

Effect of Calcium and Vitamin Administration on Premenstrual Syndrome

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Abstract: The aim of the study was to determine the effect of calcium (Ca) and vit D on premenstrual levels of estradiol, progesterone and cortisol, also the minerals calcium, phosphorous and magnesium and determine the pain factor as potassium. The present research was performed on 20 females aged (30-34 years); they were divided into two groups containing 10 females each. The first group was taken as control (normal menstruation) placebo administration; the second group (affected with premenstrual syndrome) and administered a therapeutic dose of calcium and vitamin D (1200 mg + 400 Im) for two months. 10 ml of blood sample was withdrawn from all participants before the administration of Ca and vit D and the control group received placebo for two months, another blood sample was withdrawn at the same time 7 days before the end of menstruation, blood was centrifuged and serum was collected and stored frozen at -20°C for subsequent analysis. Serum estradiol, progesterone and cortisol were measured using commercial kits, by radioimmunoassay technique. As for serum calcium, phosphorus, magnesium and potassium were measured using commercial kit by photometric method. The results revealed an increased level of estradiol, progesterone and cortisol followed by a decrease in hormone concentration after the calcium and vitamin D administrations, PMS, as for calcium, phosphorous and magnesium revealed a decreased concentration and return to the normal levels after calcium and vit D administrations. The finding of the present study indicated an elevated potassium concentration in case of PMS which decreased after calcium and vit D administrations. It may be concluded that calcium and vit D administrations may be of great help to PMS cases as indicated by hormonal and mineral changes together with alleviating pain associated with PMS.

Key words: Ovarian Hormones • Cortisol • Calcium • Vit D

INTRODUCTION

About every 28 days, gonadotropic hormones from the anterior pituitary gland cause about 8 to 12 new follicles to begin to grow in the ovaries. One of these follicles finally becomes mature and ovulates on the 14th day of the cycle. During growth of the follicles mainly estrogen is secreted. After ovulation, the secretory cells of the ovulating follicle develop into a corpus luteum that secretes large quantity of the major female hormones, progesterone and estrogen. After another 2 weeks, the corpus luteum degenerates, whereupon the ovarian hormones estrogen and progesterone decrease greatly, and menstruation begins. A new ovarian cycle then follows [1].

Premenstrual syndromes (PMS) are symptoms which affect the physical, behavior and psychological identity of the women in the two weeks before menses, then decrease gradually [2, 3].

Extracellular fluid calcium ion concentration normally remains tightly controlled within a few percentage points of its normal level, 2.4 me g/L. The bones, however, do not have an inexhaustible supply of calcium. Therefore, over the long term, the intake of calcium must be balanced with calcium excretion by the gastrointestinal tract and the kidneys.

The most important regulator of calcium is reabsorption at both sites in PTH. Thus, PTH regulates plasma calcium concentration through three main effects: (1) by stimulating bone resorption (2) by stimulating activation of vit D, which then increases intestinal absorption of calcium reabsorption [4].

Claps [5] stated that PMS symptoms are clinical manifestation of calcium decrease that results from increase estrogen concentration and that calcium and vit D administration might decrease PMS symptoms. Belko [6] added that vitamin D is found to act on target organs like bones, kidneys, intestinal mucosa to regulate calcium and phosphate metabolism.

The potential of minerals to play a significant role in fertility is indisputable. The minerals that are of particular importance are categorized into macroelements (Ca, P, K, Na and Mg) and trace elements (Cu, Co, Se, Mn, I and Zn). Physiological concentrations of the elements must always be maintained to assure the proper cellular functions [7].

Problem of the Study: Many women are affected with MPS in the two weeks preceding menstruation, calcium and vitamin D may play an important role to provoke the different symptoms, so, it is important to study the effect of calcium and vitamin D on PMS, and ask the following questions:

- What is the effect of calcium and vitamin D on some hormones?
- What is the effect of calcium and vitamin D on some minerals?
- What is the effect of calcium and vitamin D on pain sensation of PMS?

This study was undertaken to evaluate the effect of calcium and vitamin D administration on premenstrual syndrome in females for 2 months [8].

To Fulfill These Objectives, it Was Needed To:

- Determine the premenstrual levels of estradiol, progesterone and cortisol hormones.
- Determine the premenstrual levels of calcium, phosphorus and magnesium.
- Determine the pain factor of potassium.

MATERIALS AND METHODS

The sample comprising 20 females was chosen from those in the outpatient clinic in hospitals, aged 30-34 years. The sample was divided into two groups: group (1) affected with premenstrual syndrome, group (2) normal females (control).

Blood Sampling: 10 ml of fasting blood samples were collected from a superficial vein in the morning (at 10 a.m.) in polyethylene tubes without anticoagulant, and then they were left sloped for 2 hours at 2500 rpm for 20 minutes. Serum was collected and stored frozen at -20°C for subsequent analysis.

Hormonal Assay: Estradiol concentration in serum was measured using a commercial kit using RIA technique. Progesterone concentration in serum was measured using a commercial kit using RIA technique. Cortisol concentration in serum was measured using a commercial kit and RIA technique. All hormonal kits were purchased from Bisource, Europe, and USA.

Measurement of Calcium: Calcium was measured in the serum using Ca kit (Roche Diagnostics GmbH) Germany.

Measurement of Phosphorus: Phosphorus was measured in the serum using Phosphorus kit (Roche Diagnostics GmbH) Germany. As for magnesium, a kit from (Roche Diagnostics GmbH) Germany. A kit for Potassium determination from (Roche Diagnostics GmbH) Germany.

All women of the two groups were with no history of hormonal replacements. To assure their healthy conditions, all participants were subjected to full clinical examination at the hospitals, where blood pressure, chest, heart and abdomen were examined. The PMS affected females received Ca + vit D (200 mg + 400 IU) for 2 months, placebo for control group.

Statistical Analysis: The obtained data were calculated and presented using the statistical package for social science (SPSS, 8 Software, 2008) for obtaining mean and standard error. The data were analyzed using T test to determine the statistical significance of difference among groups. Statistical significance was assigned at 0.05 level. All data were expressed as means \pm SD.

RESULTS AND DISCUSSION

Table 3 indicated non-significant change of various parameters in 2 successive menstrual cycles.

Table 4 indicated a significant change of various parameters before Ca/ vit D administration of PMS females and control group.

Table 5 indicated non-significant change of various parameters in PMS group after Ca/vit D administration and control groups.

The main symptoms of premenstrual syndrome noted in this study were irritability, bloating, edema, emotional lability, decreased ability to concentrate, headache and constipation during the last 7-10 days of their menstrual cycles.

Table 1: General characteristics of the two groups

Parameters	Group (1) PMS	Group (2) Control	Sig.
Age (Y)	30 ± 4.2	34 ± 5.1	N.S
Weight (Kg)	65 ± 7.4	68 ± 5.9	N.S
Height (cm)	155 ± 6.4	159 ± 7.4	N.S
HB (g/dl)	12.8 ± 2.1	12.4 ± 1.6	N.S
Fasting glucose (mg/dl)	90 ± 4.5	95 ± 3.6	N.S

Data are presented as means ± SD non significant values between the two groups P < 0.05

Table 2: The mean ± SD levels of various studied parameters in PMS females before and after Ca, vit D administration

Variables	Before	After	Sig.
Estradiol (mg/ml)	95 ± 4.1	75 ± 3.6	S
Progesterone (mg/ml)	21 ± 7.2	18.4 ± 1.3	S
Cortisol (mg/ml)	22 ± 1.5	14.3 ± 1.6	S
Calcium (mg/dl)	8.1 ± 0.2	9.1 ± 0.3	S
Phosphorus	3.2 ± 0.1	3.7 ± 0.2	S
Magnesium	1.1 ± 0.09	1.6 ± 0.1	S
Potassium	4.6 ± 0.5	3.9 ± 0.2	S

P < 0.05

Table 3: The mean ± SD levels of various studied parameters in control groups in 2 successive premenstrual cycles

Variables	Control (1)	Control (2)	Sig.
Estradiol	68.1 ± 4.2	72.2 ± 5.3	N.S
Progesterone	17.3 ± 1.2	18.1 ± 2.1	N.S
Cortisol	13.4 ± 1.3	12.9 ± 1.4	N.S
Calcium	9.3 ± 0.9	9.0 ± 0.8	N.S
Phosphorus	3.5 ± 0.3	3.6 ± 0.5	N.S
Magnesium	1.3 ± 0.4	1.4 ± 0.3	N.S
Potassium	4.4 ± 0.6	4.2 ± 0.4	N.S

P < 0.05

Table 4: The mean ± SD levels of various studied parameters in PMS before Ca, vit D administration and control group

Variables	PMS	Control	Sig.
Estradiol	95 ± 4.1	68.1 ± 4.2	S
Progesterone	21 ± 1.2	17.3 ± 1.2	S
Cortisol	22 ± 1.5	13.4 ± 1.3	S
Calcium	8.1 ± 0.2	9.3 ± 0.9	S
Phosphorus	3.2 ± 0.1	3.5 ± 0.3	S
Magnesium	1.1 ± 0.09	1.3 ± 0.4	S
Potassium	4.6 ± 0.5	4.4 ± 0.6	S

P < 0.05

Table 5: The mean ± SD levels of various studied parameters in PMS after Ca, vit D administration and control groups

Variables	PMS	Control	Sig.
Estradiol	75 ± 3.6	72.2 ± 5.3	N.S
Progesterone	18.4 ± 1.3	18.1 ± 2.1	N.S
Cortisol	14.3 ± 1.6	12.9 ± 1.4	N.S
Calcium	9.1 ± 0.3	9.0 ± 0.8	N.S
Phosphorus	3.7 ± 0.2	3.6 ± 0.5	N.S
Magnesium	1.6 ± 0.1	1.4 ± 0.3	N.S
Potassium	3.9 ± 0.2	4.2 ± 0.4	N.S

P < 0.05

Farrell and Rebecca [9] stated that PMS affects 85 % of females monthly. Whereas Frackiewicz and Shiovitz [10] indicated that PMS affects 40 % of the female obviously. Freeman [2] reported that the predominant symptom may be pain sensation. The finding of the present study indicated an elevated potassium level in case of PMS (Tables 2, 4,5) which decreased after calcium and vit D administration. This result agrees with the opinion of Ganong [11] that a chemical agent (P Factor) is released during contraction that causes pain when its local concentration is high enough.

When the blood supply is restored, the material is washed out or metabolized. The identity of the P factor is not settled, but it could be K^+ .

The pain that develops may be due to ischemia and accumulation of P factor and the pain is relieved by rest and permits the blood supply to remove the P factor. It has been suggested that pain is chemically mediated and that stimuli which provoke it have in common the ability to liberate a chemical agent that stimulates the nerve endings which cause pain which have reflex connections that initiate nausea, vomiting and other autonomic reflex [12].

Elhosaini [13] reported that the causes of PMS may be due to excessive concentrations of estrogen and progesterone hormones and that cortisol hormone may depress PH and consequently increase Estrogen level. All these changes can lead to retention of water and affects circulation and decrease oxygen to the uterus and ovaries.

These were in accordance with the data presented in tables 2,4 and5 that estrogen, progesterone and cortisol were elevated in case of PMS cases and decreased after calcium and vit D administrations for two months, reaching the normal level of these hormones in control group (Tables 3, 4 and 5).

The increased premenstrual syndrome symptoms which affect the physical, behaviour and physiological identity of the women in the last two weeks before menses may be caused by ovarian hormones, over secretion such as edema, vomiting, increased glucose levels and elevated blood pressure and pulse rate, together with change in mood, headache and tension and body fluid retention [14-16].

Guyton *et al.* [17] refers to the pressure of excess fluid in the body tissue as edema, and in most instances, this edema occurs mainly in the extracellular fluid compartment, but it can involve intracellular fluid as well.

The main causes of this retention of fluid may be hormonal such as estrogen and progesterone in addition to cortisol hormone. They also added that two conditions are especially prone to cause intracellular swelling:

- Depression of the metabolic system of the tissues and
- Lack of adequate nutrition to the cells.

As when blood flow to a tissue is decreased, the delivery of oxygen and nutrients is decreased. These changes may affect the tissues negatively and affects its viability.

Larsen *et al.* [18] postulated that physiological stress increases ACTH and adrenocortical secretion, often increasing cortisol secretion as much as 30 fold. They added that pain stimuli are transmitted first upward to the brain stem and hypothalamus.

The increased ACTH is associated with B-endorphin hormones secretion by the pituitary gland to have a significant effect on the human body especially pain. Also hypersecretion of cortisol can cause increased blood glucose concentration; this results mainly from enhanced gluconcogenesis and decreased glucose utilization by the tissues.

The increased secretion of cortisol noted in this study may be blamed of many of the symptoms of premenstrual syndrome. The results in the present study showed that in addition to decreased calcium level and magnesium, there was also a decrease in phosphorus (in case of PMS which returns to the normal level after calcium and vit D administration (Tables 2,4 and 5) and that of the control females (Table 3,4,5). These results agreed with the results of Kamal [19] and Shamberger [20].

Calcium, phosphorus and magnesium functions shared many symptoms of PMS due to changes of concentrations such as a role in neuromuscular transmission and excitability of nerves and excitability of the heart together with acid base balance, energy transfer, in addition to a role in enzymes action [21].

Hofer and Brown [22] and Jones *et al.* [23] described the relationship of vitamin D and calcium, that vitamin D has a potent effect to increase calcium absorption from the intestinal tract; it also has important effects on both bone deposition and bone absorption. However, vitamin D is not the active substance that actually causes these effects. Instead, vitamin D must first be converted through a succession of secretion in the liver and

the kidneys to the final active product 1.25 dihydroxycholecalciferol which is inversely affected by the concentration of calcium in the plasma. When calcium is too high, the formation of 1.25 dihydroxycholecalciferol is depressed.

Many scientific studies reported a positive effect of food materials on PMS symptoms such as Falconoid containing some minerals, calcium, magnesium, potassium and manganese as well as Vitamins such as b6, E, D [24].

Leather *et al.* [25] and Facchinetti *et al.* [26] suggested magnesium and calcium administrations to cure PMS.

Takacs [27] suggested that potassium administration decreased PMS symptoms while Machlin [28] indicated that Vitamin E helps the suppression of PMS symptoms.

CONCLUSION

- It is concluded that calcium and vitamin D supplement may alleviate symptoms of PMS in females.
- Blood analysis of steroid hormones as estrogen, progesterone and cortisol are good markers of PMS symptoms.
- Calcium, phosphorus, magnesium can help in the diagnosis of PMS.
- Potassium level is a good indicator of pain and pain killer may be of good value.

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