



Zinc treatment prevents dysmenorrhea

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Summary Primary dysmenorrhea, menstrual cramps in otherwise well women, produces mild to debilitating cramping of the uterus. More than half, and by some estimates 90% of all American women experience menstrual cramps during the first several days of menstruation. About one in ten women are unable to perform their normal routine for one to three days each menstrual cycle due to severe uterine cramping. Although the uterus contracts and relaxes routinely, during menstruation the contractions are much stronger producing pain and "cramps". Women with dysmenorrhea have high levels of prostaglandins, hormones believed to cause menstrual cramping. Prostaglandins are believed to temporarily reduce or stop blood supply to the uterus, thus depriving the uterus of oxygen resulting in contractions and pain. One would expect zinc, like the non-steroidal anti-inflammatory drugs used to treat cramping, to reduce the production of prostaglandins. Zinc inhibits the metabolism of prostaglandins ruling out this mechanism of action, suggesting erroneously that zinc deficiency would prevent cramping. However, it is shown by case histories that zinc, in 1–3 30-mg doses given daily for one to four days prior to onset of menses, prevents essentially all to all warning of menses and all menstrual cramping. One hypothesis for a mechanism of action is that a precursor (COX-2) or metabolite of prostaglandins causes menstrual cramping and not prostaglandins themselves. Another hypothesis is that zinc has antioxidant and anti-inflammatory actions in the uterus. Improvement in micro-vessel circulation by zinc may help prevent cramping and pain. In patients consuming 31 mg of zinc per day, premenstrual tension (PMT) symptoms did not occur, while in patients consuming 15 mg of zinc, PMT symptoms did occur ($P < 0.001$). Protocols using 30 mg of zinc once to three times a day for one to four days immediately prior to menses to prevent dysmenorrhea are described and they are recommended for additional study. The side effect from the absence of all warning of pending menses due to zinc treatment was concern of possible pregnancy. The United States RDA for zinc appears to be too low to optimize women's health and prevent menstrual cramps.

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Introduction

Primary dysmenorrhea, menstrual cramps in otherwise well women, produces mild to debilitating cramping of the uterus. More than half, and by

some estimates 90% of all American women experience menstrual cramps during the first several days of menstruation. About one in ten women are unable to perform their normal routine for 1–3 days each menstrual cycle due to severe uterine cramping. Menstrual cramps have been described as being caused by "normal" contractions of the uterus. Although the uterus contracts and relaxes routinely, during menstruation the contractions

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are much stronger producing pain. Women with dysmenorrhea have high levels of prostaglandins, hormones known to cause cramping abdominal pain [1], and prostaglandins are believed to cause strong uterine contractions temporarily reducing or stopping the blood supply to the uterus, thus depriving the uterus of oxygen resulting in contractions and pain.

Primary dysmenorrhea is treated with drugs such as the non-steroidal anti-inflammatory agents including ibuprofen that inhibit prostaglandin metabolism, or is treated with oral contraceptives to prevent ovulation, thus preventing menstruation and cramping. Acetaminophen helps reduce pain but it does not have an effect on prostaglandins. Regular physical exercise, beta-blockers, psychotherapeutic methods, surgical interruption of pelvic nerves, cervical dilatation and progesterone are also helpful in treating cramping in some women.

During a 1982 clinical trial of zinc gluconate lozenges for common colds (23 mg zinc each 2 wakeful hours) by Eby, Davis and Halcomb [2], women asked the physician (WWH) after the 7 day course of zinc or placebo treatment if treatment caused menstrual abnormalities. They explained that their periods started on schedule, but they did not experience any menstrual cramping or bloating or any other symptom to warn them of either pending menses or experience any cramping during menses, and their main concern was pregnancy. The feeling of total absence of any indication of pending menses appeared to these women to be identical to pregnancy. Examination of the clinical trial records showed that these comments came only from zinc-treated women and not from calcium lactate placebo treated women.

Over the intervening 24 years, 30 mg of zinc (zinc gluconate) used once to three times per day during one to four days immediately prior to expected menses has been used by many Texas women, with information being spread by word-of-mouth. There have been no side effects reported, except for nausea when multiple 30 mg doses were taken at the same time.

Methods and procedures

The following case histories are taken from observations as illustrative of the effects routinely observed.

Case history 1: A zinc gluconate tablet containing 30 mg of zinc was taken morning and evening with meals during the four days immediately prior to the date of expected menses

by a 110 pound, 17 year-old childless woman. This young woman had severe menstrual cramping prior to use of zinc and had a history of regularly missing school due to severe cramping. She had been using ibuprofen in previous months, but used no other treatment than zinc in this case.

Case history 2: A 23-year old 130 pound childless woman suffering from a severe common cold used zinc acetate throat lozenges (14 mg zinc) each two wakeful hours to treat her cold for two days immediately prior to her menstrual cycle and continued zinc for the first day of her cycle. She normally had severe menstrual cramping and consequently frequently missed work even though she used ibuprofen prior to use of zinc in this case history.

Case history 3: A 49-year old 135 pound woman having had two children, having severe menstrual cramps, severe pelvic floor muscle pain, with 8–9 days of menstrual bleeding, and 3–4 days of very heavy (overflow) bleeding with severe bloating for 5–6 days prior to menstruation through the second day of menstruation, took 60 mg of zinc (from zinc gluconate) twice a day (with breakfast and supper) starting 3–4 days prior to her expected start of menstruation. She took zinc only for 3–4 days before her periods during three consecutive monthly cycles. She had suffered these severe symptoms regularly for the preceding 35 years without significant benefit from a variety of treatments including ibuprofen over the years.

Case history 4: A 30-year old childless woman, who had taken 30 mg of zinc for one day prior to expected menses each cycle for 17 years took 30 mg of zinc a day prior to expected menses. Bloating had occurred regularly one day prior to menses for 17 years with great regularity, indicating when she should take zinc. She routinely took 30 mg of zinc on that single day (or perhaps two days) per menstrual cycle without other drug or nutrient treatment. Zinc caused nausea if she used it more than once or twice per cycle.

Case history 5: A 38-year old woman, having had two children, having had a prior history of severe menstrual cramps illustrated by missing one or two days of school per cycle as a teenager, missing a day or two of work per cycle as an adult until birth control was initiated, which alleviated most cramping and bloating, with severe menstrual cramping reoccurring after terminating birth control for a few years, used 30 mg of zinc for 3–5 days prior to expected onset of menses.

Results

Case history 1: In the 17-year old woman, menstrual cramping did not occur and there was no warning of pending menses. She had nausea when she took two tablets at the same time, but not when she took one with each meal. She did not take zinc at any time except for the four days before menses and the first day of menses. She did not have bleeding different than previous periods. She did not miss school.

Case history 2: The 23-year old woman's cold symptoms were very mild and resolved completely in three days, and she noted that her usual menstrual cramps did not occur, thus she missed no work from either the cold or menstrual cramps. She used an average of nine lozenges a day, totaling 126 mg zinc per day. Use of zinc acetate lozenges throughout the day did not cause nausea and did not alter bleeding, but she was concerned for a few days that she was pregnant since there were no symptoms that would suggest pending menses.

Case history 3: The 49-year old woman experienced reduction in bloating, elimination of pelvic floor muscle pain, elimination of heavy over-flow bleeding, shortening of the menstrual period back to a normal 5 days/period, and prevention of all menstrual cramps. During the following five months (to the time of this writing) serum zinc levels remained normal, yet menstrual cramping remained absent, pelvic floor muscle tension did not re-occur, menstrual flow remained normal (no overflow) and periods remained shortened without further zinc treatment. Salt cravings were also eliminated and bloating was lessened but not eliminated during those 5 months after zinc treatment. She required no other treatment.

Case history 4: The 30-year old woman was able to greatly reduce the severity of menstrual cramps with a single 30-mg zinc tablet taken one day prior to expected menses with no other treatment. She had no other menstrual complaints, and no premenstrual complaints at any time. Using zinc, she never needed to take any drugs or use any other treatment. She used zinc to manage her cycles for 10 years. On rare occasions when zinc was unavailable, her menstrual cramps and pain were debilitating, and 1000 mg doses of ibuprofen were required to reduce her pain and cramping.

Case history 5: The 38-year old woman was not able to predict the onset of menses, thus she averaged more days taking zinc than some other

women. Menses started without any bloating, cramps or pain or any other symptom of pending menses other than menstrual flow. Menstrual flow was heavy only on the first day. There was no other change in the volume of menstrual flow from previous cycles without zinc. She used zinc for 10 years without using any other treatment for menstrual cycles.

Generally, zinc treatment when started one to four days prior to the expected onset of menses prevented menstrual cramping and was beneficial in other ways related to the menstrual cycle (helped prevent bloating, pelvic floor pain and over flow) without side effects except for occasional nausea from taking doses over 30 mg, although frequent, smaller 14 mg doses as throat lozenges taken a few hours apart did not cause nausea. None needed additional drug treatment to prevent cramps.

Discussion

Since excess production of prostaglandins is believed to be the cause of menstrual cramping, one would expect zinc to reduce the production of prostaglandins. According to Kelly and Able [3], zinc inhibits the metabolism of prostaglandins ruling out this mechanism of action. They found that concentrations of zinc in the range of 1×10^{-5} mol/l, which is in the physiologic range of concentrations in uterine tissues, inhibited the metabolism of prostaglandins, suggesting that zinc deficiency might prevent cramping, not the opposite as is described here. This disconnect poses serious implications for our understanding of the role played by prostaglandins in the uterus.

In semi-support of these observation, Goei et al. [4] showed in 1982 that in patients consuming 31 mg of zinc per day, premenstrual tension (PMT) symptoms did not occur, while in patients consuming 15 mg of zinc, PMT symptoms did occur ($P < 0.001$). The United States recommended daily allowance (RDA) for zinc has been 15 mg for many years, but it has recently been lowered to 8 mg per day for women, while the median intake of zinc from food in the United States has been found to be 9 mg per day for women. Consequently, the patients of Goei et al. were consuming large amounts of zinc relative to today's dietary intake, but only those receiving twice the previous RDA (four times the current RDA) of zinc did not have PMT symptoms. In direct support of these observations, Guy E. Abraham commented that "zinc was very help-

ful in clearing up cramps'' in a magazine article describing the effectiveness of treating PMT with magnesium, iron, and vitamins B6 and E [5]. He also showed that the current intake of excessive sodium and calcium and too little potassium and magnesium were harmful to women's health [6].

A surprising side effect from use of zinc lozenges in the treatment of common colds was prevention of signs and symptoms of pending menstruation. Prasad et al. [7] showed that treatment with 12.8 mg zinc (zinc acetate) lozenges taken an average of 6.2 times per day increased zinc serum concentration from 14.8 to 17.7 $\mu\text{mol/l}$ ($P < 0.001$), and suggested that these large amounts of zinc for a few days were safe and were very unlikely to cause disturbances in copper metabolism. Zinc dietary supplement tablets are also shown to be effective in 30 mg doses, 1–3 times per day. However, their action is not as immediate as when zinc is administered in lozenge form. Daily doses over 30 mg were split to avoid nausea. Treatment of existing menstrual cramping is not as effective as pretreatment to prevent dysmenorrhea.

Regardless of these observations, there remains concern for a viable hypothesis concerning the mechanism of action. One hypothesis is that menstrual discomfort is caused by a precursor (COX-2) or metabolite of prostaglandins and not directly by prostaglandins. Another hypothesis is that zinc has an action on the uterus similar to the action of zinc in the human heart when treating angina pectoris with similar amounts of zinc [8]. Zinc terminates the pain of angina pectoris and terminates Reynaud's disease by improving circulation at the micro-vessel level. Since strong uterine contractions temporarily reduce or stop the blood supply to the uterus, thus depriving the uterus of oxygen resulting in contractions and pain, perhaps improvement in micro-vessel circulation by zinc treatment is sufficient to prevent cramping and pain. Ischemia is partly caused by reperfusion, which results in the release of many active oxygen species which can cause tissue damage and pain. Thus, much of the discomfort of dysmenorrhea is likely to be due to these free oxygen radicals. The enzyme which inactivates these oxygen species is dismutase. Copper–zinc dismutase is present in the uterus [9] and zinc treatment allows for more adequate levels of this enzyme – which in turn could relieve cramping and pain. Zinc is an effective anti-inflammatory and antioxidant agent, and it can readily downregulate inflammatory cytokines [10]. Zinc protects plasma cell membranes preventing damage to cells by a wide variety of cytotoxic agents in a dose dependent manner extending far above physiologic concentrations

[11]. Zinc regulates cyclooxygenase-2 (COX-2), an enzyme involved in pain, inflammation and implicated in certain cancers (such as uterine cancers having poor prognosis) [12], and COX-2 can be lowered by zinc treatment [13]. Consequently, zinc in the doses used, is likely to be found by further research to be far more effective and produce far fewer side effects than current pharmaceutical and medical treatments.

It has been shown that it is possible to prevent dysmenorrhea with zinc treatment. A lack of response in women taking 90 mg zinc or more per day would suggest a need for a physical exam to determine the cause of symptoms. Both primary and secondary dysmenorrhea are worsened by zinc deficiency, and zinc treatment appears merited. Zinc oxide is not recommended since it has relatively poor bioavailability [14]. Larger doses of zinc may be required for heavy and older women.

The United States RDA for zinc appears to be too low to optimize women's health and prevent menstrual cramps and bloating, thus insuring continued dependence on pharmaceutical drugs and medical treatments for dysmenorrhea. Further research is merited since the lives of up to one half of the population are needlessly impacted by menstrual cramping.

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