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Systematic Review and Meta-analysis on the Efficacy of Zinc Supplementation in Reducing Dysmenorrhea Pain

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ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 September 2024 and was last updated on 7 September 2024.

INTRODUCTION

Review question / Objective Population: Women of reproductive age diagnosed with primary dysmenorrhea. Intervention: Zinc supplementation administered for the management of dysmenorrhea. Comparison: Placebo or other treatments such as nonsteroidal anti-inflammatory drugs (NSAIDs) or other dietary supplements. Outcome: Reduction in pain severity, measured using validated pain scales (e.g., Visual Analog Scale, VAS), and improvement in related symptoms such as nausea, vomiting, or fatigue.
To evaluate the efficacy of zinc supplementation in reducing pain severity in women with primary dysmenorrhea compared to placebo or other treatments, as measured by validated pain scales. The review will focus on randomized controlled trials.

Condition being studied Primary dysmenorrhea refers to painful menstrual cramps without any underlying pelvic pathology. It is a common condition affecting women of reproductive age, typically caused by uterine contractions triggered by prostaglandins. The pain usually starts with menstruation and can last for several days. Traditional management includes NSAIDs and hormonal contraceptives, but alternative treatments like zinc supplementation are also explored for pain relief.

METHODS

Search strategy A comprehensive literature search will be conducted in the following electronic databases: PubMed, Cochrane Library, EMBASE, and Google Scholar. The search will include studies published up until August 2024, without any language restrictions. The search strategy will focus on identifying randomized controlled trials (RCTs) that evaluate the efficacy of zinc supplementation in managing primary dysmenorrhea.

Participant or population Women of reproductive age diagnosed with primary dysmenorrhea.

Intervention The intervention involves the use of zinc supplements, which may include zinc sulfate or other zinc compounds, taken in various dosages and durations to reduce the severity of menstrual pain in women with primary dysmenorrhea.

Comparator The effectiveness of this intervention is compared to placebo or other standard treatments such as NSAIDs.

Study designs to be included Only randomized controlled trials (RCTs) will be included.

Eligibility criteria
Inclusion Criteria:
1. Language: Studies published in English or with English translations will be included.
2. Publication Type: Only peer-reviewed articles will be included. This includes full-text articles published in academic journals.
3. Time Frame: Studies published from the inception of the databases until August 2024 will be included.
4. Outcome Reporting: Studies must report on the primary outcome of interest (pain reduction in dysmenorrhea) using validated pain scales such as the Visual Analog Scale (VAS) or Numerical Rating Scale (NRS).
5. Population: Studies involving women of reproductive age diagnosed with primary dysmenorrhea will be included.

Information sources A comprehensive literature search will be conducted in the following electronic databases: PubMed, Cochrane Library, EMBASE, and Google Scholar.

Main outcome(s) Pain Reduction: The primary outcome of this review is the reduction in pain severity associated with primary dysmenorrhea.

Additional outcome(s) The quality assessment and risk of bias analysis for the included primary studies will be conducted using the Cochrane Risk of Bias Tool.

Data management Two independent authors extracted data from the recruited studies, encompassing demographic data, study design, details, and values. The evaluators paid special attention to the effect direction of the scale used in each trial to avoid mis-interpretation. In situations where the data was unavailable in the published articles, we contacted the corresponding authors to obtain the original data.Meta-analysis will be conducted using the Comprehensive Meta-Analysis (CMA) Version 3.7 software. The standardized mean difference (SMD) with 95% confidence intervals (CI) will be calculated for continuous outcomes related to pain severity. A random-effects model will be used to pool the SMDs due to expected heterogeneity among studies.

Quality assessment / Risk of bias analysis To investigate the methodological quality of recruited studies, we used the Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2), which consisted of 6 main items: randomization process, intervention adherence, missing outcome data, outcome measurement, selective reporting, and overall risk of bias. In the intervention adherence section of RoB 2, there are two options for literature assessment: intention-to-treat (intervention assignment) or per-protocol (intervention adherence). In this meta-analysis, we chose the per-protocol evaluation, since it fits the design of our included studies. Statistical heterogeneity will be assessed using the I^2 statistic, with values over 50% indicating substantial heterogeneity.

Strategy of data synthesis Because of the heterogeneity of the target populations in the enrolled studies, the current meta-analysis was conducted with a random-effects model, using Comprehensive Meta-Analysis software, version 3.7 . A two-tailed p value less than 0.05 was considered statistically significant. We chose Hedges' g and 95% confidence intervals (CIs) to quantify the primary outcomes (changes in fatigue scores). A Hedges' g of 0.2, 0.5, and 0.8 is considered a small, moderate, and large effect size, respectively. We chose odds ratios and their 95% CIs to investigate the secondary outcome (treatment-related adverse event rates).
The I2 and Cochran's Q statistics were used to evaluate the degree of heterogeneity among studies. An I2 value of 25%, 50%, and 75% was considered low, moderate, and high heterogeneity, respectively.
Meta-analysis will be conducted using the Comprehensive Meta-Analysis (CMA) Version 3.7 software. The standardized mean difference (SMD) with 95% confidence intervals (CI) will be calculated for continuous outcomes related to pain severity. A random-effects model will be used to pool the SMDs due to expected heterogeneity among studies.

Subgroup analysis Subgroup analyses will be conducted to explore potential sources of heterogeneity and to identify whether the effect of zinc supplementation on primary dysmenorrhea differs across specific groups. The following subgroup analyses are planned:

1. Dosage of Zinc Supplementation
2. Duration of Supplementation
3. Baseline Pain Severity
4. Age of Participants
5. Geographic Region.

Sensitivity analysis To confirm the robustness of the meta-analysis, the sensitivity analyses were performed using one-study removal method to see if there was a significant change in the summary effect size after removing a particular trial from the analysis.Sensitivity analyses will be performed to explore the robustness of the findings. Publication bias will be assessed using funnel plots and Egger's test.

Language restriction No language limit.

Country(ies) involved Taiwan.

Keywords Zinc supplementation; Dysmenorrhea; Primary dysmenorrhea; Menstrual pain; Pain management; Randomized controlled trials; Meta-analysis.

Contributions of each author

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