Efficacy of Ginger for Alleviating the Symptoms of Primary Dysmenorrhea: A Systematic Review and Meta-analysis of Randomized Clinical Trials

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Conflicts of Interest: James W. Daily III is President of Daily Manufacturing, Inc., a manufacturer of dietary supplements, no other authors have any conflicts of interest.

Author Contribution: S.P. designed the study and S.P., J.W.D., S.J., and D.S.K. searched RCT papers and reviewed the papers. S.P. and J.W.D. organized the data and the statistical analysis and contributed to writing of the manuscript. S.P. had primary responsibility for final content. The final manuscript has been read and approved by all authors.

Abstract

Objective. There has been no attempt to date to synthesize the available evidence for the efficacy of ginger for treating primary dysmenorrhea. This systematic review evaluates the current evidence for the effectiveness of ginger for treating primary dysmenorrhea.

Methods. Literature searches were conducted using 12 electronic databases including PubMed, EMBASE, Cochrane Library, Korean databases, Chinese medical databases, and Indian scientific database. Search terms used were: “ginger” or “Zingiber officinale” and “dysmenorrhea” and “pain.” Studies using ginger as a treatment of primary dysmenorrhea were considered for inclusion. The major outcome of primary dysmenorrhea was assessed using a pain visual analogue score (PVAS).

Results. Initial searches yielded 29 articles. Of these original results, seven met specific selection criteria. Four of the RCTs compared the therapeutic efficacy of ginger with a placebo during the first 3–4 days of the menstrual cycle and were included in the meta analysis. The meta-analysis of these data showed a significant effect of ginger in reducing PVAS in subjects having primary dysmenorrhea (risk ratio, 1.85; 95% CI of 2.87, 0.84, P = 0.0003). Six RCTs out of 7 exhibited low to moderate of risk of bias.

Conclusion. Collectively these RCTs provide suggestive evidence for the effectiveness of 750–2000 mg ginger powder during the first 3–4 days of menstrual cycle for primary dysmenorrhea.

Key Words. Ginger; Dysmenorrhea; Pain Visual Analogue Scale; Randomized Clinical Trials; Systematic Review

Introduction

Primary dysmenorrhea is one of the most prevalent gynaecologic disorders, affecting more than half of all women of reproductive age. Primary dysmenorrhea is defined as pain associated with menstruation in the absence of underlying organic disease [1]. It usually begins 6–12 months after menarche and it accompanies spasmodic cramping pain in the lower abdomen that can disseminate into the lower back and thighs [1]. Symptoms of dysmenorrhea can be incapacitating and women experiencing severe symptoms of dysmenorrhea...
are unable to engage in normal activity and experience increased absence from school or work. It is estimated that severe dysmenorrhea results in the loss of 600 million working hours and $2 billion in lost productivity annually [2]. The prevalence of primary dysmenorrhea varies from 30% to 90% among different ethnicities with various severities [3].

Although the cause of primary dysmenorrhea is not fully understood, it seems clear that increased production of prostaglandins derived from cyclooxygenase-2 (COX)-2 and other inflammatory mediators cause excessive contractions of the uterus with consequential pain and cramping [4,5]. Previous studies have reported that the inhibition of COX-2 by nonsteroidal anti-inflammatory drugs (NSAIDs) decreases prostaglandin synthesis, contributing to their analgesic, antipyretic and anti-inflammatory properties and making them effective for ameliorating the severity of menstrual pain in women [5–7]. However, frequent use of these medications have been reported to have a failure rate of 20–25% [8], and have adverse effects ranging from minor symptoms such as diarrhea, stomachache, and nausea to serious illness such as chronic kidney disease [9,10]. Although the majority of patients experience no ill effects from NSAIDS, many would benefit by having an alternative treatment for reducing pain treatment for primary dysmenorrhea with minimal adverse effects [11]. As some herbs have anti-inflammatory and analgesic activities, they might be useful as alternatives to NSAIDS or for decreasing the effective dose of NSAIDS for treating primary dysmenorrhea [12].

Ginger root (Zingiber officinale Roscoe.) is used worldwide as a spice and seasoning as well as a traditional medicine. Ginger contains abundant nonvolatile pungent constituents such as various types of gingerols, shogaols, zingerone, and paradol [8]. Ginger and ginger’s components have pleiotropic pharmacological activities, such as gastrointestinal, antioxidant, cardiovascular, analgesic, and anti-inflammatory activities [9]. Several studies have reported ginger to exert anti-inflammatory effects by the inhibition of inducible cyclooxygenase (COX)-2, NF-κB, and 5-lipoxygenase (5-LOX) [8,9]. Additionally, ginger and its constituents, especially shogaols, work as agonists of transient receptor potential channel subfamily V member 1 (TRPV1) that is associated with the transmission of physical and chemical stimuli [8]. TRPV1 has been a prime target for the development of novel pain relievers (analgesics). Both antagonists and agonists of the receptor are used for pain treatment. Under the prolonged exposure of its agonists such as capsaicins and shogaols TRPV1 is desensitized, which leads to the alleviation of pain [13].

There is growing evidence that ginger has anti-inflammatory and analgesic efficacy in humans with osteoarthritis, primary dysmenorrhea and other acute pains. Terry et al. [14] conducted a systemic review of research on ginger for the treatment of pains originating from different conditions, using 6 RCTs including 2 osteoarthritis trials, 1 dysmenorrhea trial and 3 acute muscle pain trials. The authors concluded that ginger may reduce subjective experience of pain in some conditions. In addition, in a recent meta-analysis of randomized placebo-controlled trials ginger was reported to have efficacy for pain relief in osteoarthritis [15]. Therefore, ginger has scientific support to justify its history of use for pain treatment as antiquity [16], especially in Chinese and Asian-Indian traditional medicine [17]. Several studies have also demonstrated that ginger may have beneficial effects for cancer prevention [18], pregnancy-related nausea and vomiting [19], chemotherapy nausea [20], nausea, and vomiting after surgery [21] and osteoarthritis [22]. However, despite the evidence supporting the use of ginger for many diseases involving inflammation, nausea and pain, the efficacy of ginger for treating or managing primary dysmenorrhea has not recently been systemically reviewed. As the previous review on ginger for pain, several randomized clinical trials of ginger supplementation have been conducted in young women. The purpose of the current review was to systemically evaluate all randomized clinical trials of ginger for treating primary dysmenorrhea and to elucidate the efficacy of ginger for alleviating the symptoms of primary dysmenorrhea. To the best of our knowledge this is the first systematic review and meta-analysis of RCTs on the effectiveness of ginger for primary dysmenorrhea.

Methods

Data Sources and Selection Criteria

The following electronic databases were searched: PubMed, EMBASE, Cochrane Library, Korean databases such as DBPia, the Research Information Service System (RSS), and the Korean Studies Information Service System (KISS), Chinese medical databases such as China National Knowledge Infrastructure (CNKI) and the Chinese Scientific Journals Database, the Indian Medical Journals and the Indian Journals. Dissertations were also included. The keywords and Medical Sub Headings (MeSH) were: “ginger,” (Primary) “Zingiber officinale,” “dysmenorrhea,” “pain,” “randomized,” “placebo,” “controlled trial,” and “clinical trial.” All randomized clinical trials that studied the effects of ginger on primary dysmenorrhea in young women were included. Studies that investigated the effects of complex herbal remedies that included ginger as an ingredient were excluded.

Data Extraction, Quality and Validity Assessment

The search was conducted in the databases with proper languages of English, Korean and Chinese with the following key words of mesh terminology: ginger, pain, and dysmenorrhea. Three independent reviewers (SJ, SP, DSK) screened the papers. In the first screening the related papers were identified by the titles and abstracts of the papers and the relevant articles were retrieved in full text and validated for inclusion in the
systemic review. The fourth reviewer (JWD) independently validated the selected papers.

**Eligibility Criteria for Studies for This Review**

All prospective randomized clinical studies using ginger for the treatment of dysmenorrhea in women having primary dysmenorrhea were included for this systematic review. Exclusion criteria included in vitro studies of ginger for primary dysmenorrhea, studies with only an abstract available, nonclinical trial studies, studies in which primary dysmenorrhea was not the primary outcome measured, and then we eliminated the duplicates. A flow diagram of the article selection process is shown in Figure 1. Although no language barriers were imposed, all studies included in this review were written in English. Dissertations about randomized clinical studies were included.

**Subjects and Intervention**

This systematic review included all RCTs that investigated the effect of ginger powder on the symptoms of primary dysmenorrhea in young women. The age of subjects varied among the studies but within the range of 13–30 years of age. Most subjects were teenagers. Although the exclusion criteria also varied among the studies, most studies excluded subjects with irregular menstrual cycles, those using hormonal medication, birth control pills or intrauterine contraceptive devices and having a history of pregnancy and strenuous exercise. The eligibility of subjects was somewhat different among the studies, but in all of the studies, the subjects had primary dysmenorrhea but not secondary dysmenorrhea. Primary dysmenorrhea is defined as having pain during at least 50% of menstrual cycles or first 3 days and pain score of 3-4 based on 10 visual analog scales. Furthermore, each study consisted of 2 cycles. Subjects in the experimental group were provided 750–2,000 mg ginger powder capsules per day for the first 3 days of the menstrual cycle, whereas those in the control group received placebo capsules such as lactose [23–26]. In three studies analgesic medications such as mefenamic acid [27,28] or exercise [29] were used as positive controls. Five RCTs had a two-arm parallel design: 4 RCTs contained ginger powder and placebo groups [24–27], but 1 RCT included ginger powder + exercise and exercise group [29]. Two RCTs adopted a three-arm parallel design including ginger powder group and two control groups: 1 RCT contained two analgesic groups using mefenamic acid and ibuprofen [28] whereas 1 RCT included one placebo and one analgesic group (zinc sulfate) [23].

**Outcome Measures**

Outcome measures to be included in the meta analysis were severity and duration of pain during menstruation. The severity of pain was assessed before and after intervention by a visual analogue scale. The pain visual analog scale (PVAS) is a tool widely used to measure pain. The PVAS is a valid measure that has been used in many studies to evaluate the severity of pain including menstruation [30,31]. Its reliability varies from 0.76 to
of the pain, as PVIS, and the duration of the pain, mean meta-analysis were a continuous variable of the severity used for the meta-analysis. As the data used for the cycles of all studies except the Jenabi study [24] were prior to the menstruation and lasting for 5 days. Both cycle began providing ginger or placebo from 2 days the same as the rest of the protocol but the second study [23] used different methods: the first cycle was methods for each cycle. However, the Kashefi et al. consisted of 1 cycle. Five studies contained the same six studies contained two cycles and one study [24] included in the meta-analysis.

Quality Assessment of the Articles

The Cochrane tool was used to assess quality of the RCT articles included in this systematic review by determining the risk of bias [34]. This validated tool consisted of the following 7 categories: "Random sequence generation," "Allocation concealment," "Blinding of participants," "Incomplete outcome data," "Selective outcome reporting," and "Other bias." Each category was scored as H, high risk of bias (ROB), U, uncertain ROB, or L, low ROB. Three independent reviewers (DSK, SP, SJ) performed the quality assessment and disagreement on scores were resolved through discussion.

Data Analysis

The response rates in the ginger and placebo arms were used for calculating the risk ratio, or relative risk (RR) (weighted according to sample size). RR and 95% confidence interval (CI) were calculated using the response rates for ginger (success of pain relief) as a basis. Standard mean differences (SMD) and 95% CI were also calculated for a pain visual analogue scale (AVS) using the Cochrane Collaboration’s software (RevMan Version 5.0 for Windows, Copenhagen: The Nordic Cochrane Centre). The variance of the change was calculated using a correlation factor of 0.4 as suggested by the Cochrane Collaboration. If appropriate, we then pooled data across studies using random effects models, if excessive statistical heterogeneity did not exist, the tau2 was pooled using a random-effects model because of clinical heterogeneity between each study such as age, dose of ginger and treatment duration. The meta-analysis included data from parallel-group design studies. The duration of treatment, the first 3 days of the menstrual cycle, was equivalent in all groups and the dosage was also quite similar at 750–2000 mg/day. However, the control group was different among groups and the control group was divided into placebo, analgesic (mefenamic acid, ibuprofen or zinc sulfate) and exercise.

Six studies contained two cycles and one study [24] consisted of 1 cycle. Five studies contained the same methods for each cycle. However, the Kashefi et al. study [23] used different methods: the first cycle was the same as the rest of the protocol but the second cycle began providing ginger or placebo from 2 days prior to the menstruation and lasting for 5 days. Both cycles of all studies except the Jenabi study [24] were used for the meta-analysis. As the data used for the meta-analysis were a continuous variable of the severity of the pain, as PVIS, and the duration of the pain, mean differences and standard deviations were used for the meta-analysis. Two studies gave the percentage of subjects who improved due to the treatments [27,28], and one study did not provide standard deviations of PVIS scores [25]. Thus, four studies [23,24,26,29] were included in the meta-analysis.

Heterogeneity of the included studies was tested using the Higgins $I^2$ test and meaningful heterogeneity was determined by 50% of $I^2$ value. When $I^2$ value was greater than 50, a random-effect model was used for the meta-analysis. Funnel plots were used to detect reporting biases for this systematic review as the number of studies induced was less than 10.

Subgroup Analysis

Each study had two cycles and each cycle was considered as an individual study. In addition, the studies contained different control treatments: four studies had a placebo control [23–26], two studies had mefenamic acid [27,28]; and one study had exercise [29] as positive controls. According to control treatments, studies were divided into two subgroups: placebo studies and analgesic studies. The study containing exercise as the control group was considered more like an analgesic group, but because the two studies having an analgesic control groups did not provide means and standard deviations, the exercise group in the Gupta study [29] was considered a placebo control.

Results

Summary of Included Studies

In the initial electronic searches a total of 29 studies were found and 7 duplicates were removed. After 12 studies (7 in vitro studies, 2 that were not clinical trials, 2 that did not have primary dysmenorrhea as an outcome—mixed cases of primary and secondary dysmenorrhea) were excluded, 10 studies remained. Finally, 7 RCTs met the inclusion criteria after removing 3 non-RCT studies (Figure 1). The 7 RCTs were used for the systematic review [23–29]. The main data from included RCTs were summarized in Table 1. Surprisingly, 6 RCTs were conducted in Iran [23,24,26–29] and 1 RCT was from India, although ginger is commonly consumed worldwide [25]. Five RCTs had a two-arm parallel design (ginger powder and placebo groups) [23–26,29] and 2 RCT adopted a three-arm parallel design including ginger powder [27,28]. In three-arm parallel studies, Ozgoli et al. included two analgesic groups such as mefenamic acid and ibuprofen as the control groups without a placebo group [28] and Kashefi et al. contained a placebo and one analgesic group (zinc sulfate) [27].

Risk of Bias

The risk of bias assessment for the included RCTs is presented in Table 2. Among 7 RCTs, 2 RCTs were classified as high quality [24,26], 4 RCTs had a
<table>
<thead>
<tr>
<th>First author year</th>
<th>Study Design</th>
<th>No. of Subjects; Age of Subjects Included</th>
<th>Excluded</th>
<th>Experimental Intervention (Dose, Duration, Source)</th>
<th>Control Intervention (Dose, Duration, Source)</th>
<th>Main Outcome</th>
<th>Experiment Results</th>
<th>Control Results</th>
<th>Effect Size</th>
<th>Author's Conclusions</th>
<th>Adverse effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shirvani et al.; 2015</td>
<td>RCT 2 Parallel arms</td>
<td>22; 18 and over; (Ginger mean: 26.6 ± 2.0; Placebo mean: 26.6 ± 2.1)</td>
<td>Ginger (n = 11), Placebo (n = 11) Primary dysmenorrhea for at least 50% of menstrual cycles lasting for 1 day. Pain intensity &gt;40 mm based on a 100 mm visual analog scale (VAS)</td>
<td>Ginger powder: 250 mg/capsule; Every 6 h until pain relief, for 2 cycles; Zintoma (ginger powder)</td>
<td>Mefenamic acid 250 mg/capsule Every 8 h until pain relief, for 2 cycles</td>
<td>Dysmenorrhea pain; Severity of dysmenorrhea N (%)</td>
<td>First cycle 1.39 ± 0.63 22 (53.9) second cycle 1.62 ± 0.71 33 (55.0)</td>
<td>First cycle 1.60 ± 0.80 19 (46.3) second cycle 1.49 ± 0.78 27 (45.0)</td>
<td>P &gt; 0.05</td>
<td>Ginger is as effective as Mefenamic acid for pain relief in primary dysmenorrhea. Ginger is an alternative treatment for primary dysmenorrhea None</td>
<td></td>
</tr>
<tr>
<td>Kashefiet al.; 2014</td>
<td>RCT 3 Parallel arms</td>
<td>150; 15–18; (Ginger mean: 12.8 ± 1.1; Zinc sulfate mean: 13 ± 1.0; Placebo mean: 12.4 ± 1.2)</td>
<td>Ginger (First cycle n = 47, second cycle n = 45), Zinc sulfate (First cycle n = 54, second cycle n = 53), Placebo (First cycle n = 45, second cycle n = 42), Regular menstrual cycles, Experiencing dysmenorrhea during the first three days of menstrual bleeding, Obtaining a score &gt;4 Based on 10 score of VAS</td>
<td>Ginger powder: 250 mg/capsule; 3 times/day/4 day for 2 cycles; Ginger powder</td>
<td>Placebo Capsule; Unknown dose; 3 times/day/4 day for 2 cycles; Lactose Zinc sulfate: 220 mg Capsule; 3 times/day/4 day for 2 cycles</td>
<td>Dysmenorrhea pain score (1–10-Score VAS)</td>
<td>First cycle 6.2 ± 1.40 second cycle 3.08 ± 1.52</td>
<td>Placebo First cycle 7.13 ± 1.3 second cycle 6.95 ± 1.67 Zinc First cycle 4.18 ± 1.7 second cycle 3.12 ± 1.2</td>
<td>P &lt; 0.001</td>
<td>Ginger and zinc sulfate had similar positive effects on the improvement of primary dysmenorrhea pain in young women. Headache, heartburn in both groups</td>
<td></td>
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<tr>
<td>First author year</td>
<td>Ref. no.</td>
<td>Study Design</td>
<td>No. of Subjects; Age of Subjects Included Excluded</td>
<td>Experimental Intervention (Dose, Duration, Source)</td>
<td>Control Intervention (Dose, Duration, Source)</td>
<td>Main Outcome</td>
<td>Experiment Results</td>
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<td>Gupta et al.; 2013</td>
<td>[29]</td>
<td>RCT 2 Parallel arms</td>
<td>64; 17–19; (Ginger mean = 14.0, Control mean = 13.3)</td>
<td>Ginger powder with exercise 500 mg 2 times/day First three days of menstruation Few muscle strengthening and stretching exercises 2 time/20 min First three days of menstruation</td>
<td>Only Exercise Few muscle strengthening and stretching exercises as per literature 2 time/20 min First three days</td>
<td>Pain score: 10-score numerical rating scale (NRS)</td>
<td>First cycle 3.85 ± 2.45</td>
<td>First cycle 4.43 ± 1.99</td>
<td>P = 0.304</td>
<td>Combined effect of ginger and exercise have higher efficacy than exercise alone.</td>
<td></td>
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<tr>
<td>Jenabi; 2013</td>
<td>[24]</td>
<td>RCT 2 Parallel arms</td>
<td>70; 13–19;</td>
<td>Ginger powder 300 mg/capsule; 1 time/day/3 day 1 cycle Ginger was purchased at pharmacy Placebo Capsule; Not reported dose and source</td>
<td>Dysmenorrhea pain score (1–10 score VAS)</td>
<td>4.81 ± 1.70</td>
<td>7.11 ± 1.12</td>
<td>P &lt; 0.001</td>
<td>Ginger is effective in minimizing the pain severity in primary dysmenorrhea.</td>
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<td>Rahnama et al. 2012;</td>
<td>[26]</td>
<td>RCT 2 Parallel arms</td>
<td>120; 18 and over (Ginger mean = 21.4 ± 2.0 Placebo mean = 21.3 ± 2.2)</td>
<td>Ginger powder 500 mg/capsule 3 times/day Protocol-1 2 days before the menstrual period and continued through the first three days Protocol-2 First three days</td>
<td>Placebo 1 Capsule Total powder 3 times/day Protocol-1 2 days before the menstrual period and continued through the first three days Protocol 2 First three days</td>
<td>Severity of pain Duration of pain (hout/based on 72 hour) (1–10-score VAS)</td>
<td>Protocol-1 5.12 ± 2.69</td>
<td>Protocol-1 5.72 ± 2.69</td>
<td>P = 0.015</td>
<td>Treatment of primary dysmenorrhea in students with ginger for 5 days had a statically significant effect on relieving intensity and duration of pain.</td>
<td>None</td>
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</table>

**Table 1 Continued**
<table>
<thead>
<tr>
<th>First author year</th>
<th>Study Design</th>
<th>No. of Subjects; Age of Subjects Included Excluded</th>
<th>Experimental Intervention (Dose, Duration, Source)</th>
<th>Control Intervention (Dose, Duration, Source)</th>
<th>Main Outcome</th>
<th>Experiment Results</th>
<th>Control Results</th>
<th>Effect Size</th>
<th>Author's Conclusions</th>
<th>Adverse effect</th>
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<tr>
<td>Halder; 2011 fig 25</td>
<td>RCT 2 Parallel arms</td>
<td>75; Not reported age range and average;</td>
<td>Ex1 (n=25), Ex2 (n=25), Control (n=25)</td>
<td>Irregular or infrequent menstrual cycle, Using an intrauterine contraceptive device or taking oral contraceptive pill.</td>
<td>Placebo control group (source was not reported)</td>
<td>Dysmenorrhea pain score (5-score Likert scale)</td>
<td>Ex1 1.36</td>
<td>Ex2 1.04</td>
<td>Not reported SD-value</td>
<td>Not reported</td>
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<tr>
<td>Ozpoli et al. 2009 [28]</td>
<td>RCT 3 Parallel arms</td>
<td>150; 18 and over; Mefenamic acid (n = 50), Ibuprofen (n = 50), Ginger (n = 50)</td>
<td>Pre-existing diagnosed disease, History of gestation or taking oral contraceptive, medicinal or herbal sensitivities, BMI &lt;19 or &gt;26, mild dysmenorrhea</td>
<td>Ginger rhizome powder 250 mg/capsule 4 times/day First three days of menstruation Zintoma;</td>
<td>Mefenamic acid capsule 250 mg 4 times/day First three days of menstruation Ponstan; Ibuprofen 400 mg/capsule 4 times/day First three days of menstruation Grufen;</td>
<td>A verbal multidimensional scoring system</td>
<td>62% got better</td>
<td>66% got better</td>
<td>Not reported</td>
<td>Not reported</td>
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Ex, Experiment group; Con, Control group.
### Table 2  Risk of bias in included trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Random Sequence Generation</th>
<th>Allocation Concealment</th>
<th>Patient and Practitioner Blinding</th>
<th>Assessor Blinding</th>
<th>Reporting Drop-out or Withdrawal</th>
<th>Intention-to-Treat Analysis</th>
<th>Selective Outcome Reporting</th>
<th>Other Potential Bias</th>
<th>No. of Reference</th>
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<tr>
<td>Shirvani et al. (2014)</td>
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<td>Jenabi (2013)</td>
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<td>Rahnama et al. (2012)</td>
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<td>Halder (2011)</td>
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Figure 2  Forest plot of the meta-analysis for the scores of the pain visual analog scale. (A) Inclusion of both cycles of the 4 randomized clinical studies. (B) Inclusion of the one cycle of the 4 randomized clinical studies. Each study is identified by first author and year. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
moderate quality and 1 RCT had a low quality [29]. Two studies used a proper method for randomization of the subjects such as coin flipping and computer generated random numbers [24,26] but the remaining studies did not describe how the subjects were randomized. In addition, 3 RCTs used blinding of patients and practitioners [23,26,28] but the remaining 4 RCTs did not mention their method of blinding. The drop-out rates were not high and all RCTs included in this review gave the reasons for withdrawals.

**Outcomes**

The severity of pain from primary dysmenorrhea was scaled by PVIS and the results were given as the scores in 5 RCTs [23–26,29] but two RCTs reported scores as a percent better than the baseline [27,28]. As one of the remaining five studies did not include standard deviations, four studies [23,24,26,29] were included in the meta-analysis. The pooled results of PVAS scores from the 4 RCT studies are provided in Figure 2A and B as a forest plot. In the meta analysis with pooling of both cycles of the 4 RCTs, the pain scores were significantly lower in the ginger group (n = 266) than the control group (n = 228) (Figure 2A; P = 0.0003). In addition, the results of the pain scores were the same when pooling one cycle of 4 RCTs (Figure 2B; P < 0.000001). However, as the RCT of Gupta et al. [29] used an exercise group rather than a placebo group as the control, it was deleted from the meta analysis. The pools of the remaining three RCT groups with the placebo group as the control were used for meta-analysis (Figure 3A and B): the PVIS scores were significantly lower in the ginger group (n = 198) as compared to the placebo control group (n = 168) including both cycles if available (P = 0.0001) (Figure 3A). In studies containing only one cycle, the consumption of ginger (n = 139) resulted in lower PVAS scores than that of the placebo (n = 122) (P = 0.0003) (Figure 3B).

Among the RCTs, 2 RCTs [27,28] used an analgesic treatment as the control group. Each study calculated the percentage of the PVAS improvement from the baseline. Both studies showed similar percentages of improvement in the ginger and analgesic groups (Table 1). In addition, in one study [29] the exercise group was considered as the control group. The PVAS pain score was similar between the exercise and ginger groups in the first cycle but it was lower in the ginger group than the exercise group in the second cycle (P = 0.039). Therefore, subjects treated with ginger powder experienced less pain from primary dysmenorrhea than the placebo supplemented subjects, furthermore the pain in the in the ginger group was less than in the exercise group and similar to the analgesic groups.

**Publication Bias**

An asymmetrical funnel plot was produced by this meta-analysis (the hollow circles in Figure 4), which indicated publication bias.
Numerous studies have investigated ginger for the amelioration of pain and inflammation in various diseases, and recent reviews and studies support its efficacy for pain relief in rheumatoid arthritis [35], osteoarthritis [36], burn injury [37], migraine headache when combined with Feverfew herb [38], acetic acid-induced pain [39], and chronic low back pain [40]. However, even though ginger has been shown to be effective for many types of pain, it is not necessarily efficacious for all pain. Studies of the use of ginger for exercise induced pain have yielded inconsistent results with some showing modest effects [41,42] and some no effects at all [43–45] for treating exercise-induced muscle soreness. Although the results are inconsistent, an observation by Black and O’Connor [45] may provide an explanation. They observed that the lack of effect of ginger on cycling exercise-induced pain in quadriceps muscle is consistent with a lack of effect of aspirin in similar muscle pain. They noted that the ineffectiveness of aspirin suggests that prostaglandins may not play a major role in exercise-induced skeletal muscle pain. As mentioned in the Introduction, suppressing the production of prostaglandins by COX-2 inhibition may be one of the major mechanisms of the analgesic and anti-inflammatory actions of ginger [6–9]. Therefore, although ginger has been demonstrated to have a wide range of analgesic efficacies, studies such as this that evaluates its effectiveness on specific types of pain are important.

Bioavailability of the active components of herbs and spices is a major limitation of most botanical medicines [46]; however ginger and its components appear to be well absorbed. One hour after oral consumption of ginger its major components: 6-shogaol, 10-gingerol, 6-gergoieral, and 8-gergoieral are detected in the plasma in rats and humans [47,48] and at 48–60 h 6-gergoierol, and 6-shogaol are excreted mainly into bile and some into urine [49].

It is important that the one RCT to report adverse effects of treatments reported only mild symptoms and with no differences between the ginger treated group and placebo group [23]. In a recent systematic review and meta-analysis of ginger for nausea and vomiting during pregnancy, the authors found 1,500 mg per day to be most effective and without any adverse effects [48], and there were no indications of adverse effects of higher doses. The oral consumption of ginger powder up to 2 g/kg body weight does not exhibit any mortality or abnormal changes in hematological parameters in rats [50]. The currently available studies indicate that ginger is very safe at optimally effective dosages.

To the best of our knowledge, this is the first systematic review and meta-analysis of RCTs on the effectiveness of ginger for primary dysmenorrhea. Even though the results indicate that ginger is highly effective for treating dysmenorrhea, there are important limitations to the study that need to be considered. The number of trials and total sample size of the primary studies are low. A standard scoring system was used to quantify the likelihood of bias inherent in the studies based on the description of randomization, blinding and withdrawals [34]. The seven RCTs included in the systematic review had low to moderate risk of bias. Three RCTs [24,27,29] reported double-blinding procedures but did not report details. No RCT...
and cognitive deficits in a mouse dementia model [51]. Furthermore, 10-gingerol has also been shown to have potent anti-neuroinflammatory capacity [52] and 6-gingerol has a wide variety of anti-inflammatory and other pharmacological activities [53]. Therefore, highly purified ginger preparations run the risk of removing important bioactive compounds and as rather modest doses of pure powder appear efficacious, use of whole powder may be prudent until more is known about the relative contributions of the different compounds. 

Conclusions

The results of our systematic review and meta-analysis provide suggestive evidence for the effectiveness of ginger in treating primary dysmenorrhea. However, the total number of RCTs that could be included in this analysis, the total sample size and the average methodological quality of the primary studies might not be sufficient to draw firm conclusions. However, the strength of the study was the consistency of benefit among all of the studies and a very highly statistically significant effect of ginger for treating pain. This research clearly demonstrates that ginger (750–2000 mg/day during the first 3–4 days of the menstrual cycle) is a very promising potential treatment for the pain and discomfort associated with primary dysmenorrhea. More high quality studies are necessary to clearly establish the efficacy of ginger for the treatment of primary dysmenorrhea.

Acknowledgment

This research was supported by the Ministry of Trade, Industry and Energy (MOTIE), KOREA, through the Education Support program for Creative and Industrial Convergence.

References


Ginger and Primary Dysmenorrhea


