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Protocol

Osteopathy in the treatment of irritable bowel syndrome symptoms in adults: study protocol for a randomized controlled trial

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ABSTRACT

Background: Osteopathy is chosen by patients as a treatment for irritable bowel syndrome (IBS) but evidence for its effectiveness is poor. The purpose of this study is to evaluate the effectiveness of osteopathy for IBS at 1 month follow-up in IBS adults.
Methods: Design: a multicenter, two-group parallel, randomized, double-blind, placebo-controlled trial. Inclusion criteria: adult IBS patients (Rome IV criteria) with similar baseline symptom severity, and comparable expectations of active and sham osteopathic treatment before. Treatment group included active osteopathic treatment. Control group included sham osteopathic treatment. Randomization was in allocation ratio 1:1. Assessment time was carried as inclusion and baseline assessment (day-1; initial visit V0), day 8, day 15 and follow-up (1 month and 3 months), treatments (day 0, day 8, day 15). Primary endpoint was effectiveness at 1 month (response to treatment defined as at least a 50-point reduction in IBS severity on the IBS-symptom severity score). Secondary endpoint was effectiveness at 3 months (response to treatment) and changes in total IBS quality of life scores up to 3 months. Sample size was 404 individuals to achieve 90% power to detect a 15% difference in treatment response at 1 month between the two groups (20% of patients lost to follow-up).
Conclusions: The two-group parallel, randomized, double-blind, placebo-controlled trial (sham therapy) in which the expectations and experiences of patients in the control group are comparable to the experimental group is the most accurate design for demonstrating the effectiveness of osteopathy on IBS symptoms. Future studies could use such a design to assert causality.
Trial registration: The trial has been registered in clinicalTrials.gov. Registration number: NCT05230277; registered on 7 February 2022.

Keywords: Osteopathy, Sham therapy, IBS symptoms, Randomized controlled trial

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional digestive disorder whose clinical picture is dominated by abdominal pain associated with changes in stool consistency and/or frequency. With a worldwide prevalence of 5-10% according to the Rome IV criteria, major impact on work absenteeism, and impaired quality of life due to chronicity of symptoms, IBS has led to increased use of conventional medical care at an estimated cost of hundreds of billions of dollars per year.[1-5] Due to the limited effectiveness of drug treatments, many patients are turning to complementary and alternative medicines, such as mind-body therapies

(hypnotherapy, mindfulness/meditation, yoga, etc.), body-directed therapies (osteopathic medicine, auriculotherapy, acupuncture, reflexology, etc.), energetic treatments and nutritional supplements.[6] Osteopathy is a manual medicine whose principle is to restore a state of balance between structure and function within the body in order to relieve pain.

A recent systematic review suggested the possible effectiveness of osteopathy on overall IBS symptoms at 6 months follow-up, compared to standard medical treatment.[7] However, only two randomized controlled trials (RCTs) evaluated the effectiveness of osteopathy versus sham therapy for IBS according to the Rome III criteria and showed significant improvement in overall symptoms and abdominal pain at day 7 for one and after 3 months of follow-up for the other.[8,9] Furthermore, the crossover design chosen by Attali et al was not the optimal design for IBS patients, as symptoms in this condition may be fluctuating.[8,10]

Similarly, the sham therapy chosen by Florance et al did not take into account the patients' expectations and was not described as an experience comparable to the osteopathic intervention, although this should have been done in order not to overestimate the treatment effect.[11] Thus, the design of these studies needs to be improved, in particular to define an optimal control group in order to clarify the impact of osteopathy on IBS.

This context leads us to set up a multicenter, two-group parallel, randomized, double-blind, placebo-controlled trial, the primary objective of which is to evaluate the effectiveness of osteopathy on the severity of IBS symptoms at 1-month follow-up in adult IBS patients. The secondary objective is to evaluate effectiveness of osteopathy on the severity of IBS symptoms and on quality of life up to 3 months of follow-up.

METHODS

Design

This was a multicenter, two-arm parallel, randomized, double-blind, placebo-controlled trial evaluating the effectiveness of osteopathy on the severity of IBS symptoms at 1-month follow-up in adult patients with IBS. The experimental group is defined by the active osteopathic treatment (AOT) and the control group by the sham osteopathic treatment (SOT). The protocol follows the SPIRIT guidelines (Standard protocol items: recommendations for interventional trials).[12]

Participants

The main inclusion criterion is adult patients with IBS (defined according to the Rome IV Criteria) and a moderate symptom severity score on the IBS symptom severity scale (IBS-SSS) (values ranging from 175 to 300). The main exclusion criteria are patients with chronic inflammatory bowel disease or digestive cancer (even if the disease is in remission), no osteopathic treatment in the past 12 months and planned or expected elective surgery during the study.

Blinding and treatments

To maintain patient blinding, no contact will be allowed between patients and osteopaths outside of the care consultations, and the evaluation will be made by the gastroenterologist who included the patient.

The SOT will be similar to the AOT in terms of patient expectation and experience. This scheme has been proposed by two recent systematic reviews to improve the evaluation of the effectiveness of non-pharmacological interventions for IBS.[7,11]

Experimental groupe: AOT

Patients will receive 3 AOT of 30 minutes each for 2 weeks in a private practice by an experienced osteopath (at least 15 years of practice and holder of the osteopathic diploma, D.O. being physicians or not physicians) who will receive prior training to optimize the quality of the AOT. Although the safety profile of osteopathy is good, so-called “rescue” medication will be taken by decision of the co-investigating physician if abdominal pain is not sufficiently relieved or if other IBS symptoms are present.[7]

Control group: SOT

Patients will receive 3 SOT of 30 minutes each for 2 weeks in a private practice by an experienced osteopath (at least 15 years of practice and holder of the osteopathic diploma, D.O. being physicians or not physicians) who will receive prior training to optimize the quality of the SOT. The positions of the patient and the practitioner will be the same as in the AOT group (see below).

If non-serious adverse events (e.g., exacerbation of abdominal pain) are reported, then so-called “rescue” drugs will be taken by decision of the co-investigating physicians.

Concurrent treatments and useful recommendations

Medications (antispasmodics, laxatives and anti-diarrhoeals) taken for several weeks or months before the start of the study will be allowed if they remain stable during the trial.

Description of the interventions

The AOT will first consist of the application of a visceral technique. The patient will lie on their stomach and the osteopath will touch the patient's abdomen with a wide two-handed grip. The action will consist of following the abdominal tissues in directions where tissue mobility is

allowed and occurs without restriction, from the surface to the depth of the abdomen. A change in the elasticity of the colon will then be perceived when the mobility restrictions of the tissues are dissipated. The osteopath will then use a technique on the sacrum according to the procedure described by Attali et al which consists in mobilizing the sacrum between the iliac bones.[8]

For SOT, the patient will lie on their stomach and the osteopath will use a wide two-handed grip on the patient's abdomen to deliberately mobilize it in an imprecise manner. Next, a technique with no apparent therapeutic effects, the light touch, first described by Licciardone et al and proposed by others to perform simulated bone manipulations, will be applied to the sacrum.[13,14]

Recruitment and follow-up

Setting and inclusion

Recruitment will take place in three hospitals (Paris, Lyon and Nice). After verification of eligibility criteria by the gastroenterologist during an initial screening visit (V0), the gastroenterologist will propose patients to participate in the study, and ensure the double-blind follow-up. AOT and SOT will be performed by 3 osteopaths (1 osteopath per center) as described above.

Randomization

The randomization sequence will be computer generated in a permuted block design. Randomization will be stratified by center in a 1:1 ratio and will take place one day before the first visit (V1) to reduce the risk of losing sight of participants. The osteopaths will be informed of the draw by email and the number assigned to each patient included in the trial. The outcome assessors (gastroenterologist) and statisticians will be blinded to group allocation.

Follow-up and data collection

The evaluation will be carried out at 5 different times: baseline (day-1, V0), day 8, day 15 and follow-up visits after the last treatment (1 month and 3 months after the initial treatment) (Table 1).

Table 1: Study procedure.

Clinical visits	Gastroenterology consultation, V0	V1	V2	V3	V4	V5
Time to 1st AOT	D-1	D0	D8	D15	D30	3 m
IC/NIC	*					
Consent	*					
Treatment		*	*	*		
Clinical data collection	*		*	*	*	*
Collection of QOL	*		*	*	*	*
Collection of AEs		*	*	*	*	*

Study period Inclusion/ randomization, follow-up post-treatment, V0 baseline assessment, V1 initial treatment, V2 second treatment (Day 8 after the initial treatment), V3 third treatment (Day 15 after the initial treatment), V4-V5 follow-up visit (1 and 3 months after the initial treatment), AOT active osteopathic treatment, IC inclusion criteria, NIC non-inclusion criteria, QOL quality of life, AEs adverse events.

Endpoints

Primary endpoint

The primary endpoint is the effectiveness (response to treatment) at 1-month follow-up. The primary endpoint was selected based on the Passos et al study published in the American journal of gastroenterology.[15]

The IBS-SSS is a specific, validated questionnaire that will be used to measure the level of symptom severity in IBS patients based on the following five items: degree of abdominal pain, frequency of abdominal pain, degree of abdominal distension, satisfaction with bowel movement, and influence on quality of life.

For each item, the score ranges from 0 to 100, with a maximum total score of 500. A patient with a score below 75 is considered to be in remission. The cut-off values for mildness, moderation and severity are 75 to 175, 175 to 300 and over 300.

A reduction of at least 50 points is associated with a clinically significant improvement, i.e., patients with a reduction of 50 points or more in the total IBS-SSS score were defined as responders.[16]

Secondary endpoints

Effectiveness at 3 months (response to treatment based on the IBS-SSS) and changes in total IBS-quality of life (IBS-QOL) scores up to 3 months. QOL is measured using an irritable bowel syndrome specific quality of life questionnaire.[17] The IBS-QOL is a 34-item questionnaire that assesses the degree of impact of IBS on a subject's quality of life over the past 30 days. Each item is rated on a Likert scale from 1 to 5, with higher values indicating lower quality of life. The scores are added together to give a total score between 34 and 170.[18]

Statistical considerations

Sample size

The sample size was determined to detect a 15% difference in treatment response at 1-month follow-up between the two groups, such that the responder rates, in the treatment group is 30% and, in the control, group is 15%. This difference, based on a previous report, was considered clinically significant. With a significance level of 0.05, 90% power, assuming that 20% of patients will be lost to follow-up, it is necessary to include 404 patients (202 per group).[19]

Data analysis

The proportion of treatment response at 1 month will be calculated for each group and compared using the chi^2 test or Fisher exact test. The same procedure will be applied for effectiveness at 3 months.

The changes in IBS-QOL at 1 month and 3 months will be assessed using analysis of covariance and adjusted for total IBS-QOL at baseline. We will perform subgroup analyses by centre to assess the effects of osteopath type (physician or non-physician) on the proportion of treatment response at 1 month. All analyses will be based on the intention-to-treat population and missing data will be imputed using the last observation carried forward method. All data will be analyzed using SAS, version 9.4 (SAS Institute Inc). The sample size calculation was realized with nQuery version 8.6.10. Statistical tests will be two-sided and a $p<0.05$ will be considered statistically significant.

DISCUSSION

This study will be the first RCT to evaluate the effectiveness of osteopathy on IBS symptoms according to the Rome IV criteria using a large sample of 404 subjects, compared to a sham treatment with similar expectations and patient experience to active treatment.

If effectiveness is demonstrated by the innovative design based on SPIRIT guidelines, osteopathy could be integrated into the management of IBS patients. In addition, this study design takes into account recent RCTs of good methodological quality that have evaluated the effectiveness of non-pharmacological interventions such as osteopathy on functional disorders including IBS.[20]

Our choice of a control group (SOT) whose patients' expectations and experiences are comparable to the experimental group (AOT) will address the methodological weaknesses identified in the current literature and provide an optimal control group that will allow us to accurately measure the clinical effectiveness of osteopathy on IBS symptoms. Furthermore, the recruited patients will all have the same level of baseline symptom severity as a recent systematic review has suggested that these expectations may be influenced by this factor.

Due to the type of the techniques used and the fact that they are identical in their implementation, patients will have comparable experiences in both treatment arms (AOT and SOT) which should keep patients blinded to thus reduce the risk of performance bias. Therefore, we chose SOTs already used in other studies for the osteopathic approach to the abdomen and bony skeleton with light touch being the gold standard sham therapy in osteopathic RCTs.[21]

Some patients in the trial may have already received one or more active osteopathic treatments for visceral or musculoskeletal symptoms related to IBS. Before analyzing the results, it will be necessary to ensure that the number of previous treatments of this type is identical in both groups. Such previous treatment could be considered as a confounding factor. However, the protocol does not include patients who have received osteopathic treatment in the past 12 months to ensure that the control group treatment (SOT) is indistinguishable from the active group treatment (AOT) to the patients.

Osteopaths participating in the trial as co-investigators will all have the same experience (at least 15 years of practice) and will hold a diploma of osteopath D.O. The objective is to harmonize practices in order to reduce the risk of interaction between the size of treatment effects and the type of osteopath. Clinically, the choice of our primary endpoint will follow several well-established elements.

The selection criteria for the subjects included in our trial are based on the Rome IV criteria, the latest iteration of Rome criteria for functional digestive diseases. The evolution from Rome III to Rome IV criteria emphasizes pain as a discriminating factor between IBS and functional diarrhea or functional constipation. For this purpose, the IBS-SSS is a widely used tool in IBS research and considered to have good reproducibility and sensitivity to change.[22]

Furthermore, according to the literature, the follow-up time after the last osteopathic treatment is at least 3 weeks and the number of sessions is between two and five.[23] To be consistent with these previous results, we suggest that three sessions of treatment be spread over a period of 2 weeks. The measurement of our primary outcome will therefore be performed at 4 weeks after the first treatment. Regarding follow-up times, the 3-month follow-up period (secondary endpoint) will allow measuring the medium-term effect of osteopathy excluding the possibility of remission by the disease itself, a hypothesis to be explored in future studies. In order to accurately define the disease experience, we complement this primary endpoint with another effectiveness endpoint, namely quality of life.

CONCLUSION

The results of this two-arm, randomized, double-blind, placebo-controlled, parallel trial, in which the expectations and experiences of patients in the control group are comparable to those in the experimental group, should confirm that osteopathy may be a new treatment for IBS.

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REFERENCES

1. Oka P, Parr H, Barberio B, Black CJ, Savarino EV, 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(10):908-17.
2. Hungin APS, Chang L, Locke GR, Dennis EH, Barghout V. Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact. Aliment Pharmacol Ther. 2005;21(11):1365-75.
3. Ringel Y, Williams RE, Kalilani L, Cook SF. Prevalence, Characteristics, and Impact of Bloating Symptoms in Patients With Irritable Bowel Syndrome. Clin Gastroenterol Hepatol. 2009;7(1):68-72.
4. Canavan C, West J, Card T. Review article: the economic impact of the irritable bowel syndrome. Aliment Pharmacol Ther. 2014;40(9):1023-34.
5. McFarland LV. State-of-the-art of irritable bowel syndrome and inflammatory bowel disease research in 2008. World J Gastroenterol. 2008;14(17):2625.
6. De Ponti F. Drug Development for the irritable bowel syndrome: Current Challenges and Future Perspectives. Front Pharmacol. 2013. Available at: http://journal.frontiersin.org/article/10.3389/fphar.2013.00007/abstract. Accessed on 9 May 2021.
7. Amsallem F, Sanchez S, Armoiry X, Mion F. Effectiveness of Non-Pharmacological Interventions for Irritable Bowel Syndrome: A Systematic Review. Evid Based Complement Alternat Med. 2021;2021:4404185.
8. Attali T-V, Bouchoucha M, Benamouzig R. Treatment of refractory irritable bowel syndrome with visceral osteopathy: short-term and long-term results of a randomized trial. J Dig Dis. 2013;14(12):654-61.
9. Florance B-M, Frin G, Dainese R, Nébot-Vivinus M-H, Marine Barjoan E, Marjoux S et al. Osteopathy improves the severity of irritable bowel syndrome: a pilot randomized sham-controlled study. Eur J Gastroenterol Hepatol. 2012;24(8):944-9.
10. Vitton V, Benezech A, Honoré S, Sudour P, Lesavre N, Auquier P et al. CON-COUR study: Interferential therapy in the treatment of chronic constipation in adults: study protocol for a randomized controlled trial. Trials. 2015;16(1):234.
11. Billings W, Mathur K, Craven HJ, Xu H, Shin A. Potential Benefit with Complementary and Alternative Medicine in Irritable Bowel Syndrome: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2020;S1542356520312969.
12. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K et al. SPIRIT 2013 Statement: Defining Standard Protocol Items for Clinical Trials. Ann Intern Med. 2013;158(3):200.
13. Licciardone JC, Minotti DE, Gatchel RJ, Kearns CM, Singh KP. Osteopathic manual treatment and ultrasound therapy for chronic low back pain: a randomized controlled trial. Ann Fam Med. 2013;11(2):122-9.
14. Nguyen C, Boutron I, Zegarra-Parodi R, Baron G, Alami S, Sanchez K et al. Effect of Osteopathic Manipulative Treatment vs Sham Treatment on Activity Limitations in Patients with Nonspecific Subacute and Chronic Low Back Pain: A Randomized Clinical Trial. JAMA Intern Med. 2021;181(5):620.
15. Passos MCF, Lembo AJ, Conboy LA, Kaptchuk TJ, Kelly JM, Quilty MT et al. Adequate relief in a treatment trial with IBS patients: a prospective assessment. Am J Gastroenterol. 2009;104(4):912-9.
16. Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Aliment Pharmacol Ther. 1997;11:395-402.
17. Miller LE. Study design considerations for irritable bowel syndrome clinical trials. Ann Gastroenterol. 2014;27(4):338-45.
18. Patrick DL, Drossman DA, Frederick IO, DiCesare J, Puder KL. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. Dig Dis Sci. 1998;43:400-11.
19. Pei L, Geng H, Guo J, Yang G, Wang L, Shen R. Effect of Acupuncture in Patients With Irritable Bowel Syndrome: A Randomized Controlled Trial. Mayo Clin Proc. 2020;95(8):1671-83.
20. Senna MK, Machaly SA. Does Maintained Spinal Manipulation Therapy for Chronic Nonspecific Low Back Pain Result in Better Long-Term Outcome? Spine. 2011;36(18):1427-37.
21. Licciardone JC, Stoll ST, Fulda KG, Russo DP, Siu J, Winn W et al. Osteopathic Manipulative Treatment for Chronic Low Back Pain: A Randomized Controlled Trial. Spine. 2003;28(13):1355-62.
22. Mujagic Z, Keszthelyi D, Aziz Q, Reinisch W, Quetglas EG, De Leonardis F et al. Systematic

review: instruments to assess abdominal pain in irritable bowel syndrome. Aliment Pharmacol Ther. 2015;42(9):1064-81.
23. Hundscheid HW, Pepels MJ, Engels LG, Loffeld RJ. Treatment of irritable bowel syndrome with osteopathy: Results of a randomized controlled pilot study. J Gastroenterol Hepatol. 2007;22(9):1394-8.

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