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Evaluation of the short-term efficacy of local analgesic (lidocaine) and opioid analgesic (sufentanil) on patients with centrally mediated abdominal pain syndrome: a randomized controlled trial

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Abstract

Background: Centrally mediated abdominal pain syndrome (CAPS) is characterized by continuous or frequently recurring abdominal pain and can result in functional loss across several life domains. The efficacy of the present management methods has not been established yet. We performed a prospective randomized controlled trial to explore the short-term efficacy of local analgesic (lidocaine) and opioid analgesic (sufentanil) in patients with CAPS.

Methods: We consecutively enrolled 130 patients who met the Rome IV CAPS criteria and divided them into the sufentanil + lidocaine (S + L) group and sufentanil (S) group. Patients completed the pain rating scales, including the numeric rating scale (NRS) and verbal rating scale (VRS), 60 min before colonoscopy. All the patients were initially administered sufentanil. In the S + L group, we sprayed a 5 ml solution of lidocaine on the surface of ascending, transverse, descending, and sigmoid colon during colonoscope withdrawal, while 5 ml saline was sprayed in the S group. Follow up was performed 1 day, 3 days, 1 week, 2 weeks, 1 month, and 3 months after colonoscopy, to complete the pain scaling.

Results: A comparison of the NRS and VRS showed that there were no significant differences between the S + L and S groups and within each group ($p > 0.05$).

Conclusions: Local analgesic lidocaine and opioid analgesic sufentanil showed negative efficacy during short-term observation. The opioid receptor blocker sufentanil did not worsen symptoms in patients with CAPS after colonoscopy under general anesthesia in the short term.

[chictr.org.cn, Chinese Clinical Trial Identifier, ChiCTR-IOR-16008187]

Keywords: centrally mediated abdominal pain syndrome, lidocaine, sufentanil, treatment

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Introduction

Centrally mediated abdominal pain syndrome (CAPS) is characterized by abdominal pain that is often severe and continues for more than 6 months. CAPS can impair function across several life domains. It is considered less common than other functional gastrointestinal disorders (FGIDs), with prevalence ranging from 0.5% to 2.1%. Females are 1.5–2 times more susceptible to CAPS than males; the peak age of occurrence is the fourth decade of life.[1,2] CAPS is a complicated heterogeneous condition resulting from physical stimuli and cognitive and emotional factors. If we take lessons from other FGIDs, disorders of gut–brain interaction,[3] peripheral stimulus,[4] and structural changes of responsible

brain functional regions[5] will be related to CAPS. However, unlike irritable bowel syndrome (IBS),[6] intestinal features are largely disconnected in CAPS. Cognitive and emotional features seem to play a more dominant role in the pain experience. Given the severity and chronicity of pain symptoms in patients with CAPS, structural changes in the relevant functional regions of the brain are more likely. If psychological factors amplify the experience of pain, it can provide a rationale for the use of psychological interventions for the management of CAPS. However, present related clinical trials are limited maybe due to the low incidence of CAPS, uncertain efficacy of treatments, and unclear mechanism of CAPS, etc. and not adequate to support the explanation of CAPS by structural or psychological factors.

Previous studies have found that 300 mg intrarectal lidocaine jelly could improve abdominal pain, rectal, and cutaneous pain in patients with IBS. The effects, which occurred within 5–15 min after the onset of treatment, presented for 4 h without side effects; this may be useful in the management of IBS pain symptoms, potentially *via* reduced visceral hyperalgesia and secondary cutaneous hyperalgesia.[7,8] Therefore, we conducted a prospective, double-blinded, randomized controlled trial with the intervention of local anesthetic (lidocaine) and opioid anesthetic (sufentanil) in patients with CAPS. The primary aim was to explore whether the local analgesic (lidocaine) and opioid analgesic (sufentanil) have a short-term effect on CAPS and whether CAPS could be aggravated, during short-term observation, after colonoscopy under general anesthesia, combined with sufentanil. The second aim was to compare the peripheral role and central role in mediating the pain of CAPS, to have a better understanding of its mechanism and to improve treatment methods.

Patients and methods

This was a prospective, double-blinded, randomized controlled trial registered at the Chinese Clinical Trial Registry (www.chictr.org.cn, ChiCTR-IOR-16008187). The trial was a single-center study conducted at West China Hospital, a tertiary medical center in Chengdu, Sichuan, China. The study was approved by the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University (no. 67, 2016). Written informed consent for the study was obtained from all patients.

Patients who presented in our hospital between April 2016 and January 2017 and met the Rome IV criteria of CAPS (after eliminating exceptions or alarm symptoms) based on clinical manifestations and laboratory examinations, including colonoscopy, and who were aged between 18 and 80 years were recruited. Warning symptoms included blood in stools or bloody stools, black stool, or a positive fecal occult blood test, abdominal mass, unexplained weight loss (>4.5 kg), iron-deficiency anemia, family history of colorectal cancer, and family history of inflammatory bowel disease. Patients were excluded if they had not established a diagnosis of CAPS, had organic lesions causing abdominal pain (inflammatory bowel disease, intestinal tumor, colon stenosis, fistula, hemorrhoids, anal fissure, and perianal abscess among others), had contraindications to lidocaine use (allergy to lidocaine, hepatic and renal dysfunction, congestive heart failure, hypotension, cardiac block, pre-excitation syndrome, and pulmonary insufficiency), took drugs that affected lidocaine metabolism (cimetidine, β-blockers, and barbiturates), or were pregnant or lactating. Recruited patients were assessed by anesthesiologists before colonoscopy under general anesthesia, which indicated that anesthesia was achieved by the intravenous administration of sufentanil and propofol. Sufentanil is a type of μ-opioid-receptor blocker used in intravenous anesthesia. Propofol is a type of anesthetic, which produces its anesthetic effects by activating gamma-aminobutyric acid (GABA) receptors. Lidocaine is a commonly used local anesthetic of the amide type with quick effect, wide dispersion, strong penetration, and short duration. It can be absorbed by the intestinal mucosa and combines with voltage-gated sodium channels on the sensory nerve of the submucosal center of the intestinal tract to reduce nerve excitability and increase pain threshold, thereby reducing pain.

We used a specific formula to calculate the sample size:

$$n = \frac{\left(u_{\_} + u_{\beta}\right)^2 \left(1 + 1/k\right) p\left(1 - p\right)}{\left(p_e - p_c\right)^2}$$

$$p(k = 1) = \frac{p_e + k p_c}{1 + k}$$

We expected that the difference in positive rates between p_e of the S + L group and p_c of the S group would be 25%. Taking the bilateral test $\alpha = 0.05$ (bilateral) and $\beta = 0.20$, the sample size of the experimental and control groups was 56 cases. According to the 15% shedding or elimination possibility, the sample size of the two groups increased to 65 cases. We used the random number table generated by SPSS17.0 statistical software to achieve randomization. The double-blind method was used to allocate the patients. Patients were prospectively collected and randomly divided into two groups (S + L group and S group) by the first physician according to the random number table. A nurse who knew the results of the assignment attended the examination and stopped the drug administration when necessary. Finally, the second physician completed the follow up. During the entire process, patients, operators, and the physician completing the follow up did not know the specific patient enrollment type. All the patients completed the basic information registration form, abdominal pain questionnaire, and pain rating scales, including numeric rating scale (NRS) and verbal rating scale (VRS), 30–60 min before colonoscopy. On the NRS, 0 is painless, 1–3 is mild, 4–6 is moderate, and 7–10 is severe. During colonoscopy, a gentle endoscopic approach to the ileocecal part was performed by experienced endoscopists, to minimize discomfort to patients caused by excessive pulling, improper rotation of the endoscope, and excessive gas injection. Patients in both the groups were initially administered with sufentanil (5 μg intravenous injection over 5–10 s) at first. In the S + L group, patients were then sprayed with 5 ml normal saline containing lidocaine on the surface of the ascending, transverse, descending, and sigmoid colon with spraying pipe (altogether 20 ml containing 15 ml saline + 5 ml of 2% lidocaine hydrochloride injection, with a lidocaine concentration of 0.5%, and a total lidocaine content of 100 mg). Patients in the S group were sprayed with 5 ml saline as control. The patients' blood pressure, heart rate, oxygen saturation, and other indexes were closely monitored and recorded at 15 min, 30 min, 45 min after spraying. Clinical follow up was completed by phone calls after 1 day, 3 days, 1 week, 2 weeks, 1 month, and 3 months of colonoscopy under general anesthesia, to complete NRS and VRS for the assessment of patients with abdominal pain. Patients were asked whether they had taken medication, and if they had, then the type of medication, duration of medication, and changes in symptoms after medication, were recorded in detail. Finally, we compared the constituent ratios of different severity degrees between the two groups and within each group according to the NRS and VRS methods. If significant differences were demonstrated, it would be responsible for changes in the constituent ratio caused by local analgesic (lidocaine) or central analgesic (sufentanil), which would need further explanation. (Figures 1 and 2)

Statistical analysis

Continuous variables were expressed as means and standard deviations or as median ranges. Categorical variables were expressed as frequencies and percentages. The differences in parametric variables between the two groups were compared using the Student's *t* test. The chi-squared test or Fisher's exact test was used to compare differences in categorical variables. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS v. 17.0 statistical software (IBM Corp., Armonk, New York, USA).

Results

A total of 130 patients with CAPS who met the inclusion and exclusion criteria were included in this study. Among them, eight patients did not answer the phone during the follow up and fell off. During the follow up, none of the patients took antidepressants to relieve abdominal pain. A total of 122 patients completed the follow up and were included in the outcome analysis (59 patients in the S + L group and 63 patients in the S group). Patients' baseline characteristics in the two groups are shown in Table 1, and there was no significant difference in age [S + L (43.77 ± 11.3) *versus* S (46.79 ± 9.85) $p = 0.3$], sex [S + L (female 66.1%) *versus* S (female 60.32%) $p = 0.508$], NRS (S + L *versus* S $p = 0.987$), and VRS (S + L *versus* S $p = 0.717$). No lidocaine- or sufentanil-related adverse events occurred in any patient.

Changes in abdominal pain after colonoscopy (NRS and VRS method)

Patients were followed up 1 day, 3 days, 1 week, 2 weeks, 1 month, and 3 months after colonoscopy, and the constituent ratio of the corresponding degree of abdominal pain in patients with CAPS was compared according to the NRS and VRS methods. According to the NRS method, there were no significant differences between the

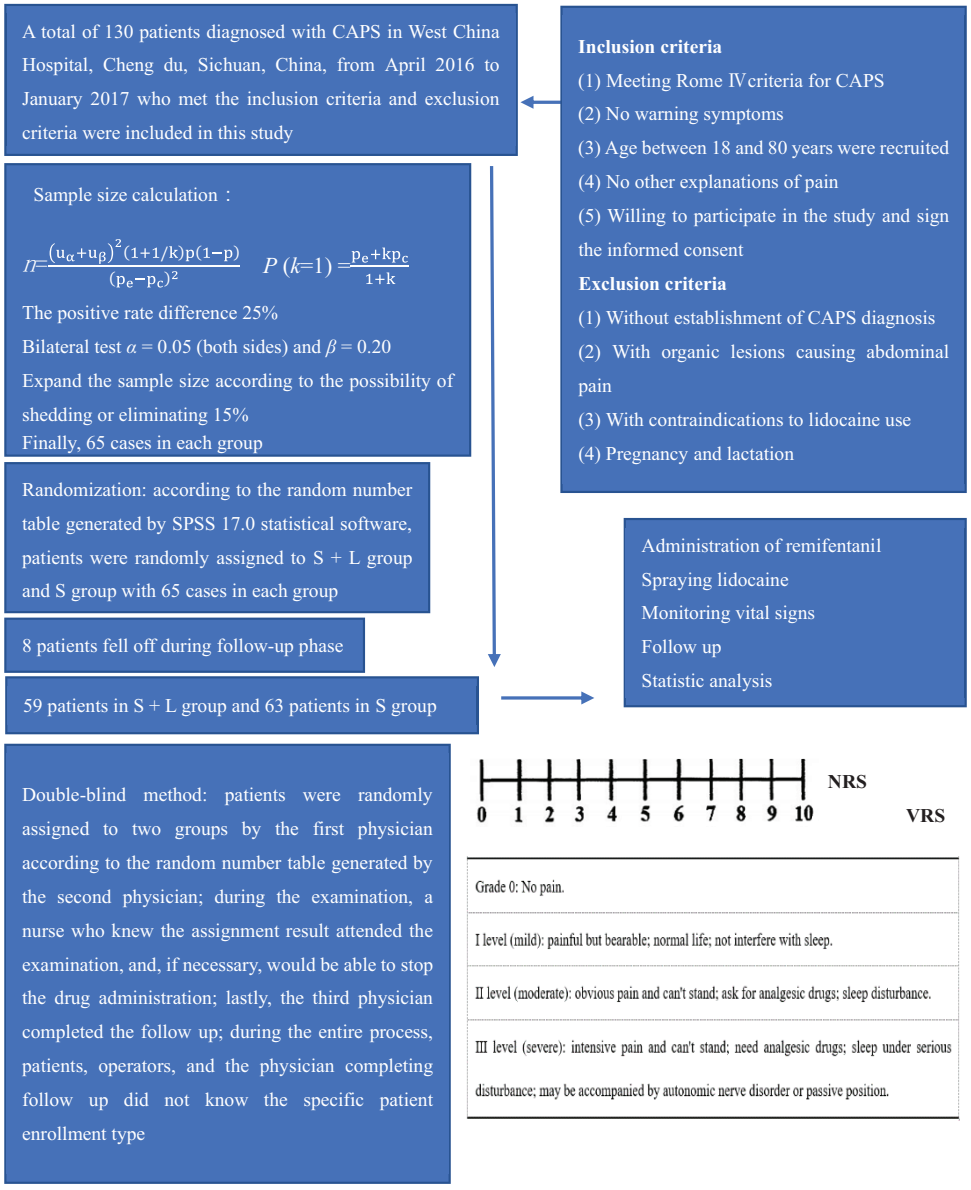

Figure 1. Flowchart of the whole study.
CAPS, centrally mediated abdominal pain syndrome; NRS, numeric rating scale; VRS, verbal rating scale; S, sufentanil; S + L, sufentanil + lidocaine; SPSS, statistical software package for social sciences.

two groups ($p_{1\,day} = 0.936$, $p_{3\,days} = 0.799$, $p_{1\,week} = 0.896$, $p_{2\,weeks} = 0.722$, $p_{1\,month} = 0.877$, and $p_{3\,months} = 0.722$; Table 2). According to the VRS method, there were no significant differences between the two groups ($p_{1\,day} = 0.835$, $p_{3\,days} = 0.992$, $p_{1\,week} = 0.853$, $p_{2\,weeks} = 0.843$, $p_{1\,month} = 0.843$, and $p_{3\,months} = 0.704$; Table 2).

Changes in abdominal pain after colonoscopy in the S + L group (NRS and VRS methods)

Intra-group analysis of abdominal pain before and after colonoscopy was conducted in the S + L group. There were no significant differences as seen in Table 3 (NRS: $p = 0.819$ and VRS: $p = 0.95$).

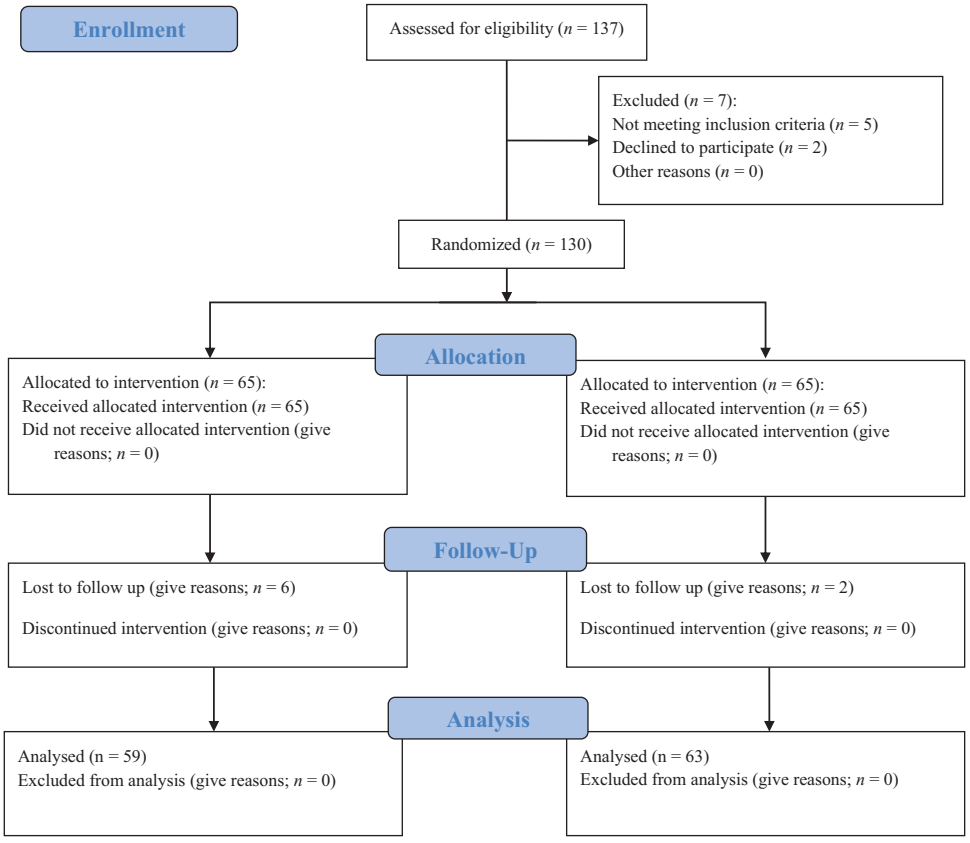

Figure 2. The CONSORT flowchart.

Changes in abdominal pain after colonoscopy in the S group (NRS and VRS methods)

Intra-group analysis of abdominal pain before and after colonoscopy was conducted in the S group. There were no significant differences, as seen in Table 4 (NRS: $p = 0.97$ and VRS: $p = 0.96$).

Small colonic polyps

Small colonic polyps do not cause abdominal pain. Therefore, patients in this study who were detected with polyps (no more than five, <0.5 cm in diameter) during colonoscopy were not excluded. After colonoscopy under general anesthesia, 18 patients in the two groups were found to have a single small colon polyp, and 14 patients had multiple small colon polyps (<5 in number), as shown in Table 5.

Discussion

In this study, we compared the constituent ratio of different severity degrees between the two groups and within each group according to the NRS and VRS methods. Local analgesic lidocaine and opioid analgesic sufentanil showed negative efficacy in a short-term observation.

As patients with CAPS usually have continuous abdominal pain with wide differential, and there is a paucity of definitive tests, colonoscopy is necessary to confirm that no alternative pathology is missed. Therefore, colonoscopy under general anesthesia is a better option for CAPS patients who need repeated or regular colonoscopy examinations, as they can receive a comparably comfortable experience and an increased possibility of careful examination. Sufentanil is commonly used and combined with propofol in colonoscopy under general anesthesia to suppress corresponding central receptors to achieve painlessness, and it is also a kind of μ-opioid receptors blocker.[9] In the management of CAPS, narcotic analgesics are not recommended because of the likelihood of addiction and the possibility of narcotic bowel

Table 1. Patients' baseline characteristics.

	S + L group (59)	S group (63)	*p* value
Age (mean ± SD)	43.77 ± 11.3	46.79 ± 9.85	0.3
Sex (percentage)			0.508
Female	39 (66.1)	38 (60.32)	
Male	20 (33.9)	25 (39.68)	
History of abdominal surgery (%)			
None	40 (67.8)	42 (66.67)	0.975
Once	14 (23.73)	16 (25.4)	
⩾Twice	5 (8.47)	5 (7.94)	
NRS			0.987
Mild (%)	4 (6.78)	4 (6.35)	
Moderate (%)	50 (84.75)	54 (85.71)	
Severe (%)	5 (8.47)	5 (7.94)	
VRS			0.717
Mild (%)	4 (6.78)	4 (6.35)	
Moderate (%)	48 (81.36)	50 (79.37)	
Severe (%)	7 (11.86)	9 (14.29)	

In NRS, 0 is painless, 1–3 is mild, 4–6 is moderate, and 7–10 is severe.
NRS, numeric rating scale; VRS, verbal rating scale; S, sufentanil; SD, standard deviation; S + L, sufentanil + lidocaine.

syndrome and other gastrointestinal (GI) side effects.[10] In our study, no adverse events occurred in any patient. There were no significant differences in the changes in constituent ratio according to the NRS and VRS methods before and after endoscopy, which meant that the patients' symptoms did not worsen. This indicated that in the short-term observation, the μ-opioid receptor sufentanil did not worsen CAPS after colonoscopy under general anesthesia in a short-term observation.

Clinically, lidocaine surface anesthesia is often used for superficial surgery or endoscopic examination of the nose, pharynx, trachea, and urethra, among others. Intrarectal infusion of lidocaine gel has been reported to effectively relieve pain in patients with IBS.[7] Submucosal injection of lidocaine achieved efficacy in controlling postoperative pain after endoscopic submucosal dissection in patients with early gastric cancer.[11] Intraperitoneal and intravenous administration of lidocaine was also effective in alleviating postoperative laparoscopic pain.[12] In our study, a negative effect was demonstrated when local analgesic lidocaine was sprayed in patients with CAPS. And in a previous study, patients with functional abdominal pain syndrome were also found to have normal rectal perceptual thresholds, a kind of visceral sense, which meant they might have normal sensitivity to painful distention.[13] Therefore, it might further indicate a different mechanism of abdominal pain of CAPS. Indeed, physiological visceral afferent input from the gut plays a lesser role in the symptom generation of CAPS, compared with other FGIDs. It differs from IBS and functional dyspepsia related to peripheral events, such as food intake or defecation. No consistent initiating triggers are noted in CAPS, and the central mediation role is dominant, which may further indicate the

Table 2. Patient number changes over time with different degrees of abdominal pain after colonoscopy in the two groups (NRS and VRS).

	S + L group, $n = 59$ (%)	S group, $n = 63$ (%)	NRS p value	S + L group, $n = 59$ (%)	S group, $n = 63$ (%)	VRS p value
1 day			0.936			0.835
Mild	11 (18.64)	11 (17.46)		9 (15.25)	9 (14.29)	
Moderate	43 (72.88)	48 (76.19)		44 (74.58)	47 (74.6)	
Severe	5 (8.47)	4 (6.35)		6 (10.17)	7 (11.11)	
3 days			0.799			0.992
Mild	10 (16.95)	9 (14.29)		7 (11.86)	8 (12.7)	
Moderate	44 (74.58)	49 (77.78)		46 (77.97)	48 (76.19)	
Severe	5 (8.47)	5 (7.94)		6 (10.17)	7 (11.11)	
1 week			0.896			0.853
Mild	9 (15.25)	10 (15.87)		8 (13.56)	8 (12.7)	
Moderate	45 (76.27)	48 (76.19)		44 (74.58)	47 (74.6)	
Severe	5 (8.47)	5 (7.94)		7 (11.86)	8 (12.7)	
2 weeks			0.722			0.843
Mild	7 (11.86)	9 (14.29)		6 (10.17)	7 (11.11)	
Moderate	46 (77.97)	48 (76.19)		46 (77.97)	49 (77.78)	
Severe	6 (10.17)	6 (9.52)		7 (11.86)	7 (11.11)	
1 month			0.877			0.843
Mild	8 (13.56)	9 (14.29)		7 (11.86)	7 (11.11)	
Moderate	45 (76.27)	48 (76.19)		46 (77.97)	49 (77.78)	
Severe	6 (10.17)	6 (9.52)		6 (10.17)	7 (11.11)	
3 months			0.722			0.704
Mild	7 (11.86)	9 (14.29)		6 (10.17)	6 (9.52)	
Moderate	46 (77.97)	48 (76.19)		47 (79.66)	49 (77.78)	
Severe	6 (10.17)	6 (9.52)		6 (10.17)	8 (12.7)	

NRS, numeric rating scale; VRS, verbal rating scale; S, sufentanil; S + L, sufentanil + lidocaine.

possibility of consistent activity of the responsible brain functional region even without peripheral afferent stimulus. On the other hand, if the chronic pain neural circuit is underlying, there is also a possibility of peripheral afferent stimulus of body parts other than the gut, which involves the association between somatogenic pain and visceral pain. For example, a study reported 81% allodynia was found in patients with chronic continuous abdominal pain (CCAP).[14] It can be further explained that if afferent pathways between allodynia and abdominal pain can converge in the posterior horn of the spinal cord or if they can enhance afferent signals, two types of pain will interact with

Table 3. Patient number changes over time with different degrees of abdominal pain after colonoscopy in the S + L group (NRS and VRS).

	Mild (%)	Moderate (%)	Severe (%)	NRS *p* value	Mild (%)	Moderate (%)	Severe (%)	VRS *p* value
Before endoscopy	4 (6.78)	50 (84.75)	5 (8.47)	0.819	4 (6.78)	48 (81.36)	7 (11.86)	0.95
1 day	11 (18.64)	43 (72.88)	5 (8.47)		9 (15.25)	44 (74.58)	6 (10.17)	
3 days	10 (16.95)	44 (74.58)	5 (8.47)		7 (11.86)	46 (77.97)	6 (10.17)	
1 week	9 (15.25)	45 (76.27)	5 (8.47)		8 (13.56)	44 (74.58)	7 (11.86)	
2 weeks	7 (11.86)	46 (77.97)	6 (10.17)		6 (10.17)	46 (77.97)	7 (11.86)	
1 month	8 (13.56)	45 (76.27)	6 (10.17)		7 (11.86)	46 (77.97)	6 (10.17)	
3 months	7 (11.86)	46 (77.97)	6 (10.17)		6 (10.17)	47 (79.66)	6 (10.17)	

NRS, numeric rating scale; VRS, verbal rating scale; S + L, sufentanil + lidocaine.

Table 4. Patient number changes over time with different degrees of abdominal pain after colonoscopy in the S group (NRS and VRS).

	Mild (%)	Moderate (%)	Severe (%)	NRS *p* value	Mild (%)	Moderate (%)	Severe (%)	VRS *p* value
Before endoscopy	4 (6.35)	54 (85.71)	5 (7.94)	0.97	4 (6.35)	50 (79.37)	9 (14.29)	0.96
1 day	11 (17.46)	48 (76.19)	4 (6.35)		9 (14.29)	47 (74.6)	7 (11.11)	
3 days	9 (14.29)	49 (77.78)	5 (7.94)		8 (12.7)	48 (76.19)	7 (11.11)	
1 week	10 (15.87)	48 (76.19)	5 (7.94)		8 (12.7)	47 (74.6)	8 (12.7)	
2 weeks	9 (14.29)	48 (76.19)	6 (9.52)		7 (11.11)	49 (77.78)	7 (11.11)	
1 month	9 (14.29)	48 (76.19)	6 (9.52)		7 (11.11)	49 (77.78)	7 (11.11)	
3 months	9 (14.29)	48 (76.19)	6 (9.52)		6 (9.52)	49 (77.78)	8 (12.7)	

NRS, numeric rating scale; VRS, verbal rating scale; S, sufentanil.

each other. It means visceral pain can be presented as somatogenic pain, and vice versa. Under this condition, spraying lidocaine on the skin surface may be effective in treating visceral pain. However, the patients in our study did not complain of somatogenic pain, and no apparent causes of abdominal pain were found. In addition, the sensory afferent pathway of allodynia can be blocked by adequate opioid analgesics with a high risk of addiction. Our results showed that the intravenous opioid analgesic sufentanil had negative efficacy, which also indicated the low possibility of peripheral afferent stimulus and the specific mechanism of CAPS distinct from the general CCAP. The negative effect of local analgesic lidocaine could confirm the dominant role of psychological intervention and antidepressants in the management of CAPS. Other ratiocinations include altered related brain functional regions, altered pain-descending pathways, and established central sensitization modulation. It is well known that electric defibrillation can eliminate the electrical activity of all myocardial cells and restore normal electrical activity. Both peripheral and central analgesic intervention could silence the electric transduction of the peripheral and central nerves. Both lidocaine and sufentanil had negative effects, which may also confirm the continuous stimulus from the higher-level center of brain. Therefore, therapies including psychological intervention and antidepressants

would be more effective[1,15] than single meditation therapy or peripheral meditation therapy. Meanwhile, a well-developed patient–physician relationship and an effective augmentation approach combined with psychological intervention are essential to help patients correctly recognize and establish new synaptic connections. Regarding psychological intervention for other FGIDs, gut–brain interaction has been shown as dominant.[3] Gut-directed hypnotherapy is recommended and is being increasingly applied to patients with IBS, which can achieve an effect similar to that of the low fermentable oligosaccharide, disaccharide, monosaccharide, and polyol diet; it can further be applied to inflammatory bowel disease to a lesser extent *via* its potential mechanism of action on the brain–gut axis.[16–18] Cognitive–behavioral therapy delivered by telephone or internet has also been shown superior to the usual treatment methods and is recommended for treating IBS.[19,20] Four classes of psychotherapy hold the most promise in CAPS: cognitive–behavioral therapy, psychodynamic interpersonal therapy, mindfulness/acceptance-based therapies and hypnotherapy,[1] although related clinical research is lacking. Due to the negative effects of lidocaine and sufentanil, psychotherapy is indispensable for the treatment of CAPS. It is also reasonable to hypothesize that a more significant curative effect may be achieved when psychotherapy is combined with antidepressants because the mechanism of CAPS is different from IBS, as it is related to the central brain functional area rather than the gut.

In our study, the overall polyp detection rate was 26% in patients with CAPS. The general polyp detection rate in other studies was less than 20%.[21,22] There are several possible reasons, such as age, family history, eating habits, alcohol use, smoking, and bowel habits, among others. Currently, there is little literature related to polyps and CAPS. No adverse effects were observed in the short term (3 months); this indicates that colonoscopy under general anesthesia could be performed when patients with CAPS, who are required to undergo colonoscopy examination to detect polyps and require surveillance after polyp resection, prefer colonoscopy under general anesthesia.

This study has a few limitations. During colonoscopy, we did not analyze the role of propofol, which is a general anesthetic used for induction of anesthesia. In the S + L group, the possible combination effect of lidocaine and sufentanil was not considered, because of their different pharmacological mechanisms and the negative effect of sufentanil. The possible effect of lidocaine at the second hour or fourth hour after application of the spray was not evaluated. We administered an adequate dose comparable with that of post-abdominal surgery because there is damage to the intraperitoneal tissue after surgery. Subgroups with different doses of lidocaine were not established, which was further restricted by the sample size. We did not restrict the practice of meditation when any patient recruited in our study had that habit. Some possible mental diseases have not been described in detail. We ensured that lidocaine was completely sprayed onto the surface of the colon to enable its fast absorption; however, it was difficult to ensure that all the lidocaine was absorbed. With regards exclusion criteria, we excluded patients who had organic lesions causing abdominal pain (inflammatory bowel disease, intestinal tumor, colon stenosis, fistula, hemorrhoids, anal fissure, and perianal abscess). However, we did not further conclude and describe these excluded patients. Further research on patients with both CAPS and organic lesions is required to explore the possible characteristics. We did not list anterior cutaneous nerve entrapment syndrome as an exclusion criterion; it is a kind of chronic abdominal pain that is mainly differentiated from CAPS and can be aggravated by any type of movement or intense use of abdominal muscles due to the anatomic position of the anterior cutaneous nerve.

Table 5. Small colonic polyps.

	S + L group ($n = 59$)	S group ($n = 63$)	*p* value
Colonic polyps	*n* (%)	*n* (%)	0.353
None	43 (72.88)	47 (74.6)	
Single	7 (11.86)	11 (17.46)	
Multiple	9 (15.25)	5 (7.94)	

S, sufentanil; S + L, sufentanil + lidocaine.

Conclusion

First, local analgesic lidocaine and central analgesic sufentanil showed negative efficacy in the short-term observation. Second, no adverse events were found in the two groups,

which indicated that the opioid receptor blocker sufentanil could not worsen the symptoms of patients with CAPS after receiving colonoscopy under general anesthesia in a short-term observation. Third, peripheral and central analgesic intervention by lidocaine and sufentanil were ineffective, which may indicate the potential dominant role of continuous central mediation and mental therapy in the management of CAPS.

Author contribution

Bing Hu, Hang Yang, and Honglin Chen designed the randomized controlled trial. Honglin Chen recruited patients. Hang Yang and Honglin Chen drafted the manuscript. And Bing Hu reviewed and revised the manuscript.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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