

LUTEAL PHASE SERUM CALCIUM AND SERUM MAGNESIUM LEVELS IN CAUSATION OF PREMENSTRUAL SYNDROME

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Abstract: Background: Premenstrual syndrome involves a variety of physical, mental and behavioural symptoms tied to a woman's menstrual cycle. It is a complex health problem and is currently defined as the cyclical occurrence of non-specific somatic, psychological or behavioural symptoms linked to luteal and premenstrual phase of the menstrual cycle and are of sufficient severity to result in deterioration of interpersonal relationships, interference with normal activities or both. The severity of symptoms varies from person to person. The aim of the study is to investigate the relationship between levels of serum calcium and magnesium and symptom severity in patients with premenstrual syndrome. **Method:** For this we have taken 50 females of age group 15-45 years out of which 25 were controls and 25 had reported symptoms of PMS. Serum calcium and serum magnesium levels were estimated during pre and post-menstrual phases and normal subjects were compared with those having premenstrual syndrome. Serum calcium was measured by Ensure biotech O-cresol phthalein complexone (OCPC) method and serum magnesium by calmagite method. **Result:** This study showed a significant decrease in serum calcium (Chi-square value-4.93 and p-value - < 0.05) and decrease in serum magnesium (Chi-square value-5.03 and p-value-<0.05) during premenstrual phase of PMS when compared with normal subjects. This study also suggested that PMS occurs in all age groups and is more prevalent in working women. **Conclusion:** This study led to a conclusion that there is a significant association between lowered serum calcium and serum magnesium levels during premenstrual phase with the severity of symptoms in PMS.

Key Words: Premenstrual syndrome(PMS),calcium, magnesium, vitamin D, Parathyroid hormone

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Introduction:

Premenstrual syndrome is a psychological and somatic disorder of unknown aetiology. It occurs during the luteal phase of the menstrual cycle. The earliest references to menstrually related mood and physical disorders come from the writings of Hippocrates and he attributed such disorders to hysteria.¹

History: The term PMS was first introduced by Dalton in 1953. In 1987, it was given the name of late luteal phase dysphoric disorder (LPDD)² which was later renamed as Premenstrual dysphoric disorder (PMDD)³

Etiology of PMS: The exact aetiology of PMS is not known. This syndrome appears to be caused by the response of CNS to the factors produced by corpus luteum^{4,5} because these symptoms are not seen in patients with anovulatory cycles. The earliest explanations included the alterations in the levels of oestrogen and progesterone⁶, oestrogen-

progesterone imbalance abnormal androgen levels and gonadotropin abnormalities⁷.

Other potential causes include prolactin excess, thyroid dysfunction, excess production of aldosterone, ADH or both and low levels of sex hormone binding globulin⁷. Endogenous opiate withdrawal has also been suggested as a mechanism for some of the symptoms of PMS⁷. GABA alterations which are induced by progesterone are also suggested in the pathogenesis or relief of PMS symptoms⁸

The role of nutritional factors in PMS was described in 1944.⁹ Micronutrients like calcium; magnesium, zinc etc are also implicated in the pathogenesis of PMS¹⁰.

Calcium: Thys-Jacobs 2000 in her study demonstrated that there is significant evidence that supports cyclic fluctuations of calcium and vitamin D during the menstrual cycle and may help explain some symptoms of PMS¹⁰. It was suggested that ovarian hormones influence calcium,

magnesium and vitamin D metabolism and it is oestrogen which regulates calcium metabolism, intestinal calcium absorption and parathyroid gene expression and secretion triggering fluctuations across the menstrual cycle.

Increasing oestrogen level would result in falling calcium concentration but to compensate the falling calcium, there is marked release of parathormone to prevent hypocalcemia¹¹. Estrogen is believed to lower serum calcium by inhibiting bone resorption in bone remodeling and promoting bone mineralization. Recent evidence suggests that oestrogen has calcium antagonistic properties, inhibiting calcium currents and increasing calcium entry into vascular smooth muscle.

Therefore, it has been suggested that women who already have low levels of serum calcium and those having symptoms of PMS are more prone for the further decrease in calcium level, during the luteal phase of menstruation. During the menstrual cycle, oestradiol has two peaks, one immediately before LH surge and ovulation and second during luteal phase. Increasing oestrogen levels would result in falling calcium concentration with compensatory rises in parathyroid hormone producing hypocalcemia.

In further studies, Thys- Jacobs observed that there is lack of responsiveness in vitamin D metabolism resulting in decline in $1,25(\text{OH})_2\text{D}$ during the luteal phase of menstrual cycle which may serve as a biological trigger for classical features of PMS.¹¹

Since extracellular calcium is the ultimate source of intracellular calcium, intracellular calcium may be perturbed resulting in abnormalities of neurotransmitter synthesis and release.¹²

Magnesium: Magnesium has been noted to fluctuate across the menstrual cycle and is involved in many cellular pathways and neuromuscular activities which affect PMS.

Magnesium is not just involved in production of cellular energy and synthesis of nucleic acids and proteins but also in hormone production and transformation, as well as for proper use of calcium and vitamin -D^{13} . Magnesium deficiencies have been noted in women with PMS. Dark chocolates are the rich sources of magnesium and that may be the root of chocolate cravings in women with PMS.

Some neurotransmitters like dopamine have also been implicated in the aetiology of PMS. Magnesium deficiency causes a specific depletion of brain dopamine without affecting brain serotonin and nor-epinephrine. Magnesium is also required for enzymatic conversion of cis-linoleic acid to gamma-linoleic acid, the rate limiting step in prostaglandin E1 synthesis which is said to inhibit the glucose induced insulin secretion in humans. This explains the craving for sweets in PMS. Magnesium is also known to increase the threshold for stressful stimuli and thus its deficiency could lead to an increased level of aldosterone in response to environmental stimuli.¹⁴

Material and Methods:

50 subjects were taken for this comparative study from gynae opd at BJ Medical College, Ahmedabad. Subjects were put to a detailed questionnaire and thoroughly examined to rule out any illness, pregnancy, diabetes, hypertension etc. Informed consent was sought and blood samples were taken within one week prior to periods and within one week after periods from normal subjects and those with PMS after seeking admission from ethics committee.

Inclusion criteria

Healthy women in reproductive age group of 15-45 years.

Having regular menstrual cycles in last six months.

Exclusion criteria

Pregnancy or post partum period

Any serious physical illness

History of Ovarian dysfunction

History of other gynaecological disorders

History of using OCP's within last 3 months A

Sample selection:

A self designed questionnaire was used based on relevant studies and test and control groups were selected.

Sample size:

25 Healthy premenopausal women with PMS in the age group of 15-45 years: (test group). 25 Healthy premenopausal women without PMS in 15-45 years: (control group).

The subjects had regular cycles and belonged to all socio-economic strata, both educated and uneducated and both married and unmarried. Serum calcium was estimated by

spectrophotometry during premenstrual phase and postmenstrual phases of their cycles.

Statistical methods:

Simple statistical methods were used like percentages, qualitative tests (chi-square) and quantitative (paired t-test) were done.

Biochemical investigations:

Serum calcium: Serum calcium was measured by the Ensure biotech OCPC (O-Cresolphthalein complexone) method.

Principle: In an alkaline medium, calcium reacts with O-Cresolphthalein complexone and forms a purple coloured complex. Intensity of colour is measured at 570nm and this corresponds to calcium concentration.

Specimen: Fresh, fasting serum is used.

Serum calcium in mg/dl = Abs. of TX 10/Abs. of S

Serum magnesium: Serum magnesium was measured by calmagite method.

Principle: Magnesium reacts with calmagite in an alkaline medium to form a red coloured complex. Intensity of colour formed is directly proportional to amount of magnesium present in the sample.

Serum magnesium in mg/dl: Abs.T/Abs.

Reference value:

Serum calcium : 8.7 – 10.5 meq/l

Aims and objectives: Aim: To study the levels of serum calcium and magnesium in PMS subject.

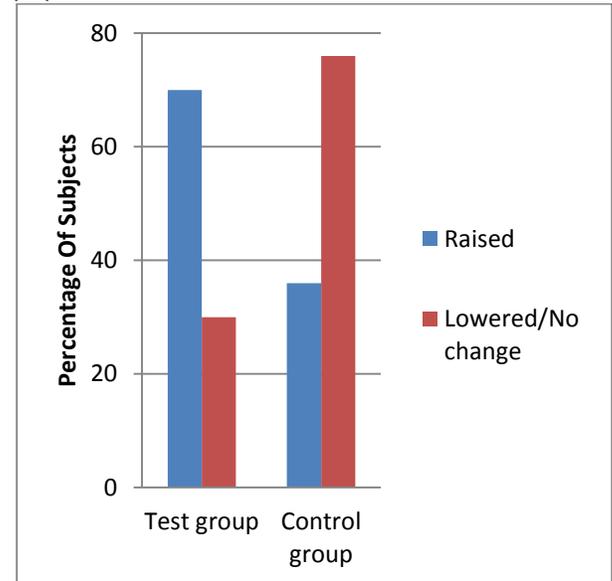
Objective: To compare the serum levels of calcium and magnesium in women with PMS and those without PMS during pre and post menstrual phases.

Result:

Subjects were divided into two groups, subjects with symptoms (Test group) and subjects without symptoms of PMS (Control group).

Studies were conducted to relate levels of serum calcium and magnesium in relation to pre and post menstrual phases and the results were subjected to statistical analysis and shown in tabular form separately.

Chart 1: variation in serum calcium levels with regard to pre and post menstrual phases in study population



The present study shows almost equal distribution of PMS in all age groups, parous and non-parous women, but a higher incidence in married, highly educated and employed women as shown in the table.

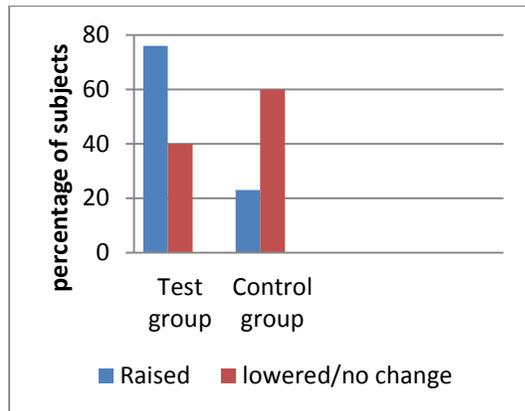
Figure 1 shows the percentage of women with variation of serum calcium levels in relation to pre and post menstrual phases i.e. those with premenstrual increase or decrease or post menstrual increase or decrease. In the test group 14 subjects had lowered premenstrual serum calcium levels. The Chi-square value is 4.91 and at 1 degree of freedom the P value is less than 0.05, which is statistically significant.

Figure 2 shows the percentage of women with variation of serum magnesium levels in relation to pre and post menstrual phases i.e. those with premenstrual increase or decrease or post menstrual increase or decrease. In the test group out of 30 subjects 13 have lowered serum magnesium levels in the premenstrual phase. The Chi-square value is 5.01 and at 1 degree of freedom, p-value is less than 0.05 which is statistically significant.

Discussion: The menstrual cycle is the most extensively studied rhythm in women. The hormonal changes during the menstrual cycle are well established and they are commonly associated

with fluctuations in electrolytes and subjective feeling in women.

Chart: 1 variation in serum magnesium levels with regard to pre and post menstrual phases in the study population.



In the present study, the percentage of women in which the mean serum calcium levels were decreased in the premenstrual period is statistically significant ($p < 0.05$)¹⁵. Fasting blood samples were drawn in the premenstrual and postmenstrual phases and it was found that levels of serum calcium varied across the cycle and declined significantly at mid cycle with increase of estradiol. This data suggests that women with PMS do have perturbations in calcium homeostasis. Susan Thys-Jacobs et al, 2000, reported that disturbances in calcium regulation underlie the pathophysiologic characteristics of PMS and calcium supplementation may be an effective therapeutic approach.

The results also show the percentage of women with PMS in this study have a statistically significant lower magnesium levels ($p < 0.05$) during premenstrual phase. Randomized, double-blind studies have shown that many women with PMS may benefit from supplementation of 200mg of magnesium per day. They reported a significant reduction of several symptoms related to PMS such as mood swings, fluid retention, abdominal bloating etc.

Conclusion: There was seen a significant association between lowered serum calcium and magnesium levels in the premenstrual phase and PMS. These findings are consistent with other

studies showing a relationship between micronutrients and PMS.

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