The efficacy of acupressure in managing opioid-induced constipation: Single-blind a randomized controlled study

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Abstract

Purpose

Opioid-induced constipation is one of the heath problems with a negative impact on the quality of life. This randomized-controlled trial aimed to investigate the effects of acupressure therapy on the management of opioid-induced constipation.

Methods

The trial was conducted on 140 patients, who were assigned to the acupressure (n = 70) and the control groups (n = 70). In addition to routine care, patients in the acupressure group received 8-min acupressure from the Zhongwan (CV12), Guanyuan (CV4) and Tianshu (ST25) acupoints once a day for 4 weeks. The outcomes included Defacationa Diary (DD), Visual Analog Scale Questionnaire (VASQ) and Patient assessment of constipation quality of life questionnaire (PAC-QOL).

Results

DD scores obtained by the acupressure and the control groups. There was a statistically significant difference between the acupressure and control groups in terms of stool consistency (2.22 ± .49 vs 1.80 ± .55) (p = 0.001), straining (1.98 ± .71 vs 2.91 ± .37) (p = 0.001), incomplete evacuation (0.37 ± .29 vs 0.61 ± .43) (p = 0.001), stool amount (0.93 ± .14 vs .95 ± .20) (p = 0.001) and the number of defecations (0.70 ± .22 vs 0.46 ± .29), (p = 0.001) measured at the fifth week. Besides, with the exception of stool amount, there was a statistically significant increase in the DD scores obtained by the acupressure group between the first and the fifth weeks. Inter-group comparison of the pre-test and post-test scores showed that acupressure group obtained statistically significantly higher scores from the PAC-QOL (p = .0001).

Conclusions

Findings of this trial suggested that 4-week acupressure was an effective way to improve the quality of life and reduce both subjective and objective constipation symptoms in patients with opioid-induced constipations.

Introduction

Opioid-induced constipation, which occurs as a result of a decrease in intestinal motility after the initiation of opioid therapy, increase in rectal sphincter tone or indifference to the stimulations of rectum related with defecation reflex is one of the important health problems with a negative impact on the quality of life [1, 2]. It may require medication change or decrease in opioid dose, which, in turn, may influence the effectiveness of therapy. The prevalence of opioid-related constipation is 39.4% [3].

Although, informing the patients about constipation, and the suggestions to increase the consumption of fibrous food, water intake, physical exercise and abdominal massage have all been suggested, none of the existing studies proposed an effective method to manage opioid-induced constipation [4]. Costs of pharmacological drugs such as laxatives and the consequences of inappropriate use of laxatives, including, fluid imbalances, loss of electrolytes and disturbances of acid-base metabolism, bring the need for non-pharmacological methods [5]. One of the methods to prevent constipation is acupressure.

Acupressure is the application of pressure or localized massage to specific sites on the body to reduce pain, maintain relief and avoid nausea or constipation [6]. Proper acupressure massage promotes gastrointestinal motility and digestive juice secretion via conduction reflex of nerves and meridians [7]. The effectiveness of acupressure has been reported by various studies [8–12]. Randomized-controlled trial of Shin and Park (2018) on patients with breast cancer found that auricular acupressure, which was received once a week for 6 consecutive weeks, resulted with significant improvements in stool form and the quality of life and reduced the constipation-assessment scores [8]. Patients with advanced cancer in the study of Wang et al. (2019) received an 8 minutes acupressure treatment for 3 consecutive days from 3 acupoints, namely, Zhongwan (CV12), Guanyuan (CV4) and Tianshu (ST25). Significant improvements in the symptoms of constipation, including colonic motility, straining during defecation, hard stools, sensation of incomplete evacuation and anorectal obstruction were observed for the intervention group (9).

Despite the existence of various studies on the effectiveness of acupressure on the management of constipation in different patient groups [8–12], no study on the management of opioid-induced constipation has been conducted yet. Consequently, this study aims to evaluate the effectiveness of acupressure on the management of opioid-induced constipation.

Methods

Study design and participants

This randomized-controlled trial was conducted in the algology clinic of a university hospital in Istanbul between August 2020 and June 2021. Registered to the Clinical Trials with the number ‘NCT 04876508’, the study conformed fully with the guidelines of the Consolidated Standards of Reporting Trials (CONSORT) Checklist (Fig. 1).

Patients diagnosed with constipation, who were at the age of 18 years and above, agreed to participate, received opioid treatment for at least two weeks, and could receive oral feeding were included to the study. Patients with communication or cooperation problems, severe thrombocytopenia (< 50.000/µl), gastrointestinal tumor, intraabdominal infection, irritable bowel syndrome, intestinal obstruction, inflammatory bowel disease, history of abdominal hernia, bowel cancer or abdominal surgery, and psychiatric problems, including delirium, anxiety, depression or panic attack, were excluded from the study.

Sample size was calculated with G Power (version 3.1.9). Sample size for 0.5 effect size and 0.05 error level was 57 participants for each group. Sample size calculation was conducted in accordance with one of the existing studies in the literature [9]. The power for the sample size was 95.1%. Given the possibility of defection, we assigned 70 participants for each group.

Data Collection Tools

Patient Information Form

Comprised of 15 questions, this form included questions on socio-demographic characteristics, diagnosis, medications, laxative consumption, daily fluid consumption, daily physical exercise, opioid usage, weekly nutrition diary, movement/activity level, fiber intake and defecation.

Defecation Diary

Prepared by Pamuk et al. (2003), Defecation Diary (DD) measured the weekly levels of straining, incomplete evacuation, < 3 defecation/week and stool consistency for five weeks [13]. For each patient, the number of weekly defecations was obtained from the diary, and for each symptom, total score in one week was divided to the number of defecations in one week, the results of which provided the mean score for each symptom for each defecation.

Visual Scale Analog Questionnaire

Prepared by Pamuk et al. (2003), Visual Analog Scale Questionnaire (VASQ) had six items on the symptoms of constipation, including the frequency of stools, stool consistency, straining and incomplete evacuation. Participants were asked to daily respond the same items by marking a score between 0 and 10. A symptom was defined to be present when it was scored a 3 on the VASQ. Daily scores obtained from the VASQ were summed for each item to calculate the weekly mean VASQ score.

Patient Assessment of Constipation Quality of Life Questionnaire

Patient assessment of constipation quality of life questionnaire (PAC-QOL) was developed by Marquis et al. (2005) to measure the effects of opioid-induced constipation on daily activities and the quality of life [14]. Validity and reliability of the Turkish version of the PAC-QOL was determined by Bengi et al. (2015). The scale had four subscales, namely, physical discomfort, psychosocial discomfort, worries and concerns and satisfaction. Higher scores obtained from the scale indicated the lower quality of life [15]. Cronbach's alpha of the PAC-QOL during the first and the fifth weeks of our study were 0.91 and 0.94, respectively.

Procedures

A total of 140 patients participated in the study. Patients were assigned to the acupressure (n = 70) or the control group (n = 70) using a computer-generated randomization list prepared by the researcher.

During the first meeting, which took about 25–30 minutes, we obtained information about fiber intake, daily fluid consumption, diet restrictions and constipation by using the patient information form. We used the PAC-QOL to evaluate the responses on the quality of life related with constipation. Medical information, including diagnosis of disease and treatment plan, was obtained via patient records.

All participants were followed by the researcher for one week without any intervention. During the first week, all participants were asked to consume normal food and beverages and continue stool softeners, such as laxatives. All participants were asked to complete the DD and the VASQ after each defecation during the first week. Following the first week, we conducted face-to-face interviews with the patients visiting the clinic.

At the beginning of the second week, participants in the acupressure (i.e. intervention) group underwent a 15-min acupressure training session administered by the researchers. To standardize and calibrate the process, one of the researchers taught the participants of the acupressure group to self-administer the acupressure methods and asked the participants to roll each acupuncture points for two minutes. Application of acupressure started with the application of Zhongwan (CV12), Guanyuan (CV4) and Tianshu (ST25) acupressure points. CV12 was on the midline, 4 cun superior to the umbilicus. CV4 was on the midline, 3 cun inferior to the umbilicus. ST25 was 2 cun lateral to the midline at the level of the umbilicus (16]. We applied 3–5 kg firm pressure with the fingertips in a circular motion at a speed of two circles per second for a duration of two minutes per acupoint. A one-minute rest was applied before moving to the next acupoint. Acupressure treatment lasted for 8 minutes. A weighing scale was used to measure the correct amount of finger pressure necessary for the acupressure treatment. Participants in the acupressure group received acupressure at home, work, or the clinic. Following the training, participants were instructed to perform 8-min acupressure once a day for four weeks.

Participants in the control group received routine treatment and were asked to complete the DD and the VASQ on a weekly basis over a course of four weeks. Assessments lasting 20–25 min were held with the patients once a week, either face-to-face or via telephone. Once the study was completed, all participants were asked to complete the PAC-QOL again. Each patient was evaluated at least 5 times during the trial. During these evaluations, participants were asked to report and bring the results of the evaluation forms requested to be completed at home to the clinic.

Data Analysis

Number, percentage, mean and standard deviation were used for descriptive statistical analysis. To compare descriptive characteristics of the control and acupressure groups, we used Pearson's Chi-square and Fischer's Exact test for categorical variables and independent samples T-test and Mann-Whitney U test for numerical variables. Frequency of constipation in the control and acupressure groups was analyzed with Pearson's Chi-square analysis. Difference between the groups in terms of the scores

obtained from the DD, VASQ and PAC-QOL was analyzed using independent T-test and Mann-Whitney U test. Mean scores obtained during the first and the fifth weeks were compared with dependent sample t-test and Wilcoxon signed-rank test. Mean scores obtained from the DD were analyzed with independent samples T-test, one-way analysis of variance and Kruskal-Wallis test. Skewness and Kurtosis values and Kolmogorov-Smirnov test were used to evaluate whether the variables followed a normal distribution. Statistical significance was set at $p < .05$.

Results

The trial started with 292 participants and concluded with 140 participants due to the exclusion of some of the participants for various reasons mentioned in Fig. 1. No negative events related with acupressure were observed. Sociodemographic and clinical characteristics of the participants in the acupressure and the control groups were similar (Table 1).

Table 1
Sociodemographic and clinical characteristics of the groups.

	Acupressure (n = 70)		Control (n = 70)			
	Min.-Max.	± SD	Min.-Max.	± SD	test	p
Age	18–90	60.93 ± 14.05	21–90	60.22 ± 12.81	t: 0.30	0.75
	n	%	n	%	χ^2	p
Gender						
Female	20	28.6	32	45.7	4.406	0.54
Male	50	71.4	38	54.3		
Marital Status						
Single	13	18.6	10	14.3	0.468	0.649
Married	57	81.4	60	95.7		
Education						
Illiterate	9	12.9	10	14.3	8.126	.149
Literate	7	10	8	11.4		
Primary school graduate	32	45.7	35	50.0		
Secondary school graduate	12	17.1	6	8.6		
High school graduate	8	11.4	3	4.3		
University graduate	2	2.9	8	11.4		
Working status						
Employed	7	10.0	29	41.4	2.146	0.59
Unemployed	63	90.0	41	58.6		
Last day of defecation						
Day 0 (Same day)	13	18.6	15	21.4	2.541	.637
1 day ago	19	27.1	16	22.9		
2 days ago	30	42.9	32	45.7		
8–10 days ago	8	11.4	7	10.0		
Diet restriction						

	Acupressure (n = 70)		Control (n = 70)			
Yes	17	24.3	19	27.1	.150	.699
No	53	75.7	51	72.9		
Fiber intake						
Yes	33	47.1	37	52.9	1.884	.170
No	37	52.9	33	47.1		
Daily fluid consumption						
10 glasses and over	21	30.0	22	31.4	.291	.865
6–9 glasses	35	50.0	32	45.7		
≤ 5 glasses	14	20.0	16	22.9		
		SD		**SD**	**t**	**p**
ECOG Performans Skoru	3.63	1.01	3.58	.91	.437	.662
Medical Diagnosis						
Lung cancer		39	55.7	35	50.0	
Genitourinary System Cancers		13	18.6	14	20.0	
Breast Cancer		4	5.7	6	8.6	
Bone Cancer		5	7.1	5	7.1	
Hematological Cancers		3	4.3	7	10.0	
The sarcoma of soft tissue		6	8.6	3	4.3	

Table 2 showed the findings on the DD scores obtained by the acupressure and the control groups. There was a statistically significant difference between the acupressure and control groups in terms of stool consistency (2.22 ± .49 vs 1.80 ± .55) (p = 0.001), straining (1.98 ± .71 vs 2.91 ± .37) (p = 0.001), incomplete evacuation (0.37 ± .29 vs 0.61 ± .43) (p = 0.001), stool amount (0.93 ± .14 vs .95 ± .20) (p = 0.001) and the number of defecations (0.70 ± .22 vs 0.46 ± .29), (p = 0.001) measured at the fifth week. Besides, with the exception of stool amount, there was a statistically significant increase in the DD scores obtained by the acupressure group between the first and the fifth weeks.

Table 2
Defecation diary scores between the acupressure and control group.

Weekly defecation diary score		Acupressure (n = 70)	Control (n = 70)		
		±SD	**±SD**	**t* / U**	**p**
Stool amount	1st week	.96 ± .13	.91 ± .21	U: 2113.5	.036
	2 nd week	.94 ± .22	.99 ± .30	U: 2078.5	.016
	3rd week	.90 ± .21	.98 ± .35	U: 2117.0	.028
	4th week	.95 ± .16	.96 ± .26	U: 2062.0	.014
	5th week	.93 ± .14	.95 ± .20	U: 2000.5	.006
	1st vs. 5th week Z	*− .115*	*1.820*		
	p	*.909*	*.089*		
Stool consistency	1st week	1.40 **±** .55	1.45 **±** .61	t: 4.991	.667
	2 nd week	1.41 ± .56	1.54 **±** .60	t: .778	.796
	3rd week	1.67 ± .68	1.61 **±** .67	t: − .340	.734
	4th week	2.24 ± .50	1.79 **±** .58	t: 5.670	.000
	5th week	2.22 ± .49	1.80 **±** .55	t: 5.444	.000
	*1st vs. 5th week t***	*-10.762*	*2.735*		
	p	*.000*	*.325*		
Straining	1st week	3.16 ± .73	2.90 ± .95	t: 1.846	.067
	2 nd week	3.15 ± .72	2.88 ± .90	t: 1.801	.074
	3rd week	2.76 ± .81	2.94 ± .88	t: − .926	.356
	4th week	2.04 ± .73	2.89 ± .98	t: -6.018	.000
	5th week	1.98 ± .71	2.91 ± .37	t: -6.559	.000
	*1st vs. 5th week t***	*11.460*	*1.428*		
	p	*.000*	*.756*		
Incomplete evacuation	1st week	.79 ± .28	.72 ± .40	t: 1.332	.185
	2 nd week	.78 ± .27	.74 ± .38	t: 1.271	.206

t*: t-test in dependent groups; t **: t -test in independent groups, Z: Wilcoxon test, U: Mann Whitney U test

	3rd week	.63 ± .33	.53 ± .38	t: -1.397	.165
	4th week	.39 ± .30	.54 ± .32	t: -5.607	.000
	5th week	.37 ± .29	.61 ± .43	t: -5.903	.000
	*1st vs. 5th week t***	*9.139*	*.721*		
	p	*.000*	*.453*		
Number of defecations	1st week	.45 ± .13	.46 ± .27	U: 2273.5	.416
	2 nd week	.44 ± .12	.45 ± .22	U: 2332.0	.587
	3rd week	.54 ± .17	.51 ± .26	U: 1672.0	.001
	4th week	.67 ± .20	.45 ± .19	U: 698.5	.000
	5th week	.70 ± .22	.46 ± .29	U: 697.0	.000
	*1st vs. 5th week t***	*-6.414*	*2.000*		
	p	*.000*	*.069*		

t*: t-test in dependent groups; t **: t -test in independent groups, Z: Wilcoxon test, U: Mann Whitney U test

Figure 2 demonstrated the comparison of the weekly mean scores obtained from the VASQ and inter-group comparison for the first and the fifth weeks. Compared to the control group, there was a statistically significant decrease in constipation (5.52 ± 1.82 vs 7.62 ± 2.04) ($p < 0.001$), straining (5.14 ± 1.82 vs 7.17 ± 2.31) ($p < 0.001$), pain (3.12 ± 1.97 vs 5.01 ± 2.81) ($p < 0.001$), feeling of fullness in the rectum (3.31 ± 1.60 vs 3.95 ± 2.14) ($p = 0.047$), and the severity of gas (4.34 ± 1.76 vs. 7.91 ± 1.75) ($p < 0.001$) in the acupressure group in the fifth week. However, there was no statistically significant difference between the two groups in terms of the severity of incomplete evacuation (4.15 ± 1.80 vs. 4.48 ± 2.49) ($p = 0.484$).

Comparison of the PAC-QOL scores obtained by the acupressure and control groups in Table 3 revealed that pre-test scores were similar but post-test scores of the acupressure group were statistically significant than the control group (60.65 ± 9.68 vs 82.00 ± 14.00) ($p = 0.001$). (Table 3). Inter-group comparison of the pre-test and post-test scores showed that acupressure group obtained statistically significantly higher scores from the PAC-QOL ($p = .0001$). However, no significant improvement was observed in the control group. Finally, we did not observe any adverse events during the study.

Table 3
PACQLQ scores between the acupressure and control group.

PACQLQ Subscales			Pre-test	Post-test		
		Groups	**± SD**	**± SD**	**t***	**p**
The Patient Assessment of Constipation Quality of Life (PACQLQ)		Acupressure	76.14 ± 10.62	60.65 ± 9.68	19.03	.0001
		Control	74.81 ± 12.77	82.00 ± 14.00	-11.93	.0001
		*t***	*.134*	*-10.486*		
		p	*.524*	*.0001*		
Subscales	Physical Discomfort	Acupressure	11.83 ± 2.24	8.77 ± 2.03	20.67	.0001
		Control	11.40 ± 2.20	12.55 ± 2.15	-6.76	.0001
		*t***	*.639*	*-10.691*		
		p	*.241*	*.0001*		
	Psychosocial Discomfort	Acupressure	21.32 ± 4.35	15.91 ± 4.08	16.88	.0001
		Control	21.14 ± 5.06	25.08 ± 4.82	-14.06	.0001
		*t***	*.233*	*-12.131*		
		p	*.816*	*.0001*		
	Anxiety	Acupressure	29.64 ± 5.35	21.97 ± 5.32	14.98	.0001
		Control	28.67 ± 6.43	31.28 ± 6.12	-12.24	.0001
		*t***	*.971*	*-10.368*		
		p	*.333*	*.0001*		
	Satisfaction	Acupressure	13.32 ± 3.35	12.05 ± 3.12	-3.83	.0001
		Control	13.60 ± 2.97	13.14 ± 2.83	1.46	.267
		*t***	*− .506*	*4.136*		

t*: t-test in dependent groups; t **: t -test in independent groups.

	p	*.613*	*.0001*	

t*: t-test in dependent groups; t **: t -test in independent groups.

Discussion

Based on our literature review, we may suggest that this study was the first randomized-controlled trial with the highest sample size on the effectiveness of acupressure on opioid-induced constipation. We found that acupressure was an effective method to manage opioid-induced constipation and improve the quality of life.

Five-week DD records of the participants using opioid in our study revealed a significant improvement in terms of stool amount and consistency, straining, incomplete evacuation and the number of defecations. Similarly, the VASQ scores obtained by the acupressure group indicated a significant improvement in the symptoms of constipation in the fifth week. Besides, acupressure therapy improved the quality of life, which was measured by the PAC-QOL.

Despite the limited number of studies in the literature, existing studies reported the positive effects of acupressure therapy on the management of constipation. Similar to our findings, the study of Wang et al. (2019) on the effects of acupressure on constipation in patients with advanced cancer reported that a 8-minutes acupressure therapy for 3 consecutive days on Zhongwan (CV12), Guanyuan (CV4), and Tianshu (ST25) acupoints alleviated the symptoms of constipation [9]. In another randomized control trial on patients with breast cancer, auricular acupressure was applied to seven auricular acupoints for six weeks. The study found that auricular acupressure was an effective method to relieve constipation in patients with breast cancer receiving chemotherapy [8]. Meta-analysis of Lee et al. (2010) on chronic functional constipation in 15 randomized-controlled trials found that moxibustion was as effective as medical therapy to change intestinal motility and improve the quality of life [17]. Wong et al. (2015) studied the effects of SP6 acupressure on pain and menstrual distress in young women with dysmenorrhea and found that SP6 acupressure had an immediate pain-relieving effect for dysmenorrhea and was effective in relieving both the pain and menstrual distress resulting from dysmenorrhea [18].

Studies on acupuncture suggest that contractility of distal colon and vagal and sympathetic stimuli may stimulate colonic motility [19, 20]. Given the fact that acupressure is based on the stimulation of basic acupuncture points and some of the patients are unconformable with acupuncture pins, we may conclude that acupressure is a more comfortable method of constipation management. Besides, we observed that the application of acupressure was easy to be learned and applied by the participants in different environments.

Conclusion

Findings of this trial suggested that 4-week acupressure was an effective way to reduce both subjective and objective constipation symptoms in patients with opioid-induced constipation. Besides, acupressure

improved the quality of life in the participants. Therefore, we suggest that acupressure may be used as a non-invasive method to manage constipation patients with opioid-induced constipation.

Declarations

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Conflicts of interest: The authors declare that they have no conflict of interest.

Availability of data and material: Data are available upon request from the corresponding author.

Code availability: N/A

Authors' contributions: D.Y.: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Validation, Visualization,Writing - review & editing. V.K.: Conceptualization, Data curation, Methodology, Validation, Visualization, Writing - review & editing. G.K.T.: Data curation, Methodology, Visualization, Writing - review & editing. All authors have read and approved the final manuscript.

Ethics approval: We obtained approval from University Ethics Committee (Number 2020/16). All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Constent to participate: Informed consent was obtained from all individual participants included in the study.

Consent for publication: N/A

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Figures

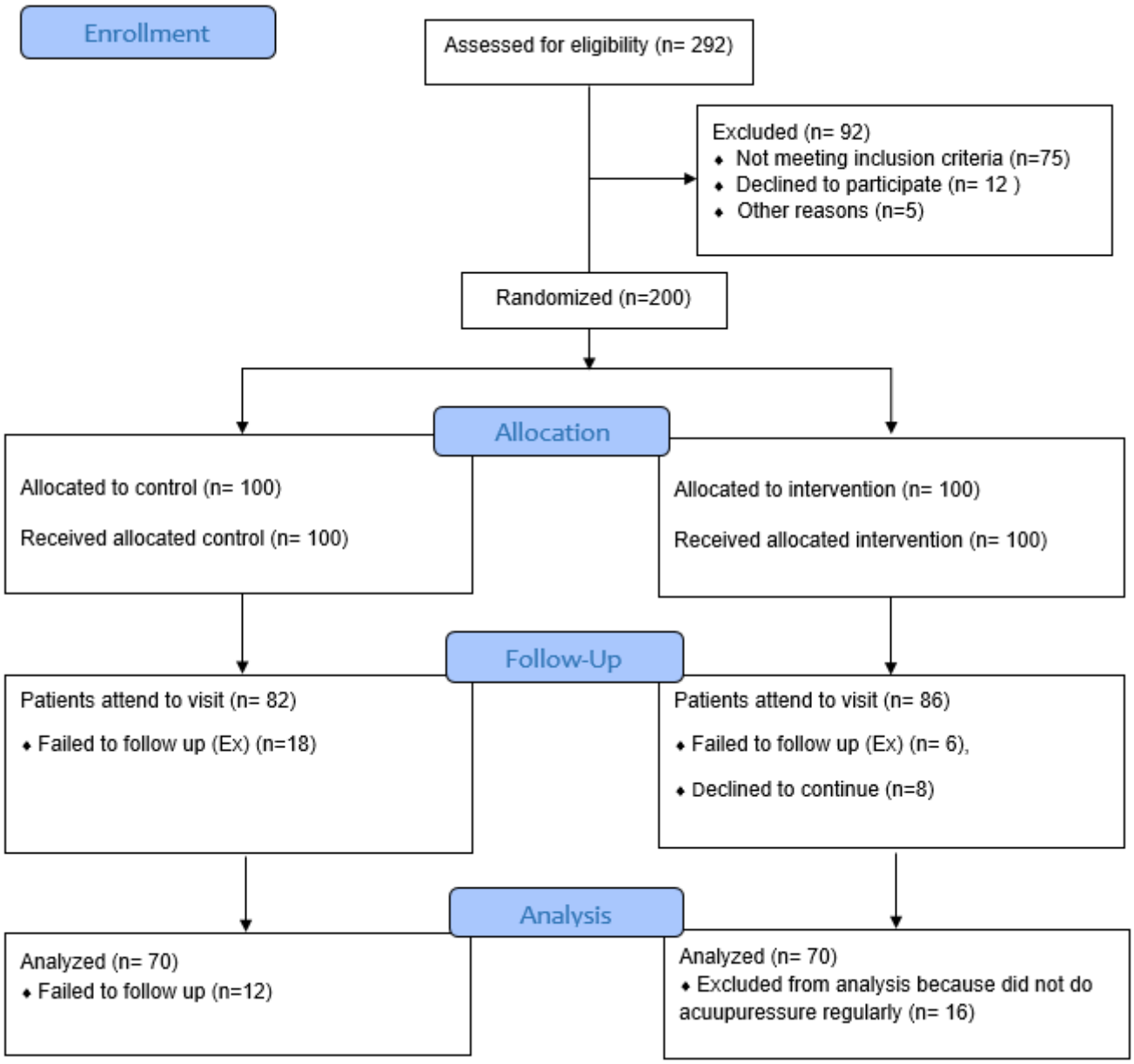

Figure 1

Consort flow diagram

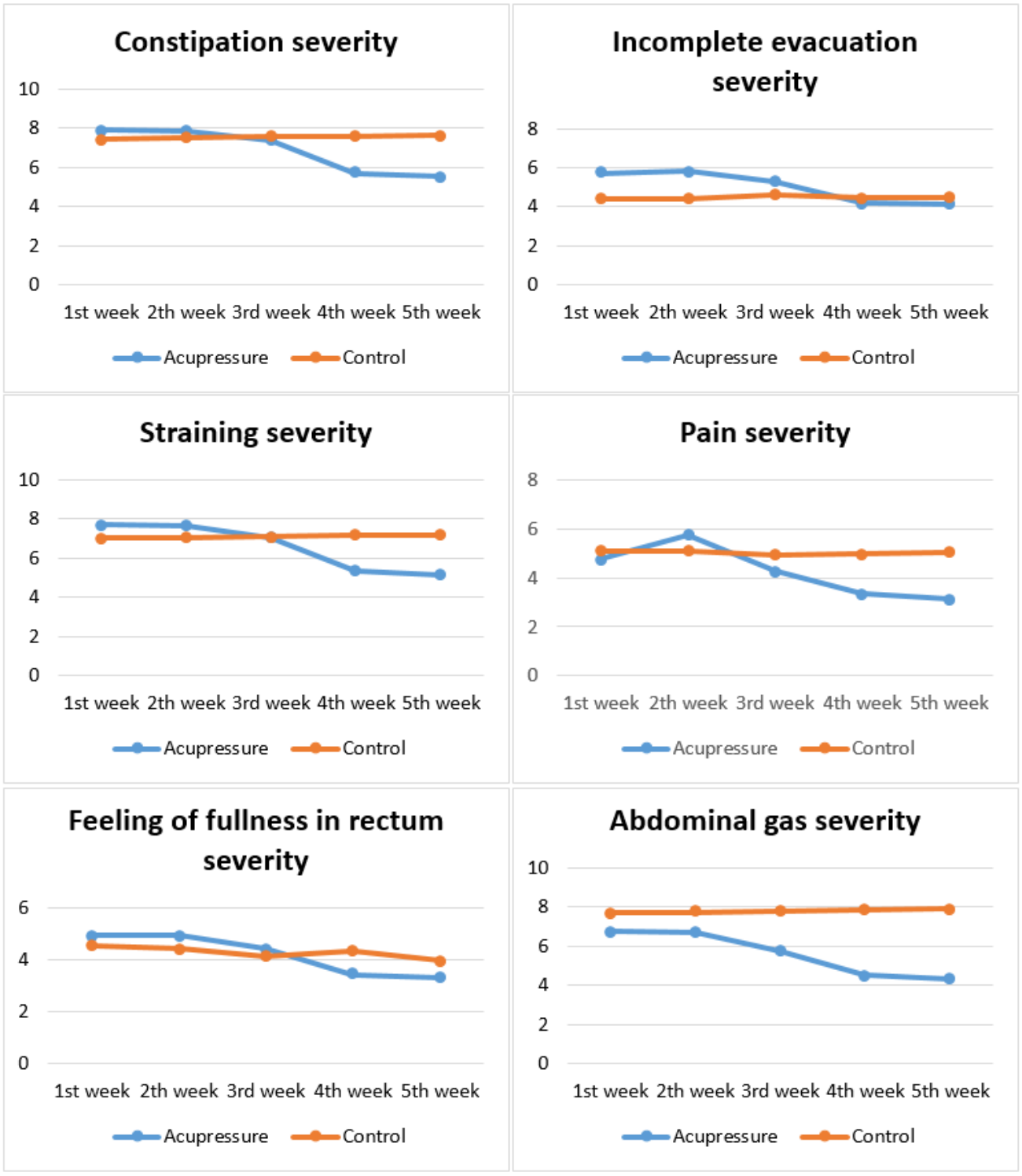

Figure 2

Mean VAS score.