Magnesium deficiency in premenstrual tension

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Zusammenfassung

Mg-Mangel ist als mögliche Ursache prämenstrueller Beschwerden (P.B.) in Betracht gezogen worden. Es wurden mittels AAS Serum-Mg und Erythrozyten-Mg bei 9 gesunden Frauen und 26 Patienten mit P.B. gemessen. Die folgenden Werte ($\bar{x} \pm$ SE) wurden ermittelt (mg %): Gesunde: 1,7 ± 0,04 bzw. 4,5 ± 0,25; Patienten mit P.B.: 1,76 ± 0,05 bzw. 3,1 ± 0,24. Bei den Patienten war das Ery-Mg signifikant erniedrigt ($P<0,05$). P.B. können zu Mg-Verlusten führen über eine streßinduzierte vermehrte Ausschüttung von Glukokortikoiden und nachfolgender verminderter intestinaler Mg-Absorption sowie erhöhter Mineralokortikoid-Spiegel mit vermehrter renaler Mg-Exkretion. Die Symptomatologie von P.B. kann weitgehend mit Mg-Mangel erklärt werden; bei der Diagnostik sollte folglich das Ery-Mg mitbestimmt werden.

Summary

Magnesium deficiency has been implicated as a possible causation factor in premenstrual tension (PMT). We have assessed serum and red blood cell magnesium concentrations in 9 normal women and 26 PMT patients, using atomic absorption spectrometry. The following mean ± SE were obtained from serum and red cell magnesium respectively in mgm%: normal subjects: 1,7 ± 0,04 and 4,5 ± 0,25; PMT patients: 1,76 ± 0,05 and 3,1 ± 0,24. Mean red cell magnesium level was significantly ($P<0,05$) lower in PMT patients. PMT may cause magnesium depletion by stressinduced glucocorticoid effect of decreased intestinal absorption and mineralo corticoid effect of increased renal excretion. Most of PMT symptomatology can be explained on the basis of magnesium deficiency. Red cell magnesium determinations should be included in the evaluation of PMT.

Résumé

Le déficit magnésique a été impliqué en tant que facteur causal possible dans la tension prémenstruelle (TPM). Nous avons évalué les concentrations du Mg sérique et érythrocytaire chez 9 femmes normales et chez 28 patientes avec TPM, en utilisant la spectrométrie d'absortion atomique. Nous avons obtenu les moyennes suivantes ± ES pour le magnésium sérique et érythrocytaire, respectivement en mg %: sujets normaux: 1,7 ± 0,04 et 4,5 ± 0,25; patientes avec TPM: 1,76 ± 0,05 et 3,1 ± 0,24. Le taux moyen de Mg érythrocytaire a été significativement plus faible ($P<0,05$) chez les patientes avec TPM. La TPM peut provoquer une déplétion du Mg par l'effet glucocorticoïde induit par le stress dans l'absorption intestinale et l'effet minéralocorticoïde de l'excrétion rénale accrue. La majeure partie de la symptomatologie de la TPM peut être expliquée sur la base d'un déficit magnésique. Des déterminations du Mg érythrocytaire devraient être comprises dans l'évaluation de la TPM.

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I. Introduction

Premenstrual tension (PMT) is a symptom complex occurring 7—10 days premenstrually, becoming progressively worse and improving with menses. Since *Frank's* original publication, [14] many symptoms have been added to this syndrome and many theories postulated in the etiology of PMT. [3] The purpose of this presentation is to propose a classification of PTM and to present recent evidence in favor of an ethiologic role for magnesium deficiency in PMT.

II. Classification of PMT

Although 150 symptoms have been added to the PMT list since *Frank's* original publication, [18] most are not common and usually represent an exacerbation of a preexisting condition. The most common symptoms for which PMT patients seek medical advice and relief can be divided into four PMT subgroups. [3]

PMT-A

The chief complaints of patients in this category are anxiety, irritability, and nervous tension, occurring as early as the mid cycle, becoming progressively worse during the luteal phase, sometimes followed by mild to moderate depression, and improving with menses.

PMT-H

PMT in this subgroup of patients is characterized by a premenstrual sensation of weight gain, abdominal bloating and tenderness, breast congestion and mastalgia, and occasionally edemia of the face and extremities. Actual premenstrual weight gain is usually less than 3 lbs except in severe PMT-H when premenstrual weight in excess of 4 lbs is observed. With increased age, the weight gain is not completely lost with menses and overweight problems occur.

PMT-C

Here PMT is characterized by premenstrual increased appetite, craving for sweets, with subsequent ingestion of relatively large amounts of

refined sugar, followed a few hours later by fainting spells, fatigue, palpitation, and headache. This indulgence in sweets occurs during stressful situations, or at least situations perceived by the patient as stressful.

PMT-D

In these patients, PMT is characterized by premenstrual depression, withdrawal, and thoughts of suicide followed by attempt at suicide. PMT-D patients complained of being lethargic, confused, incoherent, and of having difficulty verbalizing.

III. Incidence

The reported incidence of PMT in otherwise normal women varies from 21% to 39% (Table 1). The incidence of the PMT subgroups in PMT patients are on the average: PMT-A = 80%; PMT-H = 60%; PMT-C = 40%; PMT-D = 20% [3].

IV. Pathophysiology

Many theories have been proposed to explain the pathophysiology of PMT [3]. Few have been properly tested, however, and some have since been discarded.

PMT-A

A review of the literature [3] reveals that androgens and progestins induce a depressive mood in women whereas estrogen triggers a feeling of anxiety, hostility and tension. Elevated estrogens and low progesterons have been reported in PMT-A [2,12,15]. Estrogens influence monamine oxydases (MAO) activity. These enzymes are involved in the oxydation of biogenic amines such as norephinephine, epinephrine, serotonin, and dopamine. These biogenic amines affect moods [23,27]. For example, ephinephrine triggers feeling of anxiety; norepinephrine, a feeling of hostility and irritability; serotonin at high levels creates nervous tension, drowsiness, water retention, inability to concentrate and perform. Dopamine is believed to balance out the effects of these three amines by inducing a feeling of relaxation and increasing mental alertness [9]. There are two types of MAO: Type A, which deactivates all four biogenic amines mentioned above, and Type B, which only deactivates dopamine and phenylethylamine [23]. Estrogens suppress Type A and increase Type B MAO activities [8,10,17,22]. Therefore, under estrogen stimulation, the deactivation of biogenic amines would be reduced mainly for Type A MAO-sensitive amines, causing a relative imbalance with excess serotonin, norephinephrine and ephinephrine and relative deficiency in dopamine. This imbalance would then trigger PMT-A symptomatology (Figure 1). Magnesium deficiency causes a specific depletion of brain dopamine without affecting brain serotonin and norephinephrine [7]. It is likely, therefore, that magnesium deficiency is a predisposing factor in PMT-A. Indeed, *Abraham* and *Lubran* [4] reported significantly lower intracellular magnesium in PMT patients compared to normal control subjects (Table 2). In order to ascertain any differences in dietary patterns

Tab. 1: Incidence of PMT

Authors	Population Studied	No. of Subjects	Incidence %	Reference
Bickers	Female Workers in Industrial Plants	1,500	36	Tex. Rep. Biol. Med. 9: 406, 1951
Dalton	Women without History of Toxemia of Pregnancy	391	30 30	The Premenstrual Syndrome
Rees	Normal Women	61	21	J. Ment. Sci. 99: 62, 1953
Suarez-Murias	Student Nurses	107	29	Intern. Record Med. 166: 475, 1953
Sweeney	Normal Women	42	30	J. A. M. A. 103: 234, 1934
Sutherland and Stewart	University Students	150	39	Lancet 1: 1180, 1965

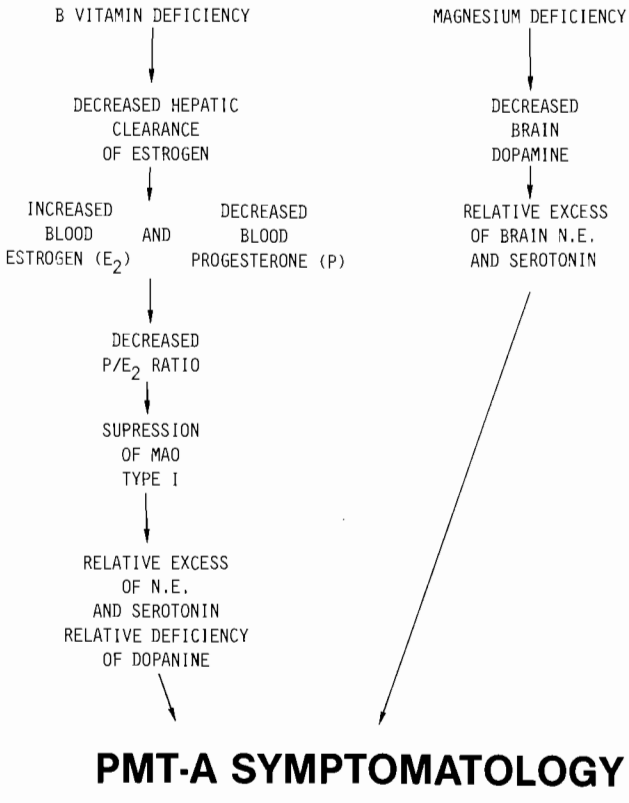

Fig. 1: Postulated pathophysiology of PMT-A

between PMT-A patients and other PMT patients, a dietary survey was performed in 39 PMT patients [6], using a computer-assisted program developed by Minera Lab Inc., Hayward, California. PMT-A was present in 30 of the 39 patients. The mean daily intake ± S. E. for calcium, magnesium and Ca/Mg ratio were: No PMT-A: 857 ± 146, 241 ± 22; 3.4 ± 0.4. For PMT-A patients: 2740 ± 660; 434 ± 46; 6.4 ± 0.93. The mean daily intake of calories, proteins, dairy products and refined sugar were significantly higher in patients with severe PMT-A compared to PMT patients without PMT-A (Table 3). It is of interest that *Seelig* reported a negative affect on magnesium absorption and retention by dairy products and refined sugar [25]. These substances increase the need for magnesium. This increased need is not met by the average diet of the PMT-A patients since dairy products contain 10 times more calcium than magnesium and calcium interferes with magnesium absorption [25,26]. For these reasons, balance studies of magnesium in PMT are required to obtain meaningful information. Dietary intake of magnesium may be adequate but due to other nutritional factors interfering with absorption and increasing renal excretion of magnesium, magnesium deficiency may be present.

Tab. 2: Red cell and serum Mg in patients with PMT

	Normal Females (9) X ± SE	PMT Patients (26) X ± SE	P Value
Serum Magnesium (Mg/100 ML)	1.7 ± 0.04	1.76 ± 0.05	N. S.
Red Cell Magnesium (Mg/100 ML)	4.5 ± 0.25	3.1 ± 0.24	< 0.01

Tab. 3: Daily intake of calories and macronutrients in 39 PMT patients according to PMT-A symptomatology

Group	N	PMT-A Symptomatology	Calories % RDA	Carbohydrates % RDA	% Cal From Fat	Protein % RDA	Dairy Servings	Refined Sugar (T. S. F.)
I	9	None or Mild						
		$\bar{X}$	122	92	42.0	140	1.33	16 ± 4.5
		SE	20	16	1.2	15	0.41	
II	16	Moderate						
		$\bar{X}$	125	89	40.8	239	2.8	15 ± 4.6
		SE	21	15	1.1	28	0.50	
III	14	Severe						
		$\bar{X}$	209	141	41.6	376	5.7	41 ± 6.3
		SE	35	28	1.4	59	0.88	
		Group I VS Group III P Value	< 0.05	NS	NS	< 0.01	< 0.01	< 0.01

PMT-H

The symptomatology of PMT-H is due to increased extracellular fluid volume secondary to sodium chloride and water retention [20,28]. The most potent sodium-retaining hormone is aldosterone, secreted by the zona glomerulosa of the adrenal cortex[1]. Aldesterone is partially under ACTH control and predominantly under the control of the renin-angiotensin system [3]. Magnesium deficiency causes hypertrophy of the zona glomerulosa of adrenal cortex with hyperaldosteronism and increased extracellular fluid volume [11]. Therefore, magnesium deficiency may play an important role in the pathophysiology of PMT-H (Figure 2).

PMT-C

Ingestion of large amounts of refined simple carbohydrates is the main factor causing the PTM-C symptomatology. Removing this craving for sweets eliminates PMT-C. This craving occurs only when patients are under stress. Normally the brain uses 20% of the total energy consumed by the body. Under stress, the brain has an increased demand for energy supply. Since the brain uses only glucose as a source of energy, there is an increased demand for glucose by the brain. This glucose comes from mainly hepatic breakdown of glycogen. In order for the liver to break down glycogen into glucose and for the brain to break down glucose into energy, many nutrients are required, mainly the B vitamins and magnesium. In patients with nutritional deficiencies, the availability and rate of metabolism of glucose would be decreased, creating an energy deficiency in the brain. In turn, the brain would signal this energy deficiency by stimulating appetite and craving for sweets. Since chocolate is rich in magnesium, chocolate craving could be a sign of magnesium deficiency (Figure 3).

The sequence of events to PMT-C would then be: (1) nutritional deficiencies (B-vitamins, magnesium); (2) decreased availability of energy to the brain to cope with stress because of decreased glycogen and glucose breakdown; (3) brain signals increased need for energy; (4) signal translated into craving for sweets; (5) increased consumption of refined sugar, (6) excess insulin release; (7) lowering of blood glucose; (8) PMT-C symptomatology.

The possible explanation for the appearance of PMT-C during the luteal phase is the fact that cells have increased capacity to bind insulin during this phase [13], resulting in an increased

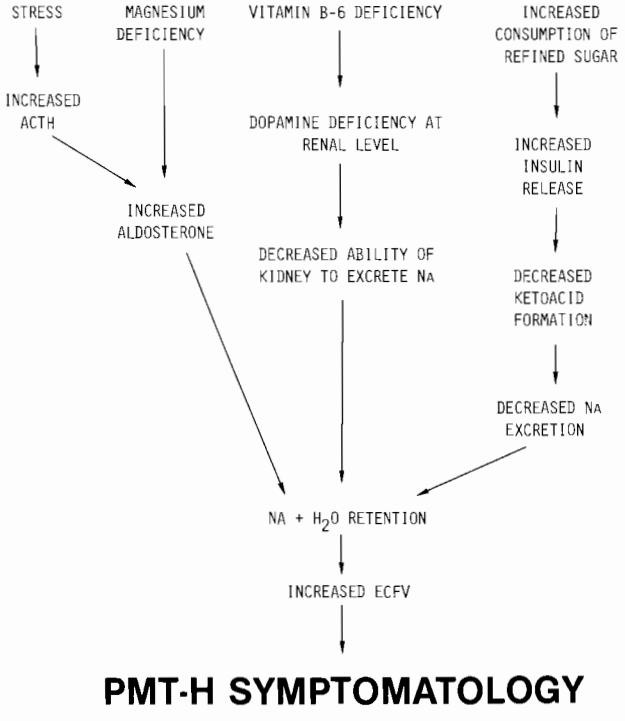

Fig. 2: Postulated pathophysiology of PMT-H

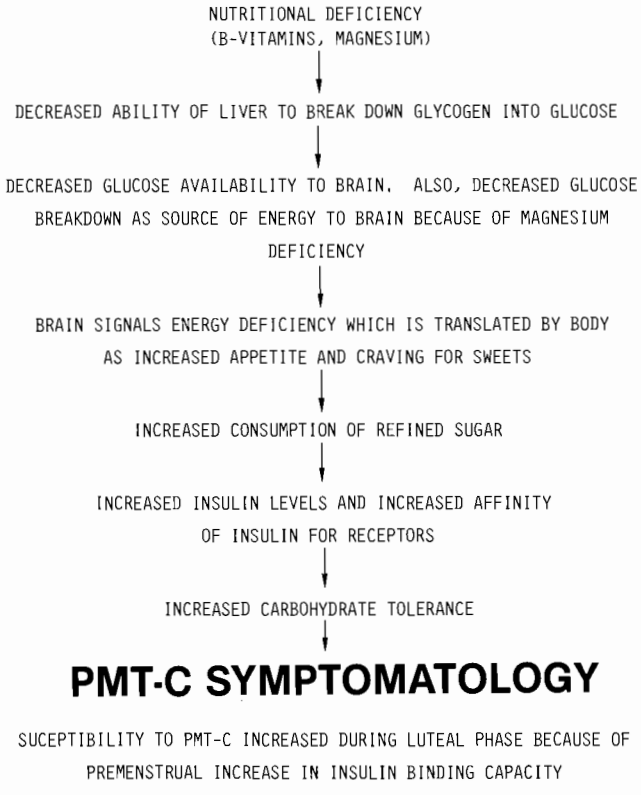

Fig. 3: Postulated pathophysiology of PMT-C

effect of insulin during the luteal phase. Ingestion of refined sugar increased the affinity of insulin by threefold to 11-fold [19]. The increased capacity of cells for insulin during the luteal phase is the predisposing factor and the increasing affinity for insulin caused by ingestion of refined sugar, the triggering factor for PMT-C.

PMT-D

Pure PMT-D is usually associated with low blood estrogens and normal or high progesterone during the mid luteal phase [3]. A proposed explanation for PMT-D is the effect of stress on adrenal androgenes which in turns supress ovarian estrogens [3]. Although magnesium deficiency may not be the cause of PMT-D, it could play a predisposing role by increasing suceptibility to stress (Figure 4).

Out of four PMT-D patients with normal blood estrogens and progesterone, two were found to have chronic lead intoxication and the other two had elevated copper levels in hair tissue [5].

Lead blocks the effect of estrogens on target tissue [30] and copper at high levels increases the oxidation of biogenic amines, decreasing their levels in the central nervous system [21]. It is of interest that depression is usually associated low levels of biogenic amines in the brain [24]. PMT-D is associated with elevated MAO levels [16], resulting from low estrogen levels or decreased biological activity of normal estrogen levels due to lead intoxication. Elevated copper level, by its oxidations of biogenic amines would produce the same effect as elevated MAO levels.

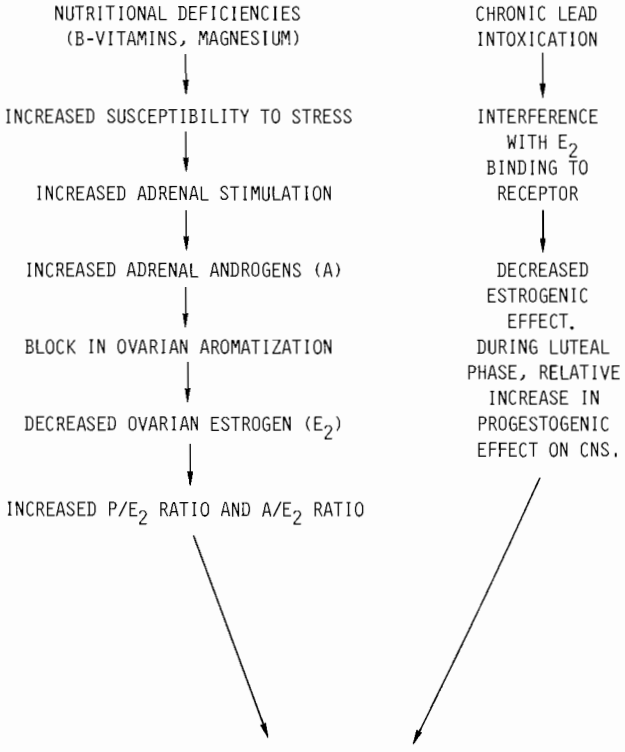

Fig. 4: Postulated pathophysiology of PMT-D

V. Conclusion

An indepth look at the pathophysiology of PMT suggest that magnesium deficiency may play a significant role by alteration of brain biogenic amines, by affecting adrenal function, by influencing glycogen und glucose breakdown and by increasing suspectibility to stress.

Future research on magnesium metabolism in PMT may be rewarding.

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Correlation of urinary magnesium excretion with blood pressure of pregnancy*)

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Zusammenfassung

Es ist ein Zusammenhang zwischen inadäquater Mg-Versorgung über die Nahrung und der Entwicklung von Schwangerschaftstoxikosen angenommen worden. Wenn dies zuträfe, würde eine verminderte Mg-Ausscheidung im Urin die mangelhafte Versorgung widerspiegeln und müßte negativ mit dem Blutdruck während der Gravidität korrelieren. Diese Hypothese wurde überprüft, indem das Urin-Mg (mEq/g Kreatinin) in Proben, die zufällig von 117 Schwangeren (Woche 10 bis 42; weiße Hautfarbe; der sozialen Mittelschicht entstammend; Alter: 14 bis 39 Jahre) gewonnen wurde, in Beziehung zum mittleren arteriellen Blutdruck (BD) gesetzt wurde. Es bestand eine signifikante negative Korrelation zwischen BD und Mg-Ausscheidung, wenn diese unter 7,0 mEq/g Kreatinin betrug, und zwar sowohl bei Mehrgebärenden (M) ($n = 25$; $r = -0{,}886$; $P < 0{,}0001$) als auch bei Primaparae (P) ($n = 32$; $r = -0{,}402$; $P < 0{,}05$), aber bei P. beruhte die Signifikanz nur auf der niedrigsten Mg-Ausscheidung bei hohem BD. P. hatten eine geringere Mg-Ausscheidung (62 % weniger als 7,0 mEq Mg/g Kreatinin) als M. (38 % unter 7,0

* Results presented at the 3rd Symposium International on Magnesium, Baden-Baden, West Germany, August 23 to 28, 1981.