

The Effects of Peppermint on Menstrual Disorders: A Systematic Review of Randomized Controlled Trials

Abstract

Background: Various aspects of women's functioning are affected by menstrual disorders. There are various treatment methods to control these conditions. This systematic review aimed to evaluate the effects of peppermint on menstrual disorders. **Materials and Methods:** A comprehensive search was performed in PubMed, EMBASE, Scopus, Web of Science, Science Direct, SID, and Google Scholar without any limitations until July 31, 2023. To identify those studies that were consistent with the main purpose of this review, the search focused on the keywords "menstruation disorders," "Mentha piperita," and their other synonyms in the title and abstract of the articles. Methodological quality was assessed using the Jadad scale. **Results:** A total of 238 articles were retrieved. After removing duplicates and irrelevant studies, 146 articles remained. After evaluating the titles and abstracts, the full text of the remaining eight articles was evaluated. At this stage, one article was excluded due to being in the Malay language, and two articles were excluded due to the use of water mint species. Finally, five Randomized Controlled Trials (RCTs) with a total of 499 participants were included. The quality rating of the included trials indicates that three studies were of high quality, and two studies were of low quality. The studies examined primary dysmenorrhea and premenstrual syndrome. Statistically significant reductions in pain severity, improved cognitive function, and gastrointestinal symptoms were observed. **Conclusions:** The findings suggest that peppermint may be effective in improving menstrual disorders. However, high-quality RCTs that overcome the methodological limitations of the current studies are needed.

Keywords: Menstruation disturbances, *Mentha piperita*, randomized controlled trial, systematic review, women

Introduction

Almost 45–99% of women of reproductive age worldwide suffer from menstrual disorders. These include pathological amenorrhea, oligomenorrhea, polymenorrhea, hypomenorrhea, hypermenorrhea, menorrhagia, metrorrhagia, dysmenorrhea, and premenstrual syndrome (PMS), which are often associated with various physiological and psychological symptoms that negatively impact various aspects of women's functioning and quality of life. Without suitable follow-up and treatment, they can have long-term consequences for an individual's health and impose economic burdens on society.^[1-4]

Today, many women with menstrual disorders, due to the severe side effects of chemical drugs, tend to control and treat their condition using low-risk methods such as Complementary and Alternative

Medicine (CAM). Among different CAM methods, medicinal plants, due to their long history of use in treating menstrual disorders, have gained considerable attention.^[5-7]

Peppermint (*Mentha × piperita*) is one of the most popular medicinal plants in traditional medicine since ancient Greek, Roman, and Egyptian civilizations. It has long been used in several ways to treat symptoms such as nasal congestion, cough, sore throat, toothache, migraine headaches, musculoskeletal pains, stress, and anxiety, itching, nausea and vomiting, indigestion, bloating, and abdominal pain. In addition, this herb has been used to induce menstruation and alleviate dysmenorrhea.^[8,9] Today, peppermint has been shown to have antioxidant, anti-inflammatory, antimicrobial, antispasmodic, analgesic, and anxiolytic

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properties.^[10-12] Its analgesic and antispasmodic effects can be attributed to menthol, the main and major component of peppermint, which acts on the nervous and smooth muscle tissues of various body systems through the transient receptor potential cation channel subfamily M member 8 (TRPM8). At low to moderate concentrations, menthol activates TRPM8 in sensory neurons, causing a cooling sensation in the skin and mucosal membranes, as well as reducing a wide range of body pains. Moreover, activation of the endogenous kappa-opioid signaling pathways also plays a role in the analgesic effects of menthol. Additionally, by blocking and inhibiting voltage-gated calcium channels and assisting calcium release from the sarcoplasmic reticulum and Golgi apparatus, menthol helps relax smooth muscles.^[13,14] Based on *in vitro* studies, menthol along with other monoterpenes can affect the central nervous system through acetylcholinesterase inhibitory properties, modulation of Gamma – Amino Butyric Acid (GABA) and Serotonin 5-Hydroxy Tryptamine-3 (5 – HT₃), and interaction with Glutamate N-Methyl-D-Aspartic acid (NMDA) and nicotinic receptor binding properties, leading to improved mood and cognitive function.^[15,16]

In this regard, results from several studies conducted in recent years indicate the effects of peppermint on physiological and psychological symptoms related with menstrual disorders.^[17,18] However, the results of some others do not fully support these findings.^[19-21]

Given the above, the effects of peppermint on improving menstrual disorders and related symptoms are unclear. Thus, to confirm and support the therapeutic effects of this herb, we need high-quality evidence. Therefore, the present systematic review aimed to evaluate all Randomized Controlled Trials (RCTs) that assessed the effects of peppermint on menstrual disorders.

Materials and Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,^[22] and its protocol was registered with the code CRD42022344146 on the PROSPERO website. A comprehensive search was performed in the English databases such as PubMed, EMBASE, Scopus, Web of Science, Science Direct, Persian database SID, and Google Scholar search engine without any limitations until July 31, 2023. To identify those studies that were consistent with the main purpose of this review, the search focused on the keywords of “menstruation disorders”, “Mentha piperita,” and other synonyms of keywords in the title and abstract.

Additionally, a secondary search was performed in the reference lists of all the articles that were initially identified. All studies retrieved at this stage that met the following selection criteria were included.

Inclusion and exclusion criteria were based on the Cochrane Handbook for Systematic Reviews of Interventions.

Women of reproductive age with menstrual disorders, including pathological amenorrhea, oligomenorrhea, polymenorrhagia, hypomenorrhea, hypermenorrhea, menorrhagia, metrorrhagia, dysmenorrhea, PMS, and premenstrual dysphoric disorder were included in the study.

All trials that used peppermint for the treatment of menstrual disorders were included. There was no limitation in dose, route of administration, and duration of treatment. Studies that used a combination of peppermint with other herbal medicines, as well as studies that used other species of mint were excluded.

Studies that used a placebo for the control group were included. Comparisons with other herbal medicines and conventional treatment methods were also acceptable.

All studies that assessed the symptoms of any type of menstrual disorder were included.

All RCTs with parallel or crossover designs that were written in the English or Persian language were included. Non-randomized studies (observational, cohort, case-control, case report, and case series), qualitative studies, and uncontrolled trials were excluded. Moreover review articles, abstracts, letters, book chapters, *in vitro*, and animal studies were also excluded.

In this review, information such as participants' characteristics, intervention and control groups, measured outcomes, and results were extracted from each article. Methodological quality and risk of bias of included studies were assessed using the Jadad scale.^[23] This scale consists of three main domains (randomization, blinding, withdrawals, and dropouts) and five questions (Was the study described as randomized? Was the randomization method appropriate? Was the study described as blinding? Was the blinding method appropriate? And Were withdrawals and dropouts reported including numbers and reasons in each group? If there were no withdrawals, was it stated in the article?).

Each question entails a Yes or No response. A Yes response receives 1 point, and a No response receives 0 points. Furthermore, if the method of randomization and blinding is not reported, questions 2 and 4 receive no points. Studies with scores higher than 3, equal to 3, and lower than 3 are considered high, moderate, and low quality, respectively.

The entire process of study selection and data extraction from each article, as well as quality assessment, was performed independently by two authors (first and second authors). Any disagreement was resolved by discussion. The third author acted as an arbitrator in unresolved disputes.

Due to heterogeneity in participants, interventions, outcomes measured, and methods of measurement, a meta-analysis could not be performed.

Ethical considerations

This study was approved by the Research Ethics Committee of Gonabad University of Medical Sciences, Gonabad, Iran (IR.GMU.REC.1401.120). This manuscript has no plagiarism. The results of the analysis were completely honest. Any data fabrication has been avoided.

Results

Search results

In the process of searching databases, a total of 238 articles were retrieved. After removing duplicates and irrelevant studies, 146 articles remained. After evaluating the titles and abstracts of the articles, 138 articles were excluded due to duplication or incompatibility with the inclusion criteria. Then, the full text of the remaining eight articles was evaluated. At this stage, one article was excluded due to being in the Malay language and lack of the researchers' proficiency in this language, and two articles were excluded due to the use of other mint species (watermint). Finally, five studies that met the inclusion criteria were included in this review.^[17-21] The flow diagram of study selection is presented in Figure 1. The characteristics of the included studies are presented in Table 1.

Quality assessment

The methodological quality assessment of the included studies is presented in Table 2. The quality rating of the included trials in this review indicates that three studies are of high quality, and two studies are of low quality. Randomization was performed in all studies; however, the method of randomization was reported only in three studies. These studies used computer-based randomization programs, block approach, and random number table for random sequence generation. Moreover, these three studies had a double-blind design and drug and placebo capsules with similar appearance. In the other two studies,

blinding was not mentioned. Although, the intervention in one of these studies was aromatherapy massage, and even if blinding was mentioned in it, due to the nature of aromatherapy, it may be difficult to deceive the participants because of the smell of essential oils. Withdrawals and dropouts with reasons were reported in four trials, while one study did not report this information.

Participants and settings

All studies were published in English journals between 2013 and 2020; three studies were conducted in Iran, one study in Pakistan, and one study in Egypt. Moreover, one study was on PMS, and four studies were on primary dysmenorrhea. The target group was students^[17] in one study, university students^[19-21] in three studies, and a combination of students and university students^[18] in one study. The age range of participants in these studies varied between 13 and 26 years. The sample size included in each study ranged from 61 to 126 participants, and a total of 499 individuals (214 in the peppermint group) participated in these five studies.

Design and interventions

Among the included RCTs, four studies had a parallel design,^[17-19,21] and one study had a crossover design.^[20] Peppermint was administered orally in four studies; of these, two studies used enteric-coated Colpermin capsules (peppermint oil).^[17,20] Furthermore, one study used 1.5% pure peppermint essential oil for aromatherapy massage. The administered dose of peppermint ranged from 374 to 990 mg/day. Peppermint was consumed three times a day^[18,19] in two studies, two times a day^[17] in one study, and once a day^[20,21] in two studies. Two studies compared the therapeutic effects of peppermint with placebo, one study compared its effects with mefenamic acid, and two other studies compared its therapeutic effects with ginger and placebo. The intervention period was reported as 8 weeks in four studies; and in one study, the duration of the intervention was not reported.

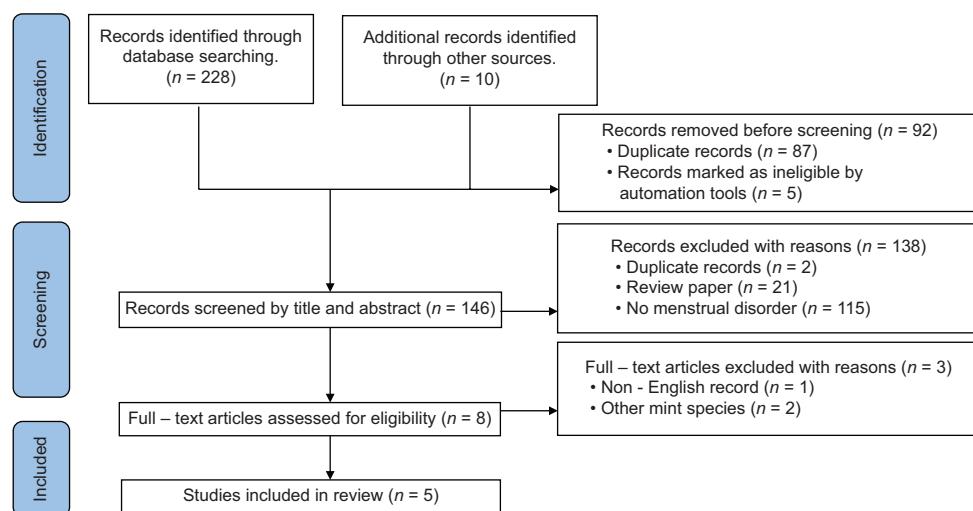


Figure 1: PRISMA flow diagram

Table 1: Characteristics of included studies

Study, year, country, reference	Disease	Participants	Interventions			Outcome measures	Results	
		Sample size	Age mean (SD)	Drop out n (%)	Duration (w)	Group	Dose	
Delavar <i>et al.</i> , (2019) Iran ^[17]	Premenstrual syndrome	30 31	17.4 (0.9) 17.0 (0.5)	11 (18.0)	8	1: Peppermint 2: Placebo	2 Cap 187 mg NR	Mood, behavioral, <i>p</i> <0.001 and physical symptoms
Heshmati <i>et al.</i> , (2016) Iran ^[19]	Primary dysmenorrhea	51 51	21.02 (1.32) 21.09 (1.49)	12 (11.70)	8	1: Peppermint 2: Placebo	3 Cap 330 mg 3 Cap 500 mg	Intensity of pain <i>p</i> <0.05 Duration of pain <i>p</i> >0.05
Masoumi <i>et al.</i> , (2016) Iran ^[20]	Primary dysmenorrhea	63 63	20.99 (0.15) 4 (3.10)	4 (3.10)	8	1: Peppermint → Mefenamic acid 2: Mefenamic acid → Peppermint	3 Cap 187 mg → 3 Cap 250 mg 3 Cap 250 mg → 3 Cap 187 mg	Intensity of pain Duration of pain Bleeding amount Nausea and vomiting Diarrhea Analgesic uses <i>p</i> <0.05 in favor of both <i>p</i> <0.05 in favor of both <i>p</i> <0.05 in favor of mefenamic acid <i>p</i> <0.05 in favor of peppermint <i>p</i> <0.05 in favor of both <i>p</i> <0.05 in favor of both
Sultan <i>et al.</i> , (2020) Pakistan ^[18]	Primary dysmenorrhea	30 30 30	17 (2.20) 17.2 (2.40) 16.4 (2.10)	NR	NR	1: Peppermint 2: Ginger 3: Placebo	3 Cap 250 mg 3 Cap 250 mg 3 Cap 250 mg	Intensity of pain <i>p</i> <0.05 in favor of both EG Blood pressure <i>p</i> <0.05 in favor of ginger Hemoglobin Calcium <i>p</i> >0.05 <i>p</i> >0.05
Rizk., (2013) Egypt ^[21]	Primary dysmenorrhea	40 40 40	17–21* 17–21* 17–21*	6 (5) 6 (5) 6 (5)	8	1: Peppermint 2: Ginger 3: Placebo	Essential oil 1.5% (3–4 drops) Essential oil 1.5% (3–4 drops) Almond oil (3–4 drops)	Intensity of pain Duration of pain Location of pain Anorexia Nausea and vomiting Diarrhea or constipation Mood swings Dizziness and fatigue Headache Daily life activities <i>p</i> <0.05 in favor of both EG <i>p</i> <0.05 in favor of peppermint <i>p</i> <0.05 in favor of peppermint <i>p</i> <0.05 in favor of ginger <i>p</i> <0.05 in favor of peppermint <i>p</i> <0.05 in favor of ginger <i>p</i> <0.05 in favor of ginger <i>p</i> <0.05 in favor of both EG

SD: standard deviation; *n*: number; w: week; EG: experimental group; *: age range

Results of individual studies

In one study that examined the effects of peppermint on PMS, a statistically significant difference was observed in

the mean total score, mean score of mood, and behavioral and physical symptoms between intervention and control groups (*p* < 0.001).^[17] The results of another study showed

Table 2: Quality appraisal of all included studies

Study, year, reference	Randomization		Blinding		Withdrawals and dropouts (5)	Total score	Qualitative rating
	(1)	(2)	(3)	(4)			
Delavar et al., (2019) ^[17]	Yes	Yes	Yes	Yes	Yes	5	High
Heshmati et al., (2016) ^[19]	Yes	Yes	Yes	Yes	Yes	5	High
Masoumi et al., (2016) ^[20]	Yes	Yes	Yes	Yes	Yes	5	High
Sultan et al., (2020) ^[18]	Yes	No	No	No	No	1	Low
Rizk., (2013) ^[21]	Yes	No	No	No	Yes	2	Low

Yes: criteria met (1); No: criteria not met (0)

that consumption of peppermint capsules significantly reduces the mean severity of menstrual pain ($p < 0.05$), but this difference in the mean duration of pain between the two groups was not significant ($p > 0.05$).^[19] In a crossover RCT that compared the effects of peppermint capsules and mefenamic acid on primary dysmenorrhea, a statistically significant difference was reported in the mean pain intensity after consumption of peppermint capsules and mefenamic acid compared to before ($p < 0.05$), but no significant difference was observed between the two groups ($p > 0.05$). Furthermore, a statistically significant difference was found in the mean duration of pain after consumption of peppermint capsules and mefenamic acid compared to before $p < 0.05$; however, this duration was lower in the mefenamic acid group ($p < 0.05$). The amount of bleeding was significantly lower in the mefenamic acid group ($p < 0.05$). Additionally, there was no statistically significant difference in the incidence of nausea and vomiting before and after consumption of mefenamic acid ($p > 0.05$), while in the peppermint group, this difference was significant, and they had a lower prevalence of nausea and vomiting ($p < 0.05$). The reduction in diarrhea was higher in the peppermint group compared to the mefenamic acid group ($p < 0.05$). Furthermore, the rate of analgesic consumption during the treatment period decreased in both groups compared to before ($p < 0.05$), but this reduction was higher in the mefenamic acid group ($p < 0.05$).^[20] In another study, a statistically significant difference was observed in the mean severity of menstrual pain after consumption of ginger and peppermint compared to before ($p < 0.05$), but this difference was not significant in the control group. Moreover, the severity of pain in the ginger group was lower than in the peppermint group ($p = 0.001$). In this study, there was a statistically significant positive correlation between blood pressure and ginger consumption ($p < 0.05$), but no significant correlation was observed in hemoglobin and serum calcium levels between the two intervention groups ($p > 0.05$).^[18] In another included study that compared the effects of abdominal massage aromatherapy using peppermint and ginger essential oils on primary dysmenorrhea, a statistically

significant reduction was observed in the intensity and location of pain in both intervention groups compared to the control group ($p < 0.05$). The duration of pain and symptoms such as anorexia, diarrhea or constipation, and mood swings in the peppermint oil group, nausea and vomiting, dizziness, fatigue, and headache in the ginger oil group significantly improved ($p < 0.05$). Additionally, daily life activities improved significantly in both intervention groups compared to the control group ($p < 0.05$).^[21]

Side effects

Only two trials assessed side effects (heartburn, mouth ulcers, and anal burning),^[17,19] and no adverse effects were reported in these two studies.

Discussion

The aim of this review was to comprehensively evaluate the evidence on the effects of peppermint on menstrual disorders. The results of all included RCTs on primary dysmenorrhea and PMS suggested the therapeutic effects of peppermint in pain management, improved mood and cognitive function, and alleviation of some related gastrointestinal symptoms. The result of each included study and comparison with other similar studies is discussed below.

In a study that examined the effect of peppermint capsules on the severity of primary dysmenorrhea, it was observed that taking 330 mg peppermint capsules, three times a day on the first 3 days of menstruation significantly reduces pain severity compared to the control group.^[19] Moreover, in a randomized crossover trial that compared the efficacy of peppermint capsules and mefenamic acid in treating primary dysmenorrhea, it was reported that taking three 187 mg peppermint capsules, once a day, for the first 3 days of menstruation, reduces the intensity and duration of menstrual cramps. In this study, nausea, vomiting, and diarrhea after consumption of peppermint were lower compared to mefenamic acid.^[20] In another study, researchers compared the effects of ginger and peppermint on adolescents with primary dysmenorrhea and stated that the severity of pain in both ginger and

peppermint groups decreased compared to before the intervention and the control group.^[18] In another clinical trial examining the effects of abdominal massage aromatherapy using peppermint and ginger essential oils on primary dysmenorrhea, it was observed that receiving 15 minutes of daily aromatherapy massage with 1.5% pure peppermint or ginger oils for five consecutive days before the onset of menstruation significantly reduced pain severity, location of pain, and improved daily life activities in both intervention groups compared to the control group. Furthermore, the duration of pain and symptoms such as anorexia, diarrhea or constipation, and mood swings significantly improved in the peppermint oil group; however, no significant reduction was observed in nausea, vomiting, dizziness, fatigue, and headache in this group.^[21] Moreover, in another clinical trial that examined the efficacy and safety of peppermint oil capsules on PMS, it was observed that taking two 187 mg peppermint capsules daily for 10 days before menstruation for 2 months decreases the severity of total, emotional, behavioral, and physical symptoms in the peppermint group compared to before the intervention and the placebo group.^[17] In this regard, an RCT evaluated the effects of aromatherapy with peppermint essential oil on pain and anxiety caused by intravenous catheterization in cardiac patients. The results showed that inhaling pure peppermint essential oil for 5 minutes significantly reduced pain in the intervention group compared to the control group and before the intervention. However, there was no statistically significant difference between the two groups in terms of anxiety levels.^[24] The findings of this study are partially consistent with the findings of the present review. The results of another study on cancer patients, with neuropathy also showed that the use of 1% topical menthol cream, twice a day for 4–6 weeks, reduce neuropathic pain and improve mood and function in these patients,^[25] which supports our study finding. In addition, in a pilot trial that evaluated the efficacy of 6% menthol gel on migraine attacks, it was observed that applying the menthol gel within 2 hours of the onset of the migraine attacks, decreased the severity of pain compared to before the intervention and the control group.^[26] This study also supports our findings. A clinical trial evaluated the effects of peppermint on the mood and cognitive function of young healthy men and women, the results showed that taking two peppermint capsules at once, improved cognitive function, and task performance and decreased mental fatigue compared to baseline, but no difference was observed in individuals' mood performance.^[16] The results of this study are partially consistent with the findings of our review. In another randomized trial, the results showed that daily use of peppermint tea (250 mg of fresh peppermint leaves), 30 minutes before sleep for 1 month, significantly decreased the mean scores of anxiety and stress in the peppermint group. Moreover, peppermint tea improves memory performance and sleep quality.^[27]

The results of the above study are also consistent with the findings of the present study. The results of another study that evaluated the effects of aromatherapy with peppermint essential oil on anxiety of patients with acute coronary syndrome showed that inhaling pure peppermint essential oil for 1 hour reduced anxiety in the intervention group compared to the control group and before the intervention^[28]; which supports the findings of our study. In another trial comparing the effects of aromatherapy with pure peppermint and lavender essential oils on fatigue and sleep quality of cardiac patients, the results showed a statistically significant difference in the mean scores of fatigue and sleep quality after the intervention compared to before the intervention in the experimental groups; however, no statistically significant difference was observed between the two intervention groups.^[29,30] In fact, fatigue and sleep disorders are symptoms of PMS and primary dysmenorrhea, and the findings of this study are consistent with the present review. The results of a clinical trial conducted on cardiac patients also showed that aromatherapy with peppermint essential oil after open-heart surgery reduces pain and improves patients' sleep quality,^[31] which supports our findings. In addition, peppermint aroma improves sleep quality in cancer patients and reduces pain and anxiety during labor.^[32,33] Moreover, the results of a double-blind clinical trial that evaluated the effect of peppermint drops on ileus after elective cesarean section showed that taking 20 drops of peppermint extract starting 4 hours after surgery and repeated at intervals of 1 hour in three doses significantly reduced the time to hear the first intestinal sounds, the first gas passing feeling time, and the first defecation feeling time compared to placebo, but there was no difference in term of nausea and vomiting between the two groups.^[34] However, the results of a literature review showed that peppermint oil is particularly effective in improving a wide range of gastrointestinal symptoms.^[35] The difference in some of the findings of the above studies with the results of the present review can be attributed to the differences in the population, dose, route of administration, and peppermint compounds used.

Overall, the findings of this review support the effects of peppermint in treating menstrual disorders such as primary dysmenorrhea and PMS. However, it seems that more research is needed in the field of the effects of peppermint on memory function as well as mood to reach more conclusive results. In this review, due to heterogeneity in participants, interventions, outcomes measured, and methods of measurement, a meta-analysis was not possible. Additionally, the sample size in one of the studies was relatively small, which limits the generalizability of the results to the general population.

The strengths of this systematic review include examining menstrual disorders separately and using a rigorous quality assessment tool. To the best of our knowledge, this is the

first comprehensive review in the world evaluating the effects of peppermint on menstrual disorders.

The limitations of the present review were also identified. The diagnosis of dysmenorrhea in all studies was based on participants' self-reports rather than clinical examination and sonographic findings. Moreover, the generalizability of the results is limited due to the small number of trials and their quality. It is suggested that future research be conducted by overcoming the limitations of the present study. However, the present review has provided a strong background for future studies and proposed peppermint as an effective and safe treatment for menstrual disorders. It also contributes to the development of knowledge in the field of complementary medicine regarding menstrual disorders.

Conclusion

In conclusion, the findings of this systematic review suggest that peppermint may be effective in improving menstrual disorders such as primary dysmenorrhea and PMS. However, high-quality RCTs that overcome the methodological limitations of the current studies, i.e. in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines, are needed.

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Conflicts of interest

Nothing to declare.

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