

Original research article

Potential Impact of Serum Magnesium and Serum Calcium on Premenstrual Distress in Students: A Case-Control Study.

Dr. Galib Sumaiya¹, Dr. Gosangari Suchithra², Dr.G.S.Prema³, Dr. Khade Yogita⁴,
Dr. D Joya Rani⁵

¹Senior resident. MD. Department of Physiology. Dr Patnam Mahender Reddy Institute of Medical Sciences and Hospital, Chevella. Rangareddy dist. Telangana. India.

²Assistant Professor. MD. Department of Physiology. Rajiv Gandhi Institute of Medical Sciences, Adilabad. Telangana. India.

³Professor. MD. Department of Physiology. Gandhi Medical College. Secunderabad. Telangana. India.

⁴Associate Professor. MD. Department of Physiology. Dr Patnam Mahender Reddy Institute of Medical Sciences and Hospital, Chevella. Rangareddy dist. Telangana. India.

⁵Prof & Head. MD. Department of Physiology. Dr Patnam Mahender Reddy Institute of Medical Sciences and Hospital, Chevella. Rangareddy dist. Telangana. India.

Corresponding Author: Dr. Gosangari Suchithra

Abstract

Aim: To evaluate and compare the serum magnesium and calcium levels in students with premenstrual distress with those of normal students.

Methodology: The present study was conducted at Gandhi Medical College, Telangana, India. Fifty medical and paramedical students of age 18-24years with regular cycles were included in the study and were given the PMS diagnostic questionnaire developed by the University of California, San Diego recommended by the American College of Obstetrics and Gynecology. Students showing premenstrual symptoms were considered as Study group (25) and those without symptoms as controls (25). 5ml of fasting venous blood samples were collected from both groups between the 15th-28thday (luteal phase) of the menstrual cycle. These samples were tested using Beckman Coulter for serum calcium and magnesium levels. Comparison between the groups was done by student's t-test and a p-value<0.05 was considered significant.

Results: Significant lower values for serum magnesium levels were observed in study group compared to controls. The prevalence of magnesium deficiency was significant in the study group.

Conclusion: Low magnesium levels are probably an important cause of premenstrual distress. Based on serum values, more than half of students with premenstrual distress were found to be deficient in magnesium.

Keywords: Luteal phase electrolytes, Magnesium deficiency, Questionnaire.

Introduction

Premenstrual distress is a term used to describe a set of behavioural, affective, cognitive, and physical symptoms that occur during the luteal phase of the circumlunar menstrual cycle and resolve almost immediately with the onset of menstruation ^[1] Its prevalence reportedly ranges between 5-76% globally ^[2]. Evidence suggests the possibility of ovarian hormones influencing electrolyte metabolism during different phases of the menstrual cycle that may, in turn, lead to premenstrual edema and psychological symptoms ^[3]. An unclear etiology makes management difficult. In this study, we assess the relationship between serum calcium and

magnesium with premenstrual distress, which might be useful to direct management strategies towards nutritional supplementation to alleviate symptoms.

Material and methods:

This study was conducted at Gandhi Medical College, Telangana, India. A total of fifty students were made a part of the study after taking informed consent and gaining ethical clearance from the institutional ethical committee. Confidentiality was maintained and assured to all the volunteers ensuring cooperation and participation.

Inclusion criteria:

Students of age 18 to 24 years having regular cycles of 27 to 33 days for at least the past 6 months were included in the study.

Exclusion criteria:

Irregular cycles, history of psychiatric or affective disorders, anxiety, depression or any other psychological issues, history of other major renal, endocrinal, gynaecological disorders or those taking hormonal pills, nutritional supplements or any other drugs for at least the past 3 months were excluded from the study.

The participants were given the PMS diagnostic questionnaire, developed by the University of California, San Diego according to the American College of Obstetrics and Gynaecology (ACOG) guidelines. At least one physical symptom and one affective symptom should be present during the 5 premenstrual days for at least three menstrual cycles to be termed as PMS according to ACOG [4]. Each woman was asked about symptom experience prior to onset of menstruation for at least 3 months with use of a checklist of 9 symptoms. The symptoms were those on the lists of the classificatory systems used in the diagnosis of PMS according to the ACOG criteria.

PMS DIAGNOSTIC QUESTIONNAIRE- UNIVERSITY OF CALIFORNIA, SAN DIEGO

1. Affective symptoms:

- Depression
- Angry outbursts
- Irritability
- Anxiety
- Confusion
- Social withdrawal

2. Somatic symptoms

- Breast tenderness
- Abdominal bloating
- Headache
- Swelling of extremities

3. RELIEF FROM SYMPTOMS FROM DAY 4 THROUGH 13 OF THE MENSTRUAL CYCLE.

Students showing symptomatology according to criteria were taken as STUDY or PMS Group (25) and those without symptoms were taken as Controls (25).

The Venous blood sample was collected from the antecubital vein (5 ml) in a disposable syringe during Luteal Phase (15th to 28th day) between 1- 2 pm to avoid diurnal variation. To avoid variations due to storage, counting was commenced within half an hour. Serum electrolytes were tested using Beckman Coulter by enzymatic method.

Statistical analysis:

Microsoft Office Excel was used for data storage, tabulation and the generation of descriptive statistics. Students' unpaired t-test was used to find the association difference between various scales. P values<0.05 was considered statistically significant.

Results:

Both the groups were age matched and no statistically significant differences were found in their basic anthropometric data. (Table1). Serum magnesium levels are significantly low in students with premenstrual distress ($p<0.005$) while serum calcium levels showed insignificant difference when compared to asymptomatic controls (Table 2). Magnesium deficiency is prevalent in the study group and is significantly higher when compared to the control group. Prevalence of calcium deficiency is not significant on comparing the two groups. (Table 3)

Table 1: Basic anthropometric characteristics of subjects

	STUDY	CONTROL	P-VALUE
	MEAN+SD	MEAN+SD	
AGE (years)	19.6+1.19	19.64+1.15	0.4
WEIGHT(kg)	54.24+ 4.44	54.32 + 5.19	0.47
HEIGHT(cm)	159 + 3.2	159.08+3.09	0.35
BMI(kg/m ²)	21.48+ 1.92	21.48+2.25	0.49

Data was presented as Mean+SD. *Indicates level of significance. $P>0.05$: not significant, $*p<0.05$: significant, $**p<0.01$ highly significant, $p<0.001$ very highly significant; BMI: body mass index

Table 2: Comparison of serum calcium and magnesium levels during luteal phase.

VARIABLES	PMS	CONTROLS	P-VALUE
	MEAN+SD	MEAN+SD	
SERUM CALCIUM(mg/dL)	9.664 +0.92	9.956+0.37	0.13
SERUM MAGNESIUM(mg/dL)	1.792+0.195	1.964+0.80	0.005*

PMS: premenstrual syndrome.

Data is presented Mean+SD.*indicates level of significance, $p>0.05$: not significant, $*p<0.05$ significant, $***p<0.001$ highly significant

Table 3: Prevalence of Calcium and Magnesium deficiency among students

SERUM LEVELS	PMS		CONTROLS		P
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE	
CALCIUM(mg/dl)					
DEFICIENCY(<8.5)	4	20%	2	10%	0.33
NORMAL	13		17		
HIGH(>11)	3		1		
MAGNESIUM(mg/dl)					
DEFICIENCY(<1.8)	16	64%	6	24%	0.004*
NORMAL(1.8-3)	9		19		

Data is presented as percentage and p value .Chi square test was used, *indicates level of significance where $p>0.05$: not significant, $*p<0.05$: significant and $***p<0.001$ is highly significant.

Discussion:

Premenstrual Syndrome, as defined by the ACOG, is a clinical condition characterized by cyclic occurrence of physical and emotional symptoms not related to any organic disease that appear during the 5 days premenstrually in each of three prior menstrual cycles and disappear within 2 days of onset of menses, without recurrence until at least day 13^[4] Despite the high prevalence of premenstrual distress among women of reproductive age, its exact aetiology remains largely obscure. Several factors like culture, socioeconomic status, cigarette smoking, alcohol consumption, exercise, dietary habits, age of menarche etc. have also been implicated^[5-8]. Prolonged stress exposure is believed to lead to persistent malfunctions of neuroendocrine system and cause PMS^[9]. Lack of micronutrients and certain hormonal agents and are also implicated in the development of PMS^[10]. Alterations in levels of hormones and neurotransmitters like GABA or transient endogenous opiate withdrawal may be associated with pathogenesis of PMS^[11] While some studies suggest imbalance in estrogen progesterone levels^[12], gonadotropin and androgen abnormalities^[11], others suggest that chemical factors released by corpus luteum act on the central nervous system. This claim is supported by the fact that premenstrual syndrome is almost never seen in anovulatory cycles^[13, 14]

Results in the present study show lowered serum magnesium levels in the luteal phase of PMS. These findings are consistent with those of Posaci et al., 1994 who reported that mean magnesium levels were significantly lower in PMS patients^[15]. Magnesium deficiency in PMS was first proposed in 1983 by Abraham^[16]. Considered potentially the most crucial micronutrient for optimal brain performance, magnesium participates in virtually every enzyme reaction, nerve signal conduction and functioning of dopamine and serotonin receptors^[17]. Magnesium, which serves as a cofactor for more than 300 enzymatic reactions, is a very important macro mineral in the diet with a multitude of roles in the human body^[18]. Magnesium is involved in the synthesis of nucleic acids, hormone production, and cell energy production also for the proper uptake of Calcium^[19]. Abnormal magnesium (Mg) metabolism has been implicated in several neuropsychiatric disorders with prominent mood and physical symptoms (e.g., migraine, epilepsy, chronic pain^[20-23]). As premenstrual syndrome is characterized by symptoms such as mood instability, fatigue, and fluid alterations, magnesium deficiency has also been implicated in the etiology of PMS^[24].

According to Dr. James Greenblatt, highest level of magnesium is found in the CNS and is thus known as the 'Mind Mineral'. Magnesium is crucial for dopamine synthesis as it activates tyrosine kinase, the rate limiting step of dopamine formation^[25]. Magnesium also binds serotonin and dopamine to their receptors^[26, 27]. Magnesium deficiency causes specific depletion of brain dopamine. It also supports the calming actions of GABA by interacting with its receptors. It also keeps glutamate, an excitatory neurotransmitter, within healthy limits. Higher magnesium levels correlate with healthy serotonin levels in the cerebrospinal fluid. In addition, it is known prevent excitotoxicity. Thus, its deficiency has been implicated in multiple neurological disorders^[28]. Low magnesium levels may theoretically potentiate glutamatergic neurotransmission, leading to a supportive environment for excitotoxicity, which can lead to oxidative stress and neuronal cell death^[29]. Historically, magnesium nitrate had been used to treat and manage premenstrual distress and essential dysmenorrhoea in 1962 by Durlach and Lerner^[30]. Hypomagnesaemia contributes to both the neurological symptoms and the psychiatric symptoms by modulating glutamatergic neurotransmission at the *N*-methyl-D-aspartate (NMDA) receptor^[31]. Magnesium also possibly controls the activity

of the hypothalamic-pituitary adrenocortical (HPA axis)^[32], which is considered to be the main stress response mechanism^[33]. In our study 64% of the subjects with PMS showed serum Mg deficiency in the luteal phase which was significantly higher than the prevalence of Mg deficiency among the controls. Thus, a magnesium deficiency in women with PMS may account for some of the symptoms of PMS.

Different studies suggest that calcium deficiency during the luteal phase of the menstrual cycle can exacerbate PMS symptoms by causing depression, hallucination, and restlessness^[34, 35]. Though our study revealed lower levels of serum calcium in the luteal phase and a higher prevalence of calcium deficiency in the PMS group, none of these findings were statistically significant when compared with the controls.

Conclusion:

The present study concludes with a strong correlation between Magnesium deficiency and premenstrual distress. Premenstrual distress can affect both physical and psychological aspects of the students, causing absenteeism, hampering their academics. Hence electrolyte evaluation among students with premenstrual distress might help to alleviate the symptoms caused due to their deficiency. Nutritional supplements with diet rich in Magnesium and calcium might be affective as preventive and therapeutic strategy. Hence measures can be taken for early detection and interventions among students.

Limitations:

The main limitation of the present study was the small sample size of the study groups. If the sample size was large enough, the differences between groups would be indicated more clearly with less random error. Besides, premenstrual distress studies have a drawback in lack of universally and uniformly accepted definitions for categorizing premenstrual distress, different methodologies used for assessing symptomatology, different ethnicity and sample characteristics, the use of varied reporting protocols, different methods used for evaluating changes in symptom severity, and subjective participant awareness of the menstrual cycle – which make the study of premenstrual syndrome and its characteristics rather challenging. This study has a scope of further follow-up by the administration of therapeutic doses of magnesium and calcium and thereby observing any alleviation of symptoms in the study population.

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