

The Effects Magnesium on PMS and PMDD

Jamie Trettel & Emily Raup Student Researchers

Dr. Diane Longstreet, Instructor / Senior Researcher

DIE 4564 Research Methods

Keiser University, Lakeland, FL 33803

September 21, 2015

## Abstract

Premenstrual syndrome (PMS) and premenstrual dysphonic disorder (PMDD) are classified by having a consistent cyclic cluster of life disrupting symptoms associated with menstruation. Approximately 80% of women experience at least one symptom of PMS and 5% experience PMDD. Magnesium (Mg) levels have been measured as lower in the follicular phase of the menstrual cycle suggestive that Mg play a role in the onset of PMS/ PMDD symptoms. Mg has been promoted as an alternative therapy for PMS and PMDD because muscle contraction and relaxation, neurological functions, and the release of neurotransmitters are Mg dependent. This systematic literature review found evidence of noticeable improvements in sufferers of PMS/PMDD when Mg supplementation was give for at least two months. However more studies are needed to clarify if Mg deficit precedes PMS / PMDD symptoms or the condition fosters the development of a deficit. A large prospective cross-over experimental design would establish how Mg supplementation might be best utilized to ameliorate PMS/PMDD symptoms.

***Suggested citation:*** Trettel, J., Raup, E. & Longstreet, D. (2015) The Effects Magnesium on PMS and PMDD. *Center for Magnesium Education and Research.*

***Keywords:*** magnesium, premenstrual syndrome, premenstrual dysphoric disorder, PMS, PMDD

The Effects Magnesium on PMS and PMDD

Premenstrual syndrome (PMS) is classified as cluster of symptoms ranging from cramps, water retention, irritability, anxiety, depression and headaches (Woman's Health, 2014). According to the American College of Obstetricians and Gynecologists, 80% of women will experience at least one of these symptoms between the ages of 20 and 40 years. Approximately 5% of women suffer from a more severe version of PMS called premenstrual dysphonic disorder (PMDD) (Brown et al., 2014). PMDD is defined as having five or more symptoms such as sadness, anger, trouble focusing, food cravings and feelings of being out of control (Woman's Health, 2014). The onset of PMS/PMDD symptoms usually surface one to two weeks before menses and usually disappear the first couple of days after the beginning of the cycle (Brown et al. 2014).

There are many over the counter and prescription drugs to help alleviate these symptoms. It has been suggested that Mg supplementation may ameliorate PMS symptoms (Brown et al. 2014). Mg is a cofactor for over 300 reactions in the body; it helps with stabilization of ATP, aids in muscle relaxation and contraction, neurological functions, and the release of neurotransmitters (Wilhelm, & Ketteler, 2012), all of which lend plausibility to the affect of Mg in PMS / PMDD.

Regarding assessment tests for adequacy or deficiency in Mg, no single test has been universally accepted as an adequate measure. Nearly 99% of Mg is found within the bones, muscles, and non-muscular tissue (Wilhelm, & Ketteler, 2012). Bazydlo, Needham, & Harris (2014) suggested that both intracellular and extracellular need to be tested to determine true deficiency or adequacy. Urine and retention tests are used best to evaluate the Mg absorption in the intestines and Mg wasting (Swaminathan, 2003). Since intestinal absorption of Mg is

increased in the presence of deficit, Mg retention tests have also been used as a proxy for deficiency. One study conducted on Mg levels during menstrual, follicular, and luteal phases of the menstrual cycle found Mg levels to be lower in the follicular phase compared to the other 2 phases (Dullo & Vedi, 2008). Since Mg levels are lower in women during the follicular phase of their menstrual cycle, there may be a contributing factor in symptoms of PMS or PMDD. According to Dullo & Vedi (2008), serum Mg was reported to be lower during the follicular phase of the menstrual cycle in PMS sufferers. This systematic literature review investigates the micro-mineral Mg and its role in the body including its influence on PMS and PMDD, and seeks to answer the question, “What is the evidence that Mg will reduce PMS and / or PMDD symptoms?”

## Methods

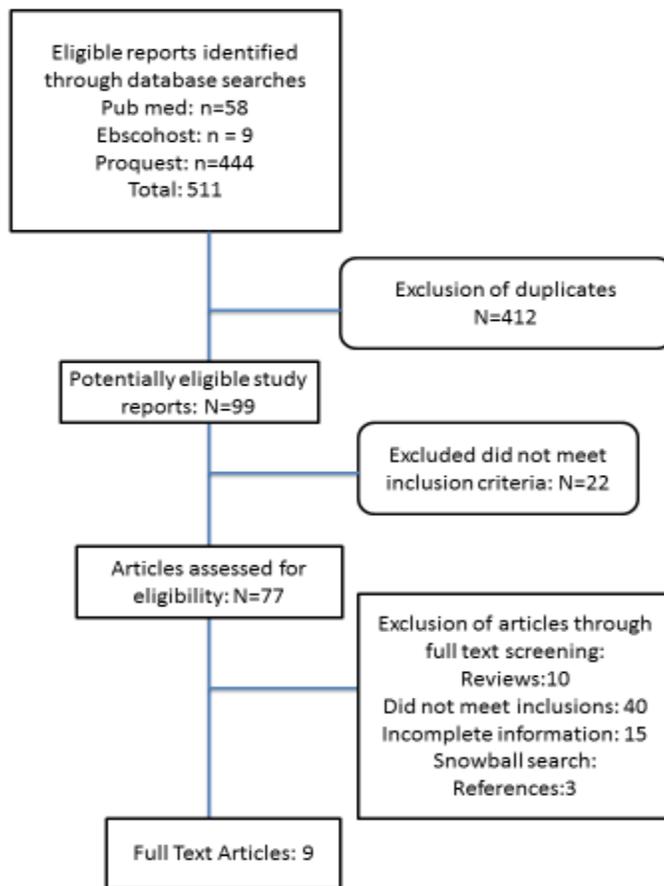
A systematic literature review was completed in September 2015 using the databases EbscoHost to include CINAHL, Cochrane, Proquest, and PubMed. The databases were searched using the keywords “magnesium”, “PMS”, “PMDD”, and “premenstrual syndrome”. The inclusion criteria were studies in the English language, humans, alternative therapy, complementary and alternative medicine, preventative treatment, magnesium, women ages 18-40, PMS symptoms, oral treatment, intravenous treatment, magnesium deficiencies, blood test, urine test, serum magnesium, intracellular magnesium, ionized magnesium, and PMS pathways. Emphasis was to identify studies that were placebo controlled, randomized, double blind, case control with crossover design. Exclusion criteria were duplicates, pregnant women, research completed by mail survey, oral contraceptives, or Mg paired with other vitamins or minerals. The exclusion process included title review, abstract review, and a full text article review. The

original search criteria were extended to not limit for date of publication in order to retrieve more studies. A “snowball” or hand search of the references was completed to find additional articles that may have been missed. The work to compile the articles for review was completed by the two lead authors. All of the full text articles were retrieved for this study and arranged into a table (see Table 1) to assist comparison of study design, number of participants, outcomes, study findings, and limitations.

### Results

Nine full text articles were identified that pertained to PMS and Mg. See Figure 1 for details on search outcome. Five studies were randomized, double blind, placebo controlled, of which three were crossover studies, one case control study, one open labeled study, and two observational of which one was a longitudinal study. Oral supplementation was given in five of studies, doses ranging from 200mg to 360mg, and one consisted of the supplementation being given intravenously. Three of the studies used only serum blood samples to test for deficiency whereas for testing deficiency it has been suggested to use both intracellular and extracellular Mg concentrations (Bazydlo, Needham, & Harris, 2014). Three studies had relatively large groups consisting of 93-150 participants, while the six other studies had smaller sample sizes consisting of 31-50 participants. All of the studies showed a significant improvement in symptoms; however the placebo control groups also showed a slight improvement, but not as significant as the experimental groups.

Figure 1. Details of literature search process



One study concluded that Mg supplementation needed to be taken for at least two months before symptoms were alleviated (Fathizadeh, Ebrahimi, Valiani, Tavakoli, & Yar, 2010). It was not identified if this finding by Fathizadeh, et al. (2010) had been replicated. If verified it may affect the validity of existing studies, and the need to have a longer lead in for supplementation to be effective.

One major limitation was most of the newer articles that were found referred back to studies completed in the 1990's by Walker, et al, (1998) and Facchinetti, et al, (1991). These studies had strong outcomes, however, the Walker et al., (1998) study had the most limitations including no blood test, mild symptoms, no check for oral contraceptive use, and had no

washouts between treatments. The Facchinetti et al., (1991) study appeared to provide the strongest evidence of effect with its only limitations being a small sample size. See Table 1 for more detail on the studies reviewed.

### Discussion

This review identified ten studies of which most reflected weak study designs or small sizes. Study limitation included small sample sizes, no crossover period between washouts, no placebo group, no random sampling, short study periods, and most of the blood tests were done using serum Mg. Serum Mg is least preferred because it is a poor reflection of total Mg concentration, a paired test is needed for best results. There appears to be a positive correlation between Mg supplementation and the reduction of PMS/PMDD symptoms. However, more studies need to be conducted utilizing oral supplementation and blood testing using the paired testing of intracellular and extracellular concentrations of Mg to validate the correlation. Also only limited number of studies specified both the dose and form of Mg supplemented, thus even establishing the best criteria for future studies have been limited. Although previous findings are suggestive, better-designed studies, to include a large prospective crossover experimental design, to clarify how Mg might be best utilized to ameliorate PMS/PMDD symptoms.

Table 1. Comparison of studies on the association of Mg with PMS/PMDD

Authors	Type of study	Number of people	Measures used	Findings	Limits
DeSouza, M.C., Walker, A.F., Robinson, P.A. & Bolland, K.	Randomized control trial (RCT) cross over design	44	Urine sample, symptom and food questionnaire, 200 mg of Mg	Treatments lead to reduction of all the symptoms	The study was only one month, no wash out period
Dullo, P., & Vedi, N.	Observational study	50	Menstrual history, blood samples and body temperature	Mg levels were lowest in the follicular phase	Small sample size
Facchinetti, F., Borella, Paola, Sances, Grazia, Fioroni, L., Nappi, R., Genazzani, A	RCT	28	Questionnaire, blood sample, 360 mg of Mg	Symptoms in the 2 <sup>nd</sup> month were decreased; the symptoms were further decreased by the 4 <sup>th</sup> month. Increase in intracellular Mg cations showed improvement in PMS symptoms	Small sample size
Fathizadeh, N., Ebrahimi, E., Valiani, M., Tavakoli, N., & Yar, M. H.	RCT	150	250 mg of Mg, Questionnaire, symptom diary	The mean scores for each symptom were reduced however the Mg plus Vitamin B6 was affected the most	No assessment of Mg status
Khine, K., Rosenstein, D.L., Elin, R. J., Niemela, J. E., Schmidt, P. J., & Rubinow, D.R	RCT with crossover	31	Blood samples serum, rbc and mbc, urine Mg infusion, urine sample, mood rating scale	The blood samples were the same, urine samples were at the lower limit for participants with PMDD, Mood rating was reduced	Age of participants, kidney absorption overload, small sample size, selection bias, infusion during luteal phase

Norhan, G., Riad, Q, & Kanan, W.	Case control study	98 students	Serum Mg levels	Serum Mg had a significant association with the PMS scale and status of serum Mg	Non purposive sampling
S. Quaranta, M. A. Bu scaglia, M. G. Meroni, E. Colombo, S. Cella	Open labeled observational trial	38	Questionnaire, symptom diary, 250 mg of Mg	35% decrease in in the total PMS symptom scores	Sample size. No placebo.
Silva Dos Santos, L.A., de Azeredo, V. B., Chaves Barbosa, D. E., & de Sa, S.A.	Observational longitudinal, randomized study	93	Daily symptom report, blood sample using colorimetric spectrophometric	Mg was had a positive association with depression and nausea, deficiency can influence PMS symptoms	Mg retention urine sample, non-compliance on the blood samples
Walker, A.F., De Souza, M.C., Vickers, M. F., Abeyasekera, S., Collins, M. L., & Trinca, L.A.	RCT, cross over	38	Questionnaire, urine sample, 200 mg of Mg	Water retention was alleviated the most but all the scores were lowered.	No blood test, only mild symptoms, didn't check for oral contraceptive, no wash out between treatments.

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