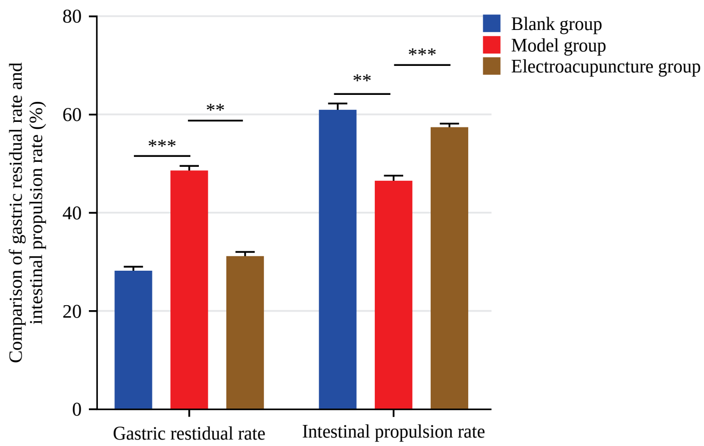

Fig. 2: Intestinal propulsion rate and gastric residual rate comparison for each group

**p<0.01 and ***p<0.001

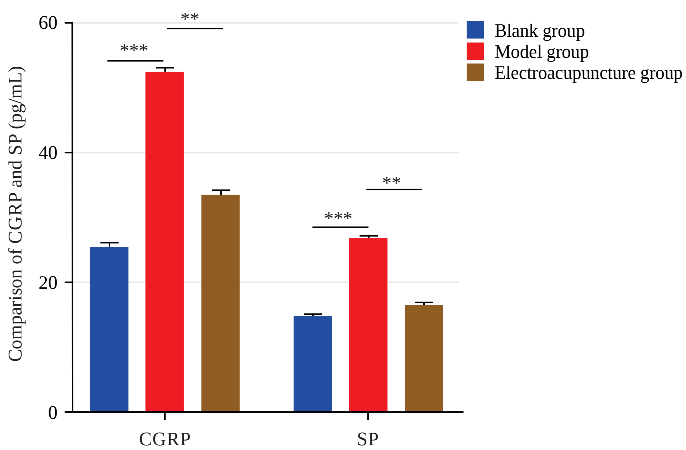

Fig. 3: Comparison of CGRP and SP in each group

**p<0.01 and ***p<0.001

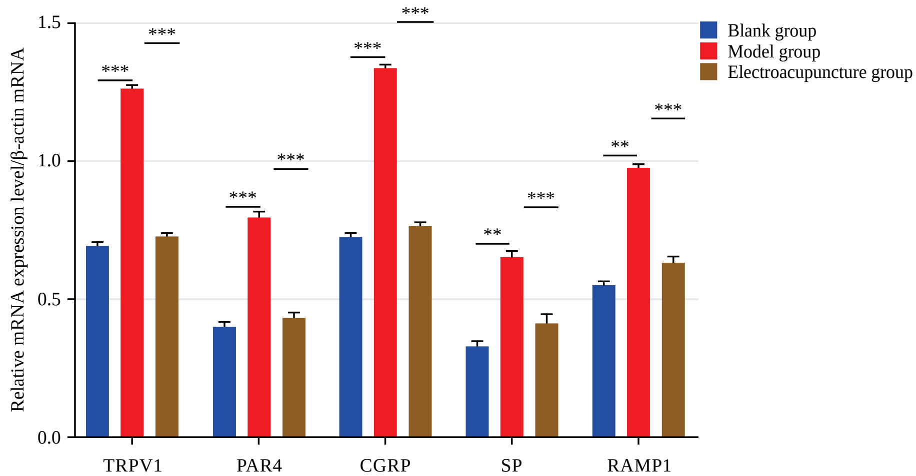

Fig. 4: mRNA expression levels of TRPV1, PAR4, CGRP, SP and RAMP1 in each group

**p<0.01 and ***p<0.001

Table 1: Comparison of score of general situation before and after electroacupuncture treatment in each group

		General situation score	
Group	Cases (n)	Pre treatment	Post treatment
Blank	20	19.24±0.23	19.28±0.26
Model	20	8.05±0.48[a]	8.10±0.96[b]
Electroacupuncture	20	7.89±0.56[a]	15.21±1.12[bcd]

[a]p<0.05 vs blank (pre treatment), [b]p<0.05 vs blank (post treatment), [c]p<0.05 vs model (post treatment) and [d]p<0.05 vs electroacupuncture (pre treatment)

Table 2: Intestinal propulsion rate and gastric residual rate comparison for each group

Group	Cases (n)	Gastric residual rate (%)	Intestinal propulsion rate (%)
Blank	10	28.54±5.18	60.78±4.12
Model	10	48.63±5.84[a]	46.25±5.78[a]
Electroacupuncture	10	31.65±4.57[b]	57.21±4.96[b]

[a]p<0.05 vs blank group and [b]p<0.05 vs model group

Table 3: Comparison of CGRP and SP in each group

Group	Cases (n)	CGRP (pg/mL)	SP (pg/mL)
Blank	10	24.78±6.54	14.58±3.64
Model	10	51.87±14.26[a]	26.43±4.81[a]
Electroacupuncture	10	32.74±14.53[b]	16.13±5.26[b]

[a]p<0.05 vs blank group and [b]p<0.05 vs model group

Table 4: mRNA expression ratio of TRPV1, PAR4, CGRP, SP and RAMP1 in each group

Group	Cases (n)	TRPV1/β actin mRNA	PAR4/β actin mRNA	CGRP/β actin mRNA	SP/β actin mRNA	RAMP1/β actin mRNA
Blank	10	0.68±0.21	0.38±0.12	0.71±0.28	0.31±0.15	0.54±0.21
Model	10	1.25±0.34[a]	0.78±0.25[a]	1.32±0.41[a]	0.63±0.18[a]	0.96±0.28[a]
Electroacupuncture	10	0.71±0.23[b]	0.41±0.15[b]	0.75±0.26[b]	0.38±0.17[b]	0.61±0.25[b]

[a]p<0.05 vs blank and [b]p< 0.05 vs model

Impact of electroacupuncture on TRPV1, PAR4, CGRP, SP and RAMP1 proteins expression in rat colon tissue: The model group's colon tissues exhibited considerably higher levels of relative expression of TRPV1, PAR4, CGRP, SP and RAMP1 proteins ($p<0.05$) when compared to the blank category. The colon tissue of the electroacupuncture group receiving treatment had substantially lower relative expression levels of TRPV1, PAR4, CGRP, SP and RAMP1 ($p<0.05$) as compared to the model category. Rats receiving electroacupuncture did not exhibit substantial variations in the relative amounts of expression of TRPV1, PAR4, CGRP, SP and RAMP1 in their colon tissue when compared to the normal cohort ($p>0.05$) (Fig. 5).

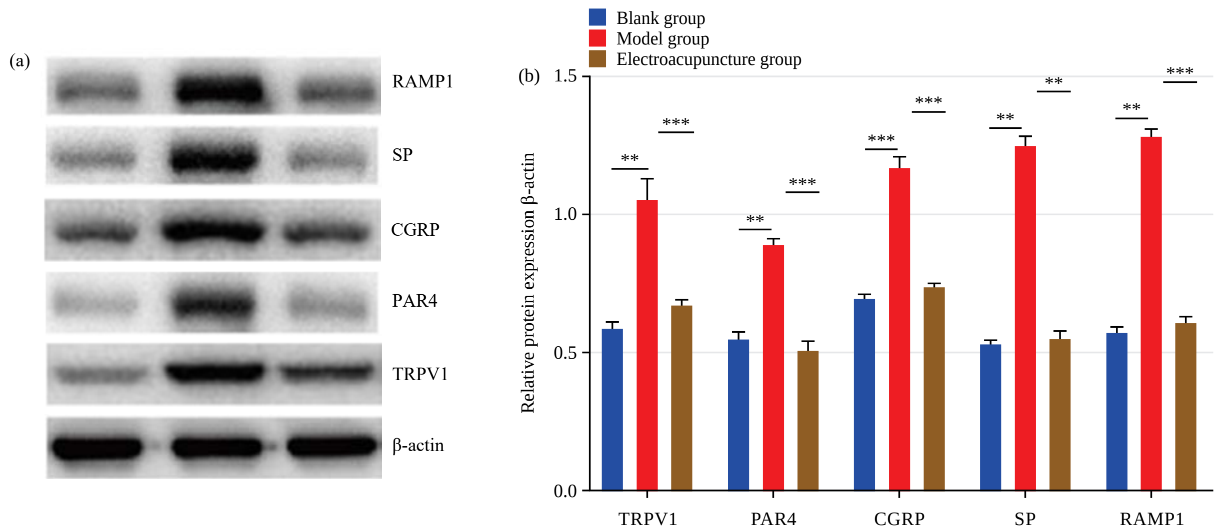

Fig. 5(a-b): Protein expression of TRPV1, PAR4, CGRP, SP and RAMP1 in each group
**p<0.01 and ***p<0.001

DISCUSSION

A functional gastrointestinal disease, or non-organic disturbance of intestinal function, is what Irritable Bowel Syndrome (IBS) is. Its primary symptoms include modifications to bowel habits and stool composition together with pain or discomfort in the abdomen. Abdominal pain, diarrhea, urgent and incomplete stools, constipation or alternating constipation and diarrhea, abdominal distension, bowel singing, sagittal gas and other symptoms are among the clinical signs[14,15]. These symptoms occur intermittently or continuously. Among them, the global prevalence of IBS-C is about 11%, with the prevalence in Asia ranging from 5.0-9.9%[15]. Due to the recurrence of symptoms and chronic prolongation of the disease, the patients' work and quality of life are diminished, healthcare costs are increased and the global healthcare burden is greatly increased. Since the pathophysiological mechanisms associated with IBS-C are controversial and there are no recognized diagnostic markers for the disease. The majority of the current standard medicines are intended to improve bowel habits and abdominal pain[14,16]. Dietary changes and the use of soluble fiber antispasmodic medications are first-line therapy. Clinical uses of visceral analgesics, motility enhancers, antidepressants and psychosocial therapies are common for individuals with varying symptoms and severity[17]. However, because therapeutic drugs can only be symptomatic and can not improve the overall symptoms of patients, a high proportion of patients (60.1%) will stop taking drugs because of this and most of the use of drugs will be accompanied by adverse reactions, even ischemic cardiovascular disease and ischemic colitis and other adverse events, so the effect of the above treatment methods is not ideal[17,18].

Traditional Chinese medicine offers significant benefits in the treatment of IBS-C since it is founded on the holistic idea and the theory of syndrome differentiation and treatment. Acupoint injections, acupuncture, enema and oral traditional Chinese medicine have all shown some therapeutic benefits in recent years. The use of TCM in the management of IBS-C is encouraging and successful. A thorough discussion of visceral hypersensitivity as well as acupuncture treatment will surely be an important area of research for IBS in the future. An increasing number of basic experimental studies have demonstrated the close relationship between the incidence of IBS-C and visceral hypersensitivity. An increasing number of clinical experimental investigations have also demonstrated the effectiveness of acupuncture in treating IBS-C. It will have important guiding significance for the diagnosis and treatment of IBS[18-20].

Gastrointestinal motility disorder and visceral paresthesia are common in IBS-C patients. Gastrointestinal motor dysfunction is a general term for a series of manifestations, such as disturbance of gastric electric rhythm, decrease of gastric emptance, decrease of gastric antral motility index and shortening or absence of the duration of transitional motor complex wave III (powerful systole) in interdigestive period. Research indicates that individuals with IBS-C experience aberrant gastric electric rhythm and delayed stomach emptying. Prompt saturation vomiting symptoms are associated with delayed gastric emptying[20]. Visceral hyperesthesia mainly refers to the stimulation that is lower than the normal threshold can cause discomfort or the physiological stimulation that is not perceived by normal people is perceived in the case of disease, mainly manifested as hyperalgesia, hyperalgesia and spontaneous pain and other reactivity enhancement or sensitization process[21]. Current studies have confirmed that in IBS-C patients, the gastrointestinal tract is highly sensitive to mechanical, physical or chemical stimulation, which makes the originally normal physiological peristaltic contraction, pain, fullness and other uncomfortable feelings. The mechanism of the visceral hypersensitivity of IBS-C is still unclear, which may be due to the change in the sensitivity of visceral mechanical receptors[22]. Studies have shown that the primary response site of visceral hypersensitivity may be the mechanical receptors in the intestinal wall and the visceral sensory information is amplified and transmitted to the center by the primary afferent nerve in the intestinal wall[18,22,23]. Furthermore, the heightened excitability of the spinal cord's dorsal horn results in abnormal nerve input sensation and a decreased central pain sensation threshold, all of which enhance the visceral sensitivity, both peripherally and in the spinal cord and central nervous system, thus leading to complexity and diversity of GI symptoms in IBS-C individuals[23,24]. Numerous prior research has demonstrated that electricity has a major therapeutic effect on IBS-C. It can greatly relieve sufferers' anxiety and despair as well as their upper abdominal fullness, poor appetite and burp symptoms[16,17,25]. Acupuncture in the treatment of functional dyspepsia with improved gastric emptying, gastric dynamic force and restoring functional dyspepsia rats' gastrointestinal hormone levels, can effectively promote digest function recovery. Numerous studies have demonstrated that acupuncture can increase the excitability of the vagus nerve while decreasing the excitability of the sympathetic nerve, thereby regulating autonomic nervous function and significantly improving visceral sensitivity in patients with IBS-C[20,21,24,25]. This study demonstrated that rats' small intestine propulsion and gastric emptying rates can both be markedly increased by electroacupuncture treatment. promote gastrointestinal absorption, reduce gastrointestinal sensitivity and improve IBS-C symptoms, which are consistent with literature reports. Therefore, it was believed that electroacupuncture has a significant and effective role in promoting gastrointestinal motility and reducing gastrointestinal sensitivity to comprehensively, safely and effectively relieve and treat various symptoms of IBS-C.

The visceral hypersensitivity mechanism of IBS-C is very complex, including cellular and molecular pathophysiological processes at central and peripheral levels[26]. The occurrence of the visceral hypersensitivity of IBS-C may be related to the abnormal up-afferent pathway or down-regulated system of the visceral sensory nerve, which may cause the dysregulation of the release of neuroregulation and transmission mediators or the increased sensitivity of the sensory nerve endings to these mediators[27,28]. The purpose of this study is to investigate the role of TRPV1, PAR4, CGRP, RAMP1 and SP in the occurrence of visceral hypersensitivity of IBS, as well as the impact of electricity on protein and mRNA expression. These factors are closely linked to visceral hypersensitivity in IBS-C. It was determined how electricity regulates IBS in both directions. The findings demonstrated that following electroacupuncture treatment, TRPV1, PAR4, CGRP, RAMP1 and SP expression levels dropped and mRNA and protein levels increased in the colonic tissue of IBS-C model rats. These findings suggested that TRPV1, PAR4, CGRP, RAMP1 and SP expression levels may be impacted by electroacupuncture. This study confirmed that electroacupuncture stimulation can improve the hypersensitivity of patients' internal organs by regulating the expression of TRPV1, PAR4, CGRP, RAMP1 and SP, which may also be one of the mechanisms by which electroacupuncture can improve the symptoms of abdominal pain or abdominal discomfort in clinical IBS-C patients.

CONCLUSION

The TRPV1, PAR4, CGRP, RAMP1, SP and IBS-C patients are closely related to visceral hypersensitivity. Electroacupuncture can effectively regulate gastrointestinal function and reduce visceral sensitivity by down-regulating the expression of TRPV1, PAR4, CGRP, RAMP1 and SP protein and mRNA in colon tissue. It helps those who have constipated IBS feel better in terms of their clinical symptoms. Furthermore, TRPV1, PAR4, CGRP, RAMP1 and SP alterations could be one of the ways that electroacupuncture treatments for IBS-C work.

SIGNIFICANCE STATEMENT

The present animal research was conducted to evaluate the effects of electricity on CGRP and RAMP1 expression, as well as its method of action. The present investigation found a strong link between visceral hypersensitivity and TRPV1, PAR4, CGRP, RAMP1, SP and IBS-C patients. Electroacupuncture may reduce the expression of TRPV1, PAR4, CGRP, RAMP1 and SP protein and mRNA in colon tissue, which improves digestive function and reduces visceral sensitivity. It helps patients with constipated IBS feel better about their clinical symptoms. Furthermore, electroacupuncture therapy for IBS-C may operate by affecting TRPV1, PAR4, CGRP, RAMP1 and SP.

ACKNOWLEDGMENT

The authors express thanks for the assistance provided by the higher authorities.

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