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Effectiveness of zinc supplementation in treating dysmenorrhea



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ABSTRACT

Background: Dysmenorrhea has a high prevalence among women, especially in young women. Zinc has been proved to have a beneficial effect in treating pain. The aim of this study is to determine the effectiveness of zinc supplementation in treating dysmenorrhoeal pain.

Method: This is an experimental study, using pre and post-test design. The study participants were medical staffs of H. Adam Malik Hospital and other satellite hospitals. This study was conducted on March 2016 to June 2016. Thirty seven patients with moderate to severe primary menstrual pain were given 30 mg of zinc per day (divided into two doses), 2 days prior to menstruation until its cessation, for two to three months. The pain was assessed with the visual analog scale (VAS).

Results: The mean age of participants was 22.95 ± 1.33 years old and the mean body weight, height, and body mass index were 55.54 ± 9.36 kg, 160.16 ± 5.46 cm, 22.02 ± 3.44 kg/m², respectively. The mean pain score is higher prior to zinc supplementation (4.92 ± 1.80 ; moderate pain) and the score decreased over three months of zinc supplementation, resulting in a mean score of 2.7 ± 2.03 (moderate pain). The differences were found to be statistically significant ($p = 0.000$).

Conclusion: Dysmenorrhea is frequently found in young women. Two to three months of zinc supplementation during menstruation is proved to be useful in reducing the intensity of dysmenorrhoeal pain.

Keywords: Dysmenorrhea, Zinc, Young Women

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INTRODUCTION

Dysmenorrhea is defined as pain or discomfort in the lower abdomen during menstruations that significantly interfere with daily activities. It is usually found in young women and it is the most common reason for young women to seek for a consultation and treatment.¹

According to previous studies, dysmenorrhea has a high prevalence. According to World Health Organisation (WHO), mean incidence of dysmenorrhea in your women is between 16.8 to 81%.² In United Kingdom, it is reported that 45 to 97% women has dysmenorrhea, similar to the other European countries.² In Indonesia, a study in Semarang, Central Java, found the incidence of mild, moderate, and severe dysmenorrhea to be 18%, 62%, and 20% respectively.³

Dysmenorrhea interferes with daily activities and causes economic burden. In the United States, the economic loss due to reduced productivity because of dysmenorrhea is up to 2 billion US dollars.⁴ While in India, of the 31.67% student with dysmenorrhea, 8.68% cannot engage in study activity.⁵ In Indonesia, a study reported that 71% women have dysmenorrhea, 5.9% of it cannot go to school or work, and 59.2% of the women experienced regression of their work productivity due to dysmenorrhea.⁶

Dysmenorrhea can be divided into primary and secondary dysmenorrhea.⁴ Primary dysmenorrhea is defined as a menstrual pain or cramp, without any pathologic abnormalities. In secondary dysmenorrhea, a pathologic abnormality (such as endometriosis) is observed. The cause of primary dysmenorrhea is unknown. One possible explanation is that the prostaglandin produced during menstruation will induce the contraction of myometrium, which then will cause ischemia of the uterus, resulting in menstrual pain.⁸

Primary dysmenorrhea manifests as a pain or discomfort in the lower abdomen, around the pelvic, that spreads to the hip and thigh. It is usually accompanied by nausea, vomiting, diarrhea, headache, and labile emotional state. The pain emerges before the menstruation begins and vanished over time until the menstruation is finished.⁹ The initial treatment is drugs that inhibit prostaglandin production; non-steroidal anti inflammation such as ibuprofen, naproxen, and mefenamic acid are the most commonly used.^{7,10} Eventually, such drugs has side effects towards the gastrointestinal system, such as dyspepsia syndrome.¹¹ Self treatment is a common finding; 30 to 70% adolescent women with dysmenorrhea treat themselves with widely available pain medication.² Concerning the

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side effects, they are at risk if they keep consuming the drugs without a consultation with a physician. Thus, alternative treatments such as herbal treatment, supplement treatment, acupuncture treatment, behavior treatment, and aromatherapy are under research to find a safer medication compared to NSAID.¹²

Zinc is known to inhibit acid-sensing ion channel 1b (ASIC1b), expressed in peripheral sensory neuron and also affect nociceptors.¹³ Zinc is also known to inhibit prostaglandin production in human endometrial tissue. A study found a higher concentration of prostaglandin metabolite in the plasma of rats with zinc deficiency.⁹ Zinc can reduce the prostaglandin production through its anti-inflammation and endogenous antioxidant catalisator effects.¹⁰ Zinc can also increase the essential fatty acid conversion into anti-inflammation, and reduce the effect of prostaglandin.¹⁴ Based on the review, zinc has a potential to be used as pain medication. Thus, the aim of this study is to determine the effectiveness of zinc supplementation in treating dysmenorrhoeal pain.

METHOD

This is an experimental study, using one group pre and post-test design. This study was conducted in H. Adam Malik Hospital and other satellite hospitals, from March 2016 to May 2016.

Study population was all female medical students and midwife students, also all medical staffs in the H. Adam Malik hospital and the satellite hospitals. This study used consecutive

sampling method. The eligibility criteria were women aged 17 to 25 years old with primary dysmenorrhea. They must also have normal menstrual cycles (24 to 35 days, with 4 to 6 days of menstruation), have not married or given birth before, and have no other abnormalities in the pelvic. Women who cannot take the zinc supplementation and women who did not have their period in 4 days since she started taking the zinc supplementation were excluded from this study. The estimated sample size was 37, calculated by using the formula below.

Eligible participants were then asked for a written informed consent in order to participate in this study. All participants were then interviewed and asked to fill the L-MMPI (Minnesota Multiphasic Personality Inventory) scale to determine the reliability of subject when they fill the pain scale, which was assessed with visual analog scale (VAS). All participants who passed the reliability test then underwent data collection, including date of last period, body height and weight, menarche age, and the initial data of pain assesment. All eligible study participant were then given oral zinc supplementation as much as 30 mg per day (15 mg of zinc, twice a day), two days prior to estimated period date until the period is over. Pain assessment was done for three consecutive menstrual cycles. The intensity of pain was categorized as mild (1-2), moderate (3-6), severe (7-8), and very severe (9-10). Data were then analyzed statistically using Wilcoxon's test and is statistically significant if $p > 0.05$. This study had been approved by University of North Sumatera's Ethics Committee.

RESULTS

Thirty seven women with moderate-severe primary dysmenorrhea were involved in this study. The mean age of participants was 22.95 ± 1.33 years old. The mean body weight, height, and body mass index were 55.54 ± 9.36 kg, 160.16 ± 5.46 cm, 22.02 ± 3.44 kg/m², respectively. Characteristics of study participant can be seen in [Table 1](#).

The mean menstrual pain score of the participants was higher before the administration of zinc; 4.92 ± 1.80 (moderate pain). The score improved every month and after 3 months period, the mean pain score decreased to 2.7 ± 2.03 (mild pain). The differences between the mean pain score are statistically significant. The data of mean menstrual pain score can be seen in [Table 2](#) and the VAS score data of every study participants can be seen in [Fig. 1](#).

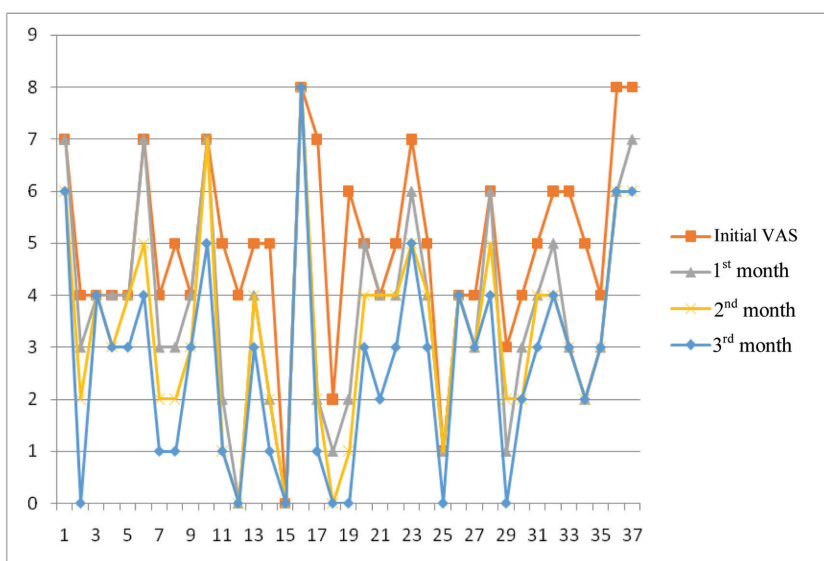


Figure 1 VAS score of every study participants, before and after zinc supplementation

Table 1 Characteristics of study participants (n = 37)

Characteristics	Mean	SD	Min	Max
Age (years)	22.95	1.33	21.00	26.00
Body weight (kg)	56.54	9.36	40.00	85.00
Body height (cm)	160.16	5.46	148.00	171.00
BMI (kg/m ²)	22.02	3.44	16.02	34.93

Table 2 Mean score of menstrual pain of study participants (n = 37)

VAS score	Mean	SD	Z		
			Initial	1 st month	2 nd month
Initial	4.92	1.80	-	-	-
1 st month	3.73	2.04	-4.292*	-	-
2 nd month	3.30	1.93	-4.762*	-3.578*	-
3 rd month	2.70	2.03	-5.068*	-4.719*	-3.947*

*p = 0,000

VAS: visual analog scale

DISCUSSION

To investigate the effectiveness of zinc in treating dysmenorrhea, an experiment was conducted on 37 women aged 17-25 years old with primary dysmenorrhea. The selection of the age group is because dysmenorrhea is more common in teenagers and adolescent women (70-90%).¹²

The zinc dosage of 30 mg/day used in this experiment follows the previous study, but in the previous study, it was given as a single dose instead of two doses. This dosage is considered to be safe since the maximal dose of zinc is 150 mg/day.⁸ In the therapeutic dose, zinc rarely causes any adverse effects. The effects are nausea, bloated, discomfort in the abdomen. In the toxic concentration, zinc will cause the inflammatory mediators to be released through the activation of the Transient receptor potential cation channel 1 (TRPA1).^{14,15} The zinc supplementation was started 2 days prior to menstruation following a previous study which also showed a similar finding.⁹

A similar finding was reported in a study, where women who received 30 mg zinc per day (single dose) had less incident of dysmenorrhea compared to the other group of women who received 15 mg of zinc per day.⁹ Another study showed that both primary and secondary dysmenorrhea will get deteriorate if the patient has a zinc deficiency.¹²

The finding of this study is related to the role of zinc in prostaglandin synthesis since prostaglandin plays a crucial role in dysmenorrhea.¹⁶ Contraction of myometrium is induced by a substance similar to natural fat, which was identified later as prostaglandin. The spasm then causes tissue ischaemia and induces the release of pain mediator, including prostaglandin.

During menstruation, there is an increasing concentration of prostaglandin, especially PGF₂α and PGE₂. At the beginning of the cycle, both are detected in low concentration. The concentration of PGF₂α will keep increasing and then decrease during the implantation window. In some pathological condition, such as dysmenorrhea and menorrhagia, the concentration of PGF₂α and PGE₂ are distinctly higher.¹⁷

The Prostaglandin F receptor (FP) is abundant in the myometrium. Increased PGF₂α production will cause vasoconstriction and spasm of the myometrium. The combination vasoconstriction and spasm will cause myometrium to be in the ischemic state, inducing the pain sensation.¹⁷

Zinc is proved to inhibit the metabolism of prostaglandin in endometrium tissue. In the uterus tissue, a concentration of 110⁻⁵ mol/l zinc can inhibit the prostaglandin metabolism.¹⁸ A study in rats showed that rats with zinc deficiency have a higher concentration of prostaglandin metabolites, compared to rats without zinc deficiency.⁹ This effect might be contributed to zinc's effect towards cyclooxygenase-2 (COX-2) enzyme. Zinc inhibits the activity of this enzyme, leading to decreasing of prostaglandin synthesis.¹⁹

Zinc's mechanism of action in reducing the menstrual cramp is supposedly toward increasing of the capillary circulation.⁹ In angina pectoris, zinc is observed to improve the capillary circulation, in which the same effect is expected in the uterus tissue.⁹ The improved capillary circulation then will help to resolve the tissue ischemia state during menstruation, leading to reduce production of prostaglandin. Besides, zinc is also a nutrient that increases the essential fatty acid conversion into anti-inflammation towards prostaglandin and also acts as antioxidant and anti-inflammation. All these effects then lead to improvement of the capillary circulation.⁹

The tissue ischemia will also cause the production of some reactive oxygen species (ROS) which will cause a further damage to the tissue. Tissue damage will then induce the production of pain mediators. In the uterus, there is copper-zinc dismutase enzyme, which will inactivate the ROS. Zinc supplementation will make sure there is an adequate zinc deposit in the uterus.²⁰

Besides those mechanisms mentioned above, zinc is also known to inhibit the acid-sensing ion channels (ASICs), a neuronal voltage-insensitive sodium channels activated by extracellular protons. So far, there has been 7 subunits of ASICs identified, encoded by 4 genes (ASIC1, ASIC2, ASIC3, ASIC4). In the nociceptor, both ASIC1a and ASIC1b are expressed. In rats, inhibition of ASIC1 resulted in the loss of pain sensation

(thermal, mechanic, chemical, inflammation, and neuropathic pain).⁸ Thus; it is thought that ASIC1 plays a role in transmitting pain sensation. An experiment in mouse showed that zinc inhibits the activity of ASIC1b channel and cystein 149 which is located extracellularly of the ASIC1b subunit.⁸ It is also showed that channel ASIC1b is a sensible target for zinc and also cystein 196 in the extracellular matrix.¹⁶

CONCLUSION

Dysmenorrhea is a common finding in young age women. Zinc supplementation at the dose of 30 mg/day, two days prior to the menstruation until its cessation, is proved to reduce the intensity of dysmenorrhea. This effect is acquired after 2 to 3 months of supplementation. This finding supports the usage of zinc as an alternative to the dysmenorrhea treatment.

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