

## Measurement of seminal and serum plasma magnesium levels in premature ejaculation

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### ABSTRACT

**Background:** Magnesium (Mg<sup>2+</sup>) is one of the trace elements present in human semen. Although premature ejaculation (PE) has been linked to Mg<sup>2+</sup> deficiency, its role and relationship with PE needs to be studied more.

**Objective:** This study was designed to determine the relationship between PE and serum as well as seminal plasma Mg<sup>2+</sup> levels.

**Methods:** Two-hundred Egyptian males complaining of PE were enrolled in this study (Group 1). Their ages ranged from 24 to 38 years. Fifty married healthy men (age and sex matched) were enrolled as controls (Group 2). Seminal as well as serum Mg<sup>2+</sup> levels were measured using atomic absorption spectrometer in both patients and controls.

**Result:** We found that mean seminal plasma Mg<sup>2+</sup> was significantly low in patients with PE (Group 1) with normal mean serum Mg<sup>2+</sup> level, while the mean serum and seminal plasma Mg<sup>2+</sup> in control group (Group 2) was normal.

**Conclusion:** This study demonstrated that PE has a significant relationship with decreased seminal plasma Mg<sup>2+</sup>. This highlights a possible role of seminal Mg<sup>2+</sup> in the pathophysiology of PE.

KEY WORDS: Seminal plasma magnesium, serum magnesium, premature ejaculation

### INTRODUCTION

Premature ejaculation (PE) is a sexual debilitating condition affecting a large number of men worldwide and leading to important dysfunctions influencing the patient's affective and emotional life.<sup>1</sup> According to some reports, it is present in about 20-30% of the male population.<sup>2,3</sup>

Trace elements in semen play an important role in male sexuality.<sup>4</sup> As calcium is one of the elements responsible for smooth muscle contraction of the vas deference and corpus cavernosum,<sup>5</sup> Mg<sup>2+</sup> may play a role in relaxation of smooth muscles of the male genital tract and the penis to delay the ejaculatory process and improve the erection.<sup>6</sup>

The normal serum Mg<sup>2+</sup> level is 1.8-2.2 mg/dL.

Out of this 60% is ionized, 10% is complexed with other ions and 30% is bound to proteins.<sup>7</sup> Magnesium is important in the maintenance of the structure of ribosomes, nucleic acids and some proteins.<sup>8</sup> There are two major roles played by magnesium in biological systems: (i) It can compete with calcium for binding sites on proteins and membranes, and (ii) It can form chelates with important intracellular anionic ligands, notably adenosine triphosphate (ATP).<sup>7,9</sup>

Magnesium acts as a cofactor for some 300 enzymes; including enzymes involved in protein synthesis, glycolysis and the transmembrane transport of ions.<sup>8</sup> A Mg<sup>2+</sup>-ATP complex is the substrate for many ATP-requiring enzymes such

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as alkaline phosphatase, hexokinase, fructokinase, phosphofructokinase, adenyl cyclase, cAMP dependent kinases, amongst others.<sup>7,8,9</sup>

The reported normal level of  $Mg^{2+}$  in seminal fluid is  $> 7$  mg/dl,<sup>10</sup> while the normal serum  $Mg^{2+}$  level is 1.8-2.2 mg/dl.<sup>7</sup> The seminal level, which is 4 or 5 fold higher than that of blood serum, do not increase significantly after  $Mg^{2+}$  therapy. It is believed that the higher  $Mg^{2+}$  level in seminal plasma is the result of an active secretion process and is maintained by the human body as a part of homeostatic balance even if  $Mg^{2+}$  intake is insufficient.<sup>11</sup>

Omu et, al<sup>12</sup> have found that  $Mg^{2+}$  is involved in semen transport through a relation between electrical activity of the vas deferens and extracellular  $Mg^{2+}$  concentration. They had proved that extracellular  $Mg^{2+}$  depletion enhanced the contractile response of the smooth muscles of vas deferens to electrical stimulation, while increasing extracellular  $Mg^{2+}$  concentration inhibited the contractions. Decreased levels of  $Mg^{2+}$  gives rise to contraction of male genital tract and this may lead to premature emission and ejaculation processes. PE is significantly related with a lower level of seminal plasma  $Mg^{2+}$  and the pathological physiology of this relationship requires more investigations.<sup>13,14</sup> In this study we aimed to determine the relationship between PE and seminal as well as serum  $Mg^{2+}$  levels.

## SUBJECTS AND METHODS

This study included 250 Egyptian males living in Cairo presented at andrology clinic of Al-Hussein university hospital. They were divided into two groups. Group 1 (PE group); included 200 males complaining of PE. Their ages ranged from 24 to 38 years. Group 2 (control group); included 50

married healthy males. Their ages ranged from 24 to 38 years.

Inclusion criteria: 1) Male patients complaining of PE (defined as brief ejaculatory latency or loss of control before sexual satisfaction of both partners); 2) Duration of marriage more than 6 months; 3) Complaint of PE more than 6 months. Patients with organic disorders e.g.; diabetes mellitus, chronic prostatitis, hyperthyroidism, renal failure and previous genitourinary surgery were excluded.

All studied subjects were subjected to: 1) Full history taking, general and local examination; 2) Estimation of seminal and serum  $Mg^{2+}$  levels. The  $Mg^{2+}$  levels were measured using atomic absorption spectrophotometry (model AA670, Shimadzu, Japan).

## STATISTICAL ANALYSIS

Statistical analysis was carried out using SPSS (version 17.0; SPSS Inc., Chicago, IL, USA). All results of the patients were statistically studied for the following: 1) *Mean X*: to measure a central value of a group of data. 2) Standard deviation (*SD*): to measure the degree of deviation of data around their means. 3) Paired t test: to test for significant difference between two sample means. Results were considered statistically significant at  $P$  value  $\leq 0.05$ .

## RESULT

This study was carried out on 250 males divided into two groups. Group 1; included 200 males complaining of PE. Their ages ranged from 24 to 38 years (mean  $\pm$  SD;  $31.63 \pm 5.99$ ). Group 2; included 50 married healthy men as controls. Their ages ranged from 24 to 38 years (mean  $\pm$  SD;  $31.75 \pm 6.97$ ).

Results of seminal and serum Mg<sup>2+</sup> levels in the two groups were as follows: (Table 1). Seminal plasma Mg<sup>2+</sup> levels in group 1 ranged from 7 to 14 mg/dl (mean = 10.53 mg/dl ± 1.56). Seminal plasma Mg<sup>2+</sup> levels in group 2 ranged from 8.1 to 14 mg/dl (mean = 11.06 mg/dl ± 1.56). There was a statistically significant decrease of Mg<sup>2+</sup> level in group 1 compared with group 2 ( $p > 0.05$ ).

Serum Mg<sup>2+</sup> levels in group 1 ranged from 1.7 mg/dl to 2.5 mg/dl (mean = 2.02 mg/dl ± 0.24). Serum Mg<sup>2+</sup> levels in group 2 ranged from 1.7 mg/dl to 2.4 mg/dl (mean = 2.04 mg/dl ± 0.24). There was no statistically significant difference between serum Mg<sup>2+</sup> levels in both groups ( $p > 0.05$ ).

**Table 1** Comparison between mean of seminal and serum Mg<sup>2+</sup> levels among cases and controls.

Mg <sup>2+</sup> level		N.	Mean	Std. Deviation	P value
Seminal Mg <sup>2+</sup>	Cases	200	10.53	1.49	0.03
	Controls	50	11.06	1.56	
Serum Mg <sup>2+</sup>	Cases	200	2.02	.25	0.63
	Controls	50	2.04	.24	

## DISCUSSION

The exact cause of PE is not fully identified and many theories have tried to explain this sexual disorder from many aspects.<sup>6</sup> As there are four PE subtypes, each with its own clinical characteristics, etiology and pathogenesis, it is assumed that the pathophysiology of lifelong PE is different from the pathophysiology of the other PE subtypes. For a full understanding of the pathophysiology of lifelong PE, there are still many questions that need to be answered by evidence-based human and animal research.<sup>15</sup>

Some studies postulate a role of seminal Mg<sup>2+</sup> in the pathogenesis of PE.<sup>13,14,16</sup> In this study we measured Mg<sup>2+</sup> in semen as well as in serum of men suffering from PE in a trial to highlight a

possible role in this sexual disorder. Our results showed that the mean seminal plasma Mg<sup>2+</sup> level was significantly lower in PE patients compared with controls (P value = 0.03). While the mean serum Mg<sup>2+</sup> level was normal in patients as in controls (P value = 0.63).

Omu *et al*<sup>16</sup> analyzed the level of Mg<sup>2+</sup> in three groups of men; with normal semen parameters, oligoathenozoospermia and PE. Agreeing with our results, their study showed that there was a significant decrease in level of Mg<sup>2+</sup> in semen of the group of men with PE. Thus, it was concluded that Mg<sup>2+</sup> is probably involved in sperm transport and PE. Also Wang *et al*<sup>17</sup> analyzed serum leptin level, Mg<sup>2+</sup> level and glans hypersensitivity measurements for patients with PE and showed that there is a possible role for Mg<sup>2+</sup> in the pathogenesis of PE.

In agreement with this study, Nikoobakht *et al*<sup>13</sup> measured Mg<sup>2+</sup> level in semen and serum in healthy men and men with PE. The results showed a significant decrease of Mg<sup>2+</sup> in semen of men with PE when compared to control cases, but there were not many differences regarding serum Mg<sup>2+</sup> level in both groups.

Another study by Aloosh *et al*<sup>14</sup> confirmed the conclusions of Nikoobakht *et al*,<sup>13</sup> where Mg<sup>2+</sup> level was measured in serum and semen of healthy men and patients with PE and the results showed that Mg<sup>2+</sup> was significantly lower in semen of men with PE than in control cases, while serum Mg<sup>2+</sup> level in both groups was nearly the same.

Low seminal Mg<sup>2+</sup> in relation to PE with normal serum Mg<sup>2+</sup> level may be due to a defect in the active transport system that transports Mg<sup>2+</sup> from blood to semen or the presence of a Mg<sup>2+</sup> -diminishing factor like chelating agents in the semen of the patients or a previous hypomagnesemia

caused by low consumption of  $Mg^{2+}$  that might contribute to the decline in seminal plasma  $Mg^{2+}$  levels.<sup>13,14</sup>

Low  $Mg^{2+}$  level might manifest as uncontrolled contractility of the male genital tract, to cause premature emission and ejaculation.<sup>14</sup> The mechanism by which hypomagnesemia may lead to PE is explained by fact that hypomagnesemia stimulates angiotensin-induced aldosterone synthesis and thromboxane-A2 over-production by phospholipase-A2 activation. Engagement of thromboxane-A2 results in  $Ca^{2+}$  influx.<sup>18,19</sup> Elevated calcium in endothelial cells promotes phosphodiesterases and decreases G-cyclase activity<sup>20</sup> resulting in decreased nitric oxide (NO) production and its release from the endothelium.<sup>18</sup> This will decrease c-GMP resulting in decreased NO production, which is a vascular smooth muscle relaxing factor. And thus, decreased levels of NO consequently lead to contraction of smooth muscles of genital tract causing rapid emission and PE.<sup>13,14</sup> A decrease of NO can lead also to contraction of cavernosal smooth muscles causing a state of erectile dysfunction (ED).

This study, with other works, hypothesizes that low seminal  $Mg^{2+}$  has a pathological role in PE and with a further decrease of  $Mg^{2+}$  it might also lead to a combination of PE and ED. Decrease in  $Mg^{2+}$  leads to a combination of PE and ED through NO system. Nitric oxide is released from the nerve and endothelial cells mainly in the corpora cavernosa so it acts first on the smooth muscles of the corpora causing their relaxation and erection. When NO level decreases, most of the residual amount will be consumed for having an erection and so ejaculation will be affected causing a state of PE and with a further decrease in level of NO, PE and ED may both occur.

## CONCLUSION AND RECOMMENDATIONS

As this study demonstrated that PE has a significant relationship with decreased seminal plasma  $Mg^{2+}$  level, we advice measurement of this trace element in the patient semen, rather than serum, whenever possible. Also we recommend that all patients complaining of PE to take  $Mg^{2+}$  supplementation as an adjuvant therapy beside the main treatment.

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