Introduction

Past decade has been distinguished by few advances with respect to the pathophysiology and prevention (1), but several modifications has been made in preeclampsia patient’s clinical treatment (2). Particularly, approval have been contrived for home or day-care management of a chosen group of patients with moderate gestational hypertension or preeclampsia (3). Three randomized clinical trials showed that anticipated management with close monitoring of maternal and fetal conditions is attainable in a selected group of patients with serious preeclampsia at less than 34 weeks' gestation (4).

Moreover, the efficacy of MgSO₄ in the control and prevention of eclamptic convulsion has been confirmed in randomized controlled trials carried out worldwide (5). In comparison, recent randomized trials was aborted to show any major potency from the habitual use of low-dose aspirin in pregnancy (6), whereas a recent meta-analysis found calcium supplementation amid pre term neonates with no effect on Ca and PTH levels.

Magnesium passes through placenta and fetal membranes and its modulation has parallel changes in the mother’s blood (12). The Mg distribution volume reaches a plateau approximately 3-4 hours after administration (10). Although it is considered safe to both mother and the newborn, but, it causes neonatal hypermagnesemia and hypocalcaemia in adult (13).

Abstract: Due to the approximate clinical and biochemical manifestations of calcium and magnesium disturbances, with regard to the regulatory effects of parathyroid hormone (PTH), this present study is designed to analyze serum calcium (Ca), magnesium (Mg), and (PTH) at the time of birth, 24 hours afterwards in newborns after the mother has been treated with Mg-sulfate. We registered 86 term and preterm neonates (43 in each group) using simple census method delivered through vagina to preeclampsia pregnant women treated with Mg-sulfate immediately before birth in Khoramabad Asali Hospital, Iran. The first specimen was obtained from umbilical cord blood at birth, followed by the second sample of 2cc peripherally obtained from blood 24 hours after birth. The mean serum Mg level was higher than normal for both specimens in both term and preterm groups with no significant difference. The mean serum Ca level was higher in term group at both occasions, which turned out to be statistically significant (P<0.000) and (P=0.001) for the first and second specimens respectively. The mean PTH level was also in normal range for both groups at both times with no statistical significance. On the other hand, magnesium level showed a significant decline at 24 hours (P = 0.005) while PTH increased significantly (p<0.000) and (p=0.005) for term and preterm groups respectively. In contrast, Ca changes were not significantly different between the two specimens. Treatment with Mg-sulfate immediately before vaginal delivery increases Mg in both term and preterm neonates with no effect on Ca and PTH levels.

Key words: Preeclampsia, neonatal hypermagnesemia, PTH, magnesium sulfate.
Table 1. Serum Ca, Mg, PTH levels in the study population immediately after birth and 24 hours after that.

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>Term at birth</th>
<th>Term 24 hours after birth</th>
<th>Preterm at birth</th>
<th>Preterm 24 hours after birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mg (mg / dl)</td>
<td>3.45 ± 1.09</td>
<td>2.96 ± 0.87</td>
<td>3.87 ± 1.35</td>
<td>3.29 ± 1.03</td>
</tr>
<tr>
<td>Ca (mg / dl)</td>
<td>9.58 ± 0.9</td>
<td>9.41 ± 0.93</td>
<td>8.84 ± 0.8</td>
<td>8.71 ± 0.97</td>
</tr>
<tr>
<td>PTH (pg / dl)</td>
<td>16.29 ± 13.08</td>
<td>28.85 ± 5.37</td>
<td>12.42 ± 13.21</td>
<td>24.29 ± 17.27</td>
</tr>
</tbody>
</table>

1 The normal ranges according to the reference lab; PTH: 6.2-29 pg / dl; Ca: 8.5-11 mg / dl; Mg: 1.8-3 mg / dl.
Calcium, Magnesium, and PTH In pre-eclampsia.

S. Vahabi et al. 2016 | Volume 62 | Issue 14

At 24 hours. There was no significant difference between these two groups (P = 0.39).

The mean Ca level in term and preterm neonates at birth and 24 hours after birth have been shown in figure 2. The t-test showed significant correlation for both groups either at birth or 24 hours after birth (p = 0.003 at birth and p = 0.001 24 hours after birth). In other words, although Ca levels were normal in both term and preterm groups, it was significantly higher in term neonates at both occasions (table 1).

We also found hypocalcaemia at birth to be 46.5 and 11.6 percent of the preterm and term offspring respectively. Interestingly, hypercalcemia was detected in 9.3 percent of term infants which was not the case in preterm neonates. There was no significant correlation between first and second specimens in term (p = 0.372) and preterm (p = 0.249) groups.

The mean PTH level in term and preterm groups at birth and 24 hours later have been presented in figure 3. Twenty four (55%) preterm and 34 (79%) term infants at birth, and 22 (51%) preterm and 32 (74%) term infants at 24 hours after birth had normal PTH levels (table 1).

The t-test showed no significant difference between groups at either first or second occasions (P = 0.42 at birth and P = 0.44 at 24 hours). However, the fisher test proved the significance of the increase in PTH levels at 24 hours in both groups (P < 0.005 for term and P = 0.005 for preterm group). The chi-square test was insignificant for both groups at both timings (P = 0.25 and P = 0.21, respectively).

Discussion

Parenteral magnesium sulfate therapy is routinely utilized for capturing prophylaxis in pre-eclampsia management. Magnesium is crucial constituent of calcium homeostasis, along with calcitonin, vitamin D, parathyroid hormone, and phosphorus (20). Even though the impact of magnesium sulfate infusion on the levels of different serum constituents have been addressed, the comprehension of maternal homeostasis is left incomplete because the levels of vitamin D have not been measured. Reports on the effects of maternal therapy on neonatal and fetal calcium homeostasis are incomplete and inaccurate, and effects on the vitamin D constituents have not been previously recorded (21).

As we have described fully in our result, both the term and preterm groups had hypermagnesemia after birth. Although the Mg level declined in both groups 24 hours after birth, which was significant in comparison to the first-hour specimen, there was no significant correlation between the two groups (22). The Ca and PTH were normal at both occasions in both groups.

Green et al. (1983) (23) in their study found hypermagnesemia with normal Ca in the offspring of Mg-sulfate treated mothers. The also described neurologic status of the newborns and concluded no difference in comparison to control group and no correlation with cord Mg or the total Mg administered (24). This is important as hypermagnesaemia may affect neurologic status of the newborn adversely, thus resulting in diagnostic confusion (25). We limited our study to neonates and avoided measurements in mothers as a matter of technical and financial difficulties, but our results are closely comparative to Green's study.

Rantonen et al., 2001 studied (15) the effects of maternal magnesium sulphate treatment on the parathyroid hormone secretory response and mineral status of neonates studied, 8 participants were exposed to MgSO4 and 27 control preterm infants amid the first 2 weeks of life (26). Hypermagnesaemia resulted during the first 3–7 days of life without influencing the concentrations of other serum constituents. They concluded that hypermagnesaemia was related with hypercalciuria at the first 3 days and PTH suppression up to the age of 2 weeks in the exposed infants (27).

To evaluate the therapeutic effects of Mg-sulfate on mineral and PTH response, Rantonen et.al (2001) found hypermagnesaemia and hypercalcemia in the first week of life with PTH suppression (28). This was in contrast to our findings which showed hypercalcemia in only a minimal of term cases. We did not detect either hypercalcemia or PTH suppression. This was the case in Van Der Hayden et.al research, who, in contrast to our study, also detected elevated potassium and calcium in cord blood immediately after birth (29).

McGumrus et.al (1980) (30) designed a case-control study on 37 neonates born to mothers treated with Mg-
sulfate for preeclampsia using serial measurements and found hypermagnesemia immediately, and at hours 2, 12, and 24 after birth. This reached has a comparable level of controls after 48 hours. Calcium levels were normal.

Donovan et al. (1980) (31) considered Ca, Mg, and PTH changes in 20 preeclampsia patients treated with Mg-sulfate, and detected hypermagnesemia in the first 72 hours concomitant with hypercalcemia and reduced PTH levels. They concluded that hypermagnesemia causes calcium shift from bone to plasma. This is important because Matsuda et al. also described hypermagnesemia as a cause for transverse bands in the metaphysis of long bones which is indicative of bone mineral loss (32).

As the Schanler et al. (1997) (32) have shown, premature neonates born to prolonged Mg-sulfate treated mothers had increased Mg, phosphorus, osteocalcin levels with concomitant hypocalcemia. We cannot comment on these findings because we did not use prolonged treatment in our study.

Calcium supplementation at the time of pregnancy decreases maternal mean arterial pressure (33) and the prevalence of preeclampsia, yet, the molecular basis is not well understood. These findings are generally support our findings. The differences in results relating to Ca and PTH level may be caused by the difference in frequency or duration of Mg-sulfate administration. However, it should be emphasized that Ca is not the only factor affecting PTH level and Mg levels are also relevant (34).

In a study by August et al., a reduction in the levels of lα, 25-dihydroxy calciferol and parathyroid hormone levels was reported not to be significantly different from controls group in nine subjects with acute preeclampsia before magnesium sulfate therapy. These findings seems to be different from ours.

Preeclampsia is associated with abnormal calcium metabolism and placental dysfunction. Yusuf (2012) (35) investigated ionized calcium levels in the umbilical cord arterial blood of women with preeclampsia and normotensive pregnancies. There was no difference in the cord pH and fetal growth restriction between the two groups. Ionized calcium levels were significantly lower in the preeclampsia group (p<0.001).

Although some studies showed significant changes in serum trace elements levels like Ca and Mg in preeclampsia and eclampsia, but we do not examine these elements before starting magnesium sulfate treatment. It can influence the exchange of circulation of Mg and Ca between mothers and neonate.

In term neonates, Mg sulfate exposure may be associated independently with NICU admission in a dose-dependent relationship. Requirements for fluid and nutritional support are common in this group, likely due to feeding difficulties in exposed neonates. Assessment of acute care needs among all neonates exposed to Mg sulfate for maternal eclampsia prophylaxis should be considered. These increasing risk for NICU admission may be as a result of serum Mg level changes in neonates that we showed in our study (36).

Although maternal and neonatal magnesium concentrations were highly correlated but we did not examine the serum Mg level in mother and neonate simultaneously, which limited our study.

It is noteworthy that we faced some limitations during the study, which might have influenced or results. First, the time schedule was limited and we encountered many mothers’ did not consent when selecting our participant. This caused reduction of the total cases. Second, we had to limit our study design to cases with no controls, which would certainly reduce the accuracy of our conclusions. There were also technical obstacles such as inability to obtain second specimens, or the delay in analysis because of occupied laboratory timetable.

If the administration of Mg-sulfate is inevitable to prevent preeclampsia adverse effects, the hypermagnesemia should be considered as an important contribution in the case of hyporeflexia, hypotonia, or coma in the newborn. In totality, we should conclude that administration of Mg-sulfate in order to prevent preeclampsia adverse effects causes hypermagnesemia in both term and preterm neonates with no effect on Ca and PTH levels. Our results also emphasize the need for further studies on the calcium status of infants born to mothers with preeclampsia.

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References
10. Green KW, Key TC, Coen R, Resnik R. The effects of maternal-
22. Iran-Pour E, Sepideh Vahabi, Mohammad Heidari, Amir Hooman Kazemi, Mehdi Birjandi (Lorestan University of Medical Sciences, Lorestan, Islamic Republic of Iran.). Assessment. 2010.