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Clinical and laboratory markers in the recovery from severe preeclampsia

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ABSTRACT

Objective: To examine the recovery from severe Preeclampsia toxemia (PET) in women treated with magnesium sulfate ($MgSO_4$) during the first 24 h postpartum as reflected by the changes in various clinical and laboratory markers.
Study design: The study population included all women diagnosed with severe PET that gave birth at the Soroka University Medical center between 2013 and 2014, and were treated with $MgSO_4$ in the first 24 h postpartum. Data were collected from the institutional computerized records. The different parameters were examined in 6 h intervals and were compared using appropriate statistical tests.
Main outcomes measures: Change in various postpartum laboratory and clinical parameters.
Results: During the study period there were 132 singleton deliveries with severe PET treated with a 24-hours postpartum $MgSO_4$ regimen. Most of the women were primigravida and delivered vaginally. Both mean systolic and mean diastolic blood pressure values have shown recovery to normal values after the first 6 h of treatment ($P < 0.001$). Urine output and proteinuria have demonstrated later recovery (after 12 h).
Conclusions: When assessing the natural recovery of severe PET features, the earliest parameter to recover during the first 24 h postpartum is hypertension followed by urine output and the proteinuria. Further larger studies are needed in order to confirm these results. Moreover, the use of these parameters may allow using shorter $MgSO_4$ treatment regimens for appropriate women showing earlier recovery and facilitating quicker mother-baby bonding and emotional recovery.

1. Introduction

Preeclampsia toxemia (PET) is a multi-system disorder prevalent among 3–8% of pregnancies worldwide [1]. It has the potential to pose great risks for morbidity and mortality for both the mother and the fetus [2]. According to the American College of Obstetricians and Gynecologists (ACOG), PET is defined as the onset of hypertension (systolic ≥140 or diastolic ≥90) and proteinuria (≥300 mg in 24 h urinary collection, or 1+ in a urine dipstick) after 20 weeks of gestation in a previously healthy woman. PET with severe features is defined as either increased values of blood pressure (systolic ≥160 or diastolic ≥110) or hypertension as defined in PET followed by any sign/symptoms of end organ failure (thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, cerebral or visual symptoms) and that even in the absence of proteinuria [3]. The management of women diagnosed with PET depends on various factors including the presence of maternal end organ dysfunction, gestational age and signs of fetal distress [4,5]. The Guidelines of ACOG support prompt delivery after maternal stabilization for any woman with severe PET past 34 0/7 weeks of gestation, or for any woman with maternal/fetal instability regardless to gestational age [3]. In addition to delivery, $MgSO_4$ prophylaxis is given to any woman diagnosed with severe PET, in order to prevent deterioration to eclampsia (convulsive phase of the disorder) [6], and additional supportive care given to treat hypertension and any preexisting complication. To date, there is no consensus regarding the treatment regimen of $MgSO_4$ in terms of loading dose, maintenance dose and maintenance duration as well as route of administration. This is most probably due to the fact that the precise maternal initial dose and continuous blood concentrations have never been established [7]. According to the World Health Organization (WHO), treatment with $MgSO_4$ usually

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begins with the onset of labor or induction and is followed by 24 h maintenance therapy postpartum (the time frame most susceptible for seizures) [8]. In past years, it has been suggested, that some women (with reduced risk of developing eclampsia) treated with $MgSO_4$ can benefit from shorter maintenance therapy regimens, given the great risk for magnesium toxicity and the need for close monitoring [9]. Few experimental studies were carried out [10–16] using different regimens. Some were randomly assigned [11–13,16] and others used different clinical and laboratory parameters to assign women to shorter regimens, or in the case of mild PET, no treatment at all. Among the parameters used were: blood pressure [10,14,15] and urinary output [10,14]. To date, there is no one clear clinical parameter known to predict the upcoming resolution of severe PET. Many challenges rise because mothers affected by severe PET who receive magnesium sulfate treatment are separated from their infants in the immediate postpartum period, not only physiological ones but mental and emotional ones as well. Early maternal separation, reduced mother infant interaction and reduced breastfeeding rates have been reported in patients with severe PET [17].

In light of the interest and need in shortening the use of maintenance therapy for appropriate women with severe PET, we decided to describe how certain clinical and laboratory parameters change during the first 24 h postpartum. Potential findings of significant early change in any of the parameters, may allow us to use it as a predictor of resolution in future studies.

2. Materials and methods

2.1. Setting

The study was conducted in the largest regional hospital in southern Israel – Soroka University Medical Center (SUMC). SUMC hosts roughly 98% of the deliveries that take place in the southern region of Israel. The study has been approved by Institutional Review Broad (in accordance with Helsinki declaration).

2.2. $MgSO_4$ treatment regimen

According to the SUMC protocol, the loading dose of $MgSO_4$ is given when the diagnosis of severe PET is made and maintained for 24 h following delivery, while the patient is closely monitored in the delivery room. The loading dose is 4 g over 20–30 min, and maintenance is 1–2 grams per hour given over 24 h. During that period the patient is monitored in a darkened room, every hour. Vital signs including blood pressure and heart rate are taken and the urinary output as measured by foley catheter is recorded and documented. In addition, every six hours blood tests that include: complete blood count, chemistry (including liver function test, creatinine and urea and $MgSO_4$ levels) and coagulation tests are drawn. The treatment with $MgSO_4$ is stopped in case of the emergence of any of the following: 1) $MgSO_4$levels exceed 7.4 mg/dL (therapeutic range is 4.7–7.4), 2) Loss of deep tendon reflexes, 3) Respiratory depression ($\leq$10 breaths per minute) and 4) oliguria ($\leq$30 cc of urine per hour) 5) 24 h from delivery if clinical improvement is noticed.

2.3. Study population

The study population included patients with the diagnosis of severe PET who were traced by the international classifications of diseases, 9th revision (ICD-9) as documented in the computerized database of SUMC. The patients selected were given the ICD-9 642.5 (Severe PET) and 642.7 (Eclampsia with pre-existing hypertension), and had a singleton delivery in SUMC between January 1st 2013 to January 1st 2014. All patients enrolled had completed 24 h of postpartum treatment with $MgSO_4$ in the delivery room. Excluded from the study were: 1) Women who did not complete a 24 h postpartum treatment, 2) Women in which the treatment with $MgSO_4$was not directly continued after delivery (the treatment was given later, after discharge to the maternity ward), 3) Women with accompanying diseases (acute infectious disease, liver disease and gestational thrombocytopenia) and 4) women with multiple gestations.

2.4. Study design

A retrospective cohort study was conducted based on information collected from the computerized database of SUMC. The potential candidates were detected using the diagnosis given by the appropriate ICD-9 codes. The following characteristics were collected from the computerized files of each woman fulfilling inclusion criteria: A) Demographic and background characteristics: maternal age, weight and height, and ethnicity (Jewish vs. Bedouin Arabs), smoking (self - reported by the patient). B) Medical and obstetrical history: chronic illnesses (e.g. hypertension, diabetes mellitus), gravity and parity, previous cesarean section. C) Obstetrical outcomes: mode of current delivery (normal vaginal delivery vs. cesarean section), stillborn, fetal gender, birth weight, low Apgar scores ($\leq$7 at 1 and 5 min). D) Laboratory parameters collected at the time of delivery and at 6 h interval in the 24 h postpartum: blood count (hemoglobin and platelets), chemistry: renal function test (urea and creatinine), liver function test (glutamate oxaloacetate transaminase – GOT, glutamate pyruvate transaminase – GPT), lactate dhydrogenase – LDH, and prothrombin time - PT and H) Different measures taken at the time of delivery and at 6 h interval in the 24 h postpartum: systolic and diastolic blood pressures, urinary protein (every 6 h a urinary sample was taken from the catheter and checked for protein presence by a urine dipstick) and urinary output (average per hour calculated at 6 h intervals).

2.5. Statistical analysis

Statistical analysis was performed, using the SPSS software, version 18. Parameters that distributed normally were evaluated using mean and standard deviation, while parameters that did not distribute normally were evaluated using median and mode. We used the student paired *t*-test in order to determine statistical significant differences in continuous variables that were normally distributed. For paired continuous variables that were not normally distributed, we used the Wilcoxon rank test. When we encountered missing values the percentages were calculated, excluding the missing values from the 100%. The P value set for statistical significance was $\leq$0.05. Each of the measures taken at 6 h intervals was compared to the measure taken at the time of the delivery that was set to be the reference point.

3. Results

During the study period 132 deliveries met the inclusion criteria and were included in the study. The Maternal characteristics are shown in Table 1. The mean maternal age was 29.55 ± 6.97 years and the majority (68.9%) of women in our study was Bedouin Arabs. While the average weight at conception was 62.88 ± 14.36 kg, the average weight at the time of delivery was 76.71 ± 16.37 kg, the difference between the weight values was found to be statistically significant. Only 4.5% of the women smoked during the pregnancy.