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Serum Magnesium Level in Severe Preeclampsia and Eclampsia Undergoing Magnesium Sulfate Therapy at Chonburi Hospital

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ABSTRACT

Objectives: To evaluate the level of serum magnesium in pregnant women with severe preeclampsia and eclampsia who received magnesium sulfate therapy and to determine the factors affecting nontherapeutic magnesium level at Chonburi Hospital.

Study design: Prospective descriptive study.

Materials and Methods: The data from 146 pregnant women with severe preeclampsia and eclampsia receiving magnesium sulfate therapy at Chonburi Hospital from October 1, 2007 to September 30, 2008 were collected. Blood sample for serum magnesium level was taken at the third hour after loading dose of magnesium sulfate. Multiple logistic regression was employed and the calculation were done on the following factors; age, body mass index (BMI), gestational age, gestational diabetes mellitus (GDM) and other underlying disease to find out the significant factors affecting nontherapeutic magnesium level.

Results: The mean of serum magnesium level was 4.9$\pm$1.9 mg/dL. Only 67 patients (45.9%) were in the therapeutic range (4.8-8.4 mg/dL). The GDM was significantly associated with non-therapeutic serum magnesium level. (p=0.03)

Conclusion: Magnesium sulfate is now the gold standard drug for preventing seizure in pregnant women with severe preeclampsia and eclampsia. In 54.1% of pregnant women who receiving the loading dose of magnesium sulfate 4 gm followed by a maintenance infusion of 1 gm/hr had inadequate therapeutic level, and GDM was a statistical significantly associated factor.

Key words: severe preeclampsia; eclampsia; magnesium sulfate; magnesium sulfate serum level

Introduction

Hypertensive disorders complicate 5-10% of pregnant women and are the leading cause of maternal mortality in the worldwide. In addition, preeclampsia is considered severe in the presence of multiorgans involvement such as pulmonary edema, oliguria (urine less than 500 mL per 24 hours), thrombocytopenia (platelet count less than 100,000/mm^3), abnormal liver enzymes in association with persistent epigastric or right upper quadrant pain, or persistent severe central nervous system symptoms (altered mental status, headaches, blurred vision or blindness).[1,2]

Corresponding to the newer literatures,[3-5] magnesium sulfate is the first choice as anti-convulsive drug in cases of severe preeclampsia and eclampsia for preventing seizure. The target of serum magnesium level was 4.8-8.4 mg/dL. As that standard dose initially 4-6 gm of magnesium sulfate, followed by 2 gm/hr intravenously for keeping serum level applied by infusion pump are recommended. Sibai, et al.[6] found that serum magnesium level rised gradually until a maximum level was reached which the level remained constant. So adjusting the maintenance dose according to the clinical response of the patient remains the best approach such as severe headache, visual disturbance, or epigastric pain.[3-5]

At Chonburi Hospital the regimen of magnesium therapy was initially start at 4 gm and maintenance with 1 gm/hr as correlate with the Royal Thai College of Obstetricians and Gynaecologists recommendation. The cause of the controversy regimen still exists regarding the optimum maintenance dose in the intravenous regimen.[2-4] According to previous study, maintenance dose at 2-3 gm/hr, the therapeutic level still did not reach the target. Usually the magnitude of magnesium distribution reach the constant level between the third and fourth hours after administration.[7] So that the samples were collected in third hour after loading dose. Norwitz and Repke,[8] showed that magnesium sulfate therapy significantly reduced the risk of seizure from 1.9 to 0.8%. The present study was designed for serum magnesium level assessment in pregnancy complicated with severe preeclampsia and eclampsia after receiving magnesium therapy at Chonburi Hospital and to determine the risk factors that affect serum magnesium level.

Materials and Methods

Our study was approved by the Chonburi Hospital Ethical Committee on Human Research. All consecutive pregnant women with gestational age (GA) of ≥ 20 weeks which were diagnosed severe preeclampsia and eclampsia, admitted to the labor room at our institution between October 1, 2007 to September 30, 2008 were eligible in the study.

The criteria used to diagnose severe preeclampsia including, recent-onset hypertension (systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg) proteinuria 2+ or more by urine protein dipstick, and 24 hour urine protein ≥ 2 gm/24 hr. Eclampsia was defined as occurrence of seizures in a women with preeclampsia that cannot be attributed to other causes. The exclusion criteria consisted of the pregnant women who received magnesium loading dose more than 3 hours before arriving Chonburi Hospital, motor weakness, myasthenia gravis, chronic renal failure, heart block, severe preeclampsia with expectant management and the dissent pregnant women. After the explanation and invitation to join our study, each of all 160 subjects or patient's relative (in cases of eclampsia) was provided written informed consent administered in Thai. Basic demographic data such as, gestational age, BMI and medical disease were recorded by interviewers. All pregnant women received standard monitoring during labor according to our institutional protocols, including continuous electronic fetal monitoring, periodic assessment of maternal blood pressure, pulse, temperature, respiratory rate, deep tendon reflex and urine output.

Pregnant women received 4 gm of magnesium sulfate infusion intravenously for loading dose over 15-20 minutes followed by a maintenance infusion of 1 gm/hr according to the standard protocol of our obstetric unit. Blood sample of 5 cc was taken at the third hour after the loading dose which was analyzed for magnesium level test by dye chemistry at the laboratory. The termination of pregnancy was done according to the obstetrics indication. No one was terminated by cesarean section within the first three hours after treatment. The magnesium sulfate infusion was still continued even in the intrapartum period and also continued for the next 24 hours postpartum. The data was collected and then analyzed by MEDCALC VERSION 11.01.0 (Copyright 1993-2009 MEDCALC Software bvba MedCalc Software Broekstraat 52 B-9030 Mariakerke Belgium.).

Multiple logistic regression was used to identify the association of magnesium level with BMI, serum creatinine level, urine output volume, gestational diabetes mellitus (GDM), and

medical diseases. Statistical significance was considered if the P value was less than 0.05

Results

From October 1, 2007 to September 30, 2008, the total of 160 pregnant women with severe preeclampsia and eclampsia were included in our study. Ten pregnant women who were transferred from other hospitals received the magnesium sulfate loading dose for more than 3 hours prior to the arrival, and four patients dissented to the research. Therefore only 146 were enrolled and only one was eclampsia. Demographic data of the pregnant women were shown in Table 1; the mean maternal age in our study was 26.1 years old, BMI 29.9 kg/m^2 and GA 264 days. Medical histories such as hypertension, epilepsy, SLE, thyroid disease were identified in 6.16% (9/146). The mean serum magnesium level was 4.9±1.9 mg/dL. Seventy nine (54.1%) pregnant women were in the nontherapeutic level group and only 67 (45.9%) pregnant women were in the therapeutic level group as shown in Table 2. The mean serum creatinine level was 0.82±0.2 mg/dL. Serum creatinine level more than 0.9 mg/dL was categorized as renal insufficiency. The mean value of urine output was 1.2 ± 0.6 cc/kg/hr, if urine output was less than 0.5 cc/kg/hr, it was defined as oliguria.

The association between nontherapeutic magnesium level with elderly gravidarum, obesity, GA, renal insufficiency, oliguria, GDM and medical disease were shown in Table 3. Multiple logistic regression showed that pregnant women complicated with GDM was associated with nontherapeutic level of magnesium, significantly. The other factors including elderly gravidarum, obesity, gestational age, preterm, term, postterm, underlying diseases and oliguria had no significant association.

In our study, four patients (2.72%) developed seizure during admission. All of them did not have any medical diseases during pregnancy.

Table 1. Baseline characteristics.

Pregnant women (N=146)	**Mean ± SD**
Age (years)	26.1 ± 5.9
Gestational age(days)	264.0 ± 20.6
Body weight (kg)	71.1 ± 11.4
Height (cm)	154.1 ± 5.8
BMI (kg/m2)	29.9 ± 4.6
Cr (mg/dL)	0.8 ± 0.2
Medical diseases	
• Hypertension	4(2.7%)
• Epilepsy	2(1.3%)
• SLE	2(1.3%)
• Thyroid disease	1(0.6%)

BMI= Body mass index

Cr= Creatinine

SLE= Systemic lupus erythematosus

Table 2. Serum magnesium level of pregnant women complicated with severe preeclampsia and eclampsia

Serum magnesium level(mg/dL)	N=146
<4.8	79(54.10%)
4.8-8.4	67(45.90%)

Table 3. Factors affecting the nontherapeutic magnesium level

Variables	Nontherapeutic level N=79 (%)	Therapeutic level N=67 (%)	P value
Elderly Gravidarum (≥35 yr)	6(7.59%)	9(13.43%)	0.37
Obesity (BMI≥30 kg/m^2)	38(48.10)%	25(37.31%)	0.25
Gestational age (weeks)			
Preterm (<37)	26(32.91%)	25(37.31%)	0.70
Term (≥37)	53(67.09%)	41(61.19%)	0.57
Postterm (≥42)	2(2.53%)	1(1.49%)	0.88
Renal Insufficiency	30(37.97%)	31(46.27%)	0.39
Oliguria (<0.5 cc/kg/hr)	1(1.27%)	8(11.94%)	0.02*
GDM	7(8.86%)	0(0%)	0.03*
Underlying disease (N=9)	6(7.59%)	3(4.47%)	0.66
● Hypertension (4)	2(2.53%)	2(2.53%)	0.73
● Epilepsy (2)	2(2.53%)	0(0.00%)	0.55
● SLE (2)	2(2.53%)	0(0.00%)	0.55
● Thyroid disease (1)	0(0.00%)	1(1.49%)	0.93

*Statistical significance

Discussion

Magnesium sulfate is now the gold standard drug for preventing seizure in pregnant women complicated with severe preeclampsia and eclampsia. The target range for seizure prevention was 4.8 to 8.4 mg/dL. At Chonburi Hospital, only 67 (45.9%) pregnant women were found to have the therapeutic level (4.8-8.4 mg/dL) with magnesium sulfate therapy. In this study, 2.7% of the subjects developed convulsion, this incidence was much more than the other study, 1.9%.[8] It cannot be concluded that magnesium sulfate regimen given at Chonburi Hospital would prevent seizure. Moreover, the study showed that half of the seizure patients had the therapeutic magnesium level and seizure can still occurred. However, the number of patients were too small to be concluded from this data.

According to the previous study,[8] the prevalence of convulsion in the pregnant women receiving a continuously intravenous infusion of magnesium sulfate at a rate of 1 gm/hr was not significantly increased in comparison with those receiving the higher dose of 2 gm/hr. Many previous studies recommended to adjust the maintenance dose up to 2 or 3 gm/hr or adjust loading dose from 4 gm to 6 gm/hr.[9,10] From Sibai's study found that when a maintenance dose of 1 or 2 g/hr was used, 98 and 50% of the respective serum magnesium values were below the levels considered therapeutic. On the other hand, therapeutic levels were achieved in all patients receiving a

maintenance dose of 3 g/h.[10] However, the major adverse effects, respiratory depression, cardiac arrest, hypotension or confusion were increasing in the higher dose groups and the recommendation was to adjust magnesium intravenous dose on the background of clinical finding with unnecessary monitor of serum magnesium. In our study, even in the nontherapeutic level group, the seizure did not occur, so clinical monitoring for signs of eminent eclampsia are more important and more easier method to monitor the patients.

Our study revealed the association between GDM pregnant women with low level of serum magnesium similarly to many previous studies.[11] Lower level of serum magnesium in GDM were probably derived from decreasing its net tubular reabsorption in diabetic patients in presence of hyperglycemia or because of their high total body volume. But we could not analyze the precise association due to small sample size.

In the future, the study should be extended and designed the regimen of magnesium therapy adjusted especially in GDM patients with subgroup analysis are far the factors affecting in GDM patients.

Conclusion

In 54.10 % of pregnant women who received the loading dose of magnesium sulfate 4 gm followed by a maintenance infusion of 1 gm/hr had an inadequate therapeutic level, GDM was the risk factor that associated with the low therapeutic level.

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ระดับแมกนีเซียมในหญิงตั้งครรภ์ที่มีภาวะครรภ์เป็นพิษอย่างรุนแรงและชักจากภาวะครรภ์เป็นพิษหลังได้รับการรักษาด้วยแมกนีเซียมซัลเฟตที่โรงพยาบาลชลบุรี

กิตติพร ปรีดาธรรม, พิมพิกา ตันสุภสวัสดิกุล

วัตถุประสงค์ *: เพื่อศึกษาระดับแมกนีเซียมในหญิงตั้งครรภ์ที่ได้รับการรักษาด้วยแมกนีเซียมซัลเฟตที่โรงพยาบาลชลบุรี และหาปัจจัยเสี่ยงที่ทำให้ระดับแมกนีเซียมไม่ถึงระดับการรักษามาตรฐาน*

รูปแบบการวิจัย *: การวิจัยเชิงพรรณา ไม่มีกลุ่มเปรียบเทียบ*

วิธีการศึกษา *: ศึกษาโดยเก็บตัวอย่างเลือด ในหญิงตั้งครรภ์ที่มีภาวะครรภ์เป็นพิษอย่างรุนแรงหรือมีภาวะชักจากภาวะครรภ์เป็นพิษที่มารับการรักษาที่ห้องคลอดโรงพยาบาลชลบุรีระหว่างวันที่ 1 ตุลาคม 2550 ถึง 30 กันยายน 2551 เพื่อหาระดับแมกนีเซียมหลังได้รับยา 3 ชั่วโมง มีการบันทึกข้อมูลของหญิงตั้งครรภ์แต่ละราย คือ ดัชนีมวลกาย อายุ โรคประจำตัว ค่าการทำงานของไต ปริมาณปัสสาวะ รวมถึง สังเกตอัตราการหายใจและความไวของข้อเข่าทุกชั่วโมง ข้อมูลรายงานเป็นค่าเฉลี่ย ค่าเบี่ยงเบนมาตรฐาน อัตราร้อยละ และการทำ multiple logistic regression*

ผลการศึกษา *: ผู้ป่วยที่ศึกษาจำนวน 146 คน มีค่าเฉลี่ยของระดับแมกนีเซียมเท่ากับ 4.9$\pm$1.9 มก./ดล. มีผู้ป่วยเพียง 67 คน (ร้อยละ 45.9) ที่ระดับแมกนีเซียมอยู่ในระดับการรักษามาตรฐาน ปัจจัยที่มีผลอย่างมีนัยสำคัญที่ทำให้ระดับแมกนีเซียมไม่อยู่ในระดับมาตรฐาน คือ การเป็นเบาหวานขณะตั้งครรภ์ หญิงตั้งครรภ์ 4 คน (ร้อยละ 2.7) ชักหลังจากรับยาแมกนีเซียม (P=0.03)*

สรุป *: แมกนีเซียมซัลเฟตเป็นยามาตรฐานหลักที่ใช้สำหรับป้องกันการชักในหญิงตั้งครรภ์ที่มีภาวะครรภ์เป็นพิษอย่างรุนแรงหรือมีภาวะชักจากภาวะครรภ์เป็นพิษที่มารับการรักษาที่ห้องคลอดโรงพยาบาลชลบุรี พบว่าในหญิงตั้งครรภ์เหล่านี้มีระดับแมกนีเซียมไม่อยู่ในระดับการรักษามาตรฐานร้อยละ 54.1 ภาวะเบาหวานระหว่างการตั้งครรภ์เป็นปัจจัยสำคัญที่ทำให้ระดับแมกนีเซียมไม่ถึงระดับมาตรฐาน*