Magnesium Sulphate Versus Labetalol for Cardioprotection in Severe Preeclamptic Parturients Undergoing Cesarean Section Under Epidural Anesthesia

AFAF A. ABDALLAH, M.D.*; NEVAN M. ELMEKAWY, M.D.*; WAEL M. SAMY, M.D.*; WAEL S. ELSHERBINEY, M.D.**; REHAM A. MOHSEN, M.D.** and YASMIN S. IBRAHIM, M.Sc.*

The Departments of Anesthesia, Surgical ICU & Pain Management* and Obstetrics & Gynecology**, Faculty of Medicine, Cairo University, Egypt

Abstract

Introduction: Preeclampsia is a state of generalized vasocostriction and hypoperfusion. It is also a risk factor of myocardial injury. Magnesium sulphate is the drug of choice for seizure prophylaxis and also it has cardioprotective effect. Labetalol can be used for control blood pressure as well as to seizure prophylaxis.

Objective: To Compare between the effects of magnesium sulphate and labetalol as cardioprotective agents in severe preeclamptic patients.

Patients and Methods: 60 patients with severe preeclampsia were enrolled in the study. They were randomly allocated into two groups. The first group received magnesium sulphate while the other group received Labetalol. Serial Troponin I (cTn I) measurements were obtained.

Results: Serum cTnI didn’t show any statistically significant differences between the two groups at different sampling times ($p>0.05$). Also, the results of this study showed that serial post-operative cTnI level did not show any significant rise if compared to the baseline in both groups.

Conclusion: Labetalol can be used as magnesium for cardioprotection in patients with severe preeclampsia as they have comparable troponin levels with magnesium sulphate during the first 24 hours following delivery by cesarean section.

Key Words: Preeclampsia – Cesarean section – Epidural anesthesia.

Introduction

PREECLAMPSIA is a pregnancy specific disorder characterized by hypertension and excess protein excretion in the urine. It affects 2-7% of healthy nulliparous women. It is a major cause of maternal and fetal morbidity and mortality. The disease is almost exclusive to humans and delivery is the only effective treatment. The disorder is probably multifactorial, although most cases of preeclampsia are characterized by abnormal maternal uterine vascular remodeling [1].

In preeclampsia perfusion is decreased to almost all organs. This is secondary to intense vasospasm resulting from an increased sensitivity of the vasculature to any pressor agent. Perfusion is also compromised by activation of the coagulation cascade, especially platelets, with microthrombi formation. Additionally, plasma volume is decreased by loss of fluid from the intravascular space [2].

As preeclampsia is a state of generalized vasocostriction and hypoperfusion, it is a risk factor to myocardial injury. Other added risk factors to myocardial injury during cesarean section are uterine bleeding, hypotension, severe anemia, tachycardia and administration of uterotonics [3].

Predictors of myocardial ischemia include ECG, continuous three channels Holter monitoring and serial analysis of CK-myocardial band isoenzyme and cardiac troponin I and T [4].

Cardiac troponin (cTn) is an inhibitory protein complex located on the actin filament in all striated muscles. It consists of three subunits T, I, and C. It coordinates striated muscle contraction in response to voltage changes. cTn I blocks the formation of actin myosin bridges [5]. Since it is not found in skeletal muscles, it is considered a highly specific indicator of myocardial injury in adults. It is important to note that cTn I is a marker of all heart muscle damage, not just myocardial infarction [6].
Patients and Methods

The study was done prospectively in the Obstetrics and Gynecology Department of Cairo University Hospitals on 60 parturients with severe preeclampsia undergoing cesarean section.

Sample size measurement:

Power analysis was performed using unpaired t-test for independent samples on troponin level because it was the main outcome variable in the present study. A pilot study was done before starting this study because there are no available data in literature for mean and standard deviation of troponin level after receiving labetalol in management of patients with severe preeclampsia. The results of the pilot study showed a mean troponin level of 0.09 in five patients who received magnesium with standard deviation 0.03, the mean troponin level in patients who received labetalol was 0.06 with standard deviation 0.03. Taking power 0.9 and alpha error 0.05, a minimum sample size of 23 patients was calculated for each group. A total number of 30 patients in each group were included to compensate for possible dropouts.

Inclusion criteria:

Severe preeclamptic patient submitted for cesarean section with singleton baby and gestational age >32 weeks. Severe preeclampsia is considered if systolic blood pressure on admission exceeds 160mmHg and/or diastolic blood pressure exceeds 110mmHg, obtained on at least two separate occasions and proteinuria on urine dipstick 3+ or more.

Exclusion criteria:

- Age >40 years.
- Multiple gestations.
- History of cardiac diseases including: chronic hypertension, patients receiving coronary vasodilators, β-blockers or calcium channel blockers.
- History of left ventricular impairment (EF <0.5 or acute pulmonary oedema).
- Hepatic insult (elevated liver enzymes more than two folds), pulmonary, vascular, renal or endocrical diseases.
- Coagulopathy or patients on anticoagulants or antiplatelet.
- Renal impairment (serum creatinine >1.5mg/L) or oliguria (<400mL/day).
- Imminent eclampsia (severe headache, visual disturbance, epigastric pain, hyperreflexia, dizziness and fainting, or vomiting).
- HELLP syndrome.
- Abruptio placenta, placenta previa, or fetal distress according to CTG scores.

Preoperative assessment and evaluation:

Patients were admitted for careful history taking, clinical examination and investigations that included: Complete blood count, liver and kidney functions tests, coagulation profile, 24hr. urine albumin, ECG and echocardiography.

Preoperative preparation:

A written informed consent was obtained. Patients were randomly allocated into 2 equal groups each containing 30 patients using computer generated numbers and concealed using sequentially numbered, sealed opaque envelope technique.

Group I: Magnesium sulphate group (M):

All patients in this group received 4gm of IV magnesium sulphate diluted in 100ml of 0.9% normal saline over 30 minutes followed by an infusion of 1g/hr (up to 24 hours postoperatively) till reaching target blood pressure (systolic 140-150mmHg, or diastolic 90-100mmHg). While patients in the other group received the same infusion rate of 0.9% saline.

Group II: Labetalol group (L):

Labetalol was given 20mg IV bolus, followed by 40mg IV if not effective within 10 minutes: Then 80mg IV every 10min. till reaching target blood pressure (systolic 140-150mmHg, or diastolic 90-100mmHg) to maximum total dose 220mg/24 hours.

The target systolic blood pressure was 140-150mmHg or diastolic blood pressure of 90-100mmHg. If this was not reached by any of the tested medications, hydralazine 2.5mg/20min. was given.

Anesthetic technique:

All patients received a standardized epidural anesthesia to attain a T4 sensory level block with catheter inserted at level of L3-L4 inter vertebral space.

Venous blood samples were collected on admission then every 6 hours for 24 hours for measuring of serum cardiac troponin I level (using an immunologic method of chemiluminescence detection) [13].

Post operative management:

The patients were admitted in ICU for the first 24 hours postoperative. The antihypertensive drugs
were continued. ECG, blood pressure, CVP and urine output were monitored closely. Post-operative analgesia by continuous epidural infusion of 0.125% bupivacaine with fentanyl 2ºg/ml at rate 8-10ml/hr.

Statistical analysis:
Data are presented as median and range, mean SD or percentage, as appropriate. Comparison between two groups is done using student- \( t \)-test and repeated measures with two-way ANOVA as post-hoc procedure for comparisons against baseline values to further investigate any statistically significant findings. Indices are analyzed using Chi-square test or Fisher’s exact where appropriate. Values less than 0.05 are considered significant. All statistical data analysis is performed using SPSS version 11.5 (SPSS, Chicago, IL).

Results

The demographic distribution of the patients in the two groups showed no statistically significant difference as regards age (group I 28 ±3yrs, group II 26±4yrs, weight (group I 85±5.8Kgs, group II 88±4.1Kgs) and gestational age (37 ± 1.3 weeks).

No statistically significant difference was found between the two groups as regard hemoglobin concentration, platelet count, creatinine, serum albumin, liver enzymes. The mean hemoglobin in both groups was around 11 g/dL. The mean platelet count in magnesium group was 190x10\(^3\)/mm\(^3\) while in labetalol group it was 202x10 \(^3\)/mm\(^3\).

There were no significant changes in the baseline or serial (6, 12, 18, 24 hours) post-operative ECGs of any patient in the two groups.

Dose of anti hypertensive:
In the labetalol group, the dose of labetalol needed to control blood pressure ranged from 60-220mg/24hr. None of the patients required hydralazine.

In magnesium group, The dose of hydralazine needed to control blood pressure ranged from 20mg to 100mg.

As regarding the Mean arterial blood pressure, the labetalol group showed statistically significant decrease in blood pressure throughout the operation and continued during the first postoperative hour. (Fig. 1).

![Fig. (1): Mean arterial blood pressure measurements in both groups.](image)

Serum troponin level:
In both groups, serum troponin levels at baseline, six hours, 12 hours, 18 hours, and 24 hours were recorded. On comparing serum troponin within each group, no statistically significant difference between every measure and the baseline (Tables 1,2).

Table (1): Group M, analysis of serial troponin measurements versus baseline measurement.

<table>
<thead>
<tr>
<th>Time</th>
<th>Troponin (ng/ml)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.132±0.053</td>
<td>0.44</td>
</tr>
<tr>
<td>6 hours</td>
<td>0.129±0.047</td>
<td>0.67</td>
</tr>
<tr>
<td>12 hours</td>
<td>0.115±0.049</td>
<td>0.62</td>
</tr>
<tr>
<td>18 hours</td>
<td>0.107±0.051</td>
<td>0.24</td>
</tr>
<tr>
<td>24 hours</td>
<td>0.09±0.06</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation (SD).

Table (2): Group L, analysis of serial troponin measurements versus baseline measurements.

<table>
<thead>
<tr>
<th>Time</th>
<th>Troponin (ng/ml)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.126±0.037</td>
<td>0.22</td>
</tr>
<tr>
<td>6 hours versus baseline</td>
<td>0.117±0.038</td>
<td>0.24</td>
</tr>
<tr>
<td>12 hours versus baseline</td>
<td>0.103±0.01</td>
<td>0.24</td>
</tr>
<tr>
<td>18 hours versus baseline</td>
<td>0.097±0.017</td>
<td>0.24</td>
</tr>
<tr>
<td>24 hours versus baseline</td>
<td>0.065±0.027</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation (SD).

On comparing both groups as regards troponin levels at every measurement, no statistically significant difference was found between the two groups (\( p \)-value >0.05) (Fig. 2).
Discussion

Patients with severe preeclampsia undergoing cesarean section are at increased risk for myocardial injury. Barton et al., described histological changes in the myocardium of patients with preeclampsia as well as microvascular abnormalities in samples of endomyocardium biopsy. Changes in the mitochondrial structure of the myometrial muscle cells were also seen in heart muscle cells [7].

Although there is substantial literature on cTnI levels in various patient groups, very few studies exist on the topic of cTnI levels in pregnancy [8,9].

In this study, 60 patients with severe preeclampsia were enrolled and divided into two groups. The mean serum cardiac troponin I (cTnI) of baseline readings in severe preeclamptic patients (n=60) was 0.12ng/ml. It was higher than the reference range (0-0.05ng/ml). This indicates some degree of myocardial injury in this population.

Due to the established specificity of this isoform of troponin T and I for cardiac tissue the most likely explanation for these findings is that some degree of myofibrillary damage occurs in association with hypertension in pregnancy. There are no data to suggest that placental production of cTnI occurs and its specificity for cardiac muscle, as distinct from vascular smooth muscle, would militate against this possibility.

While the elevated troponin levels reported here for hypertension in pregnancy are similar to those observed in acute congestive cardiac failure, the clinical significance of this for the pregnant woman is unknown. There are no clear answers concerning optimal short term and long term left ventricular function [8].

In the study of cTnI levels in preeclamptic and gestational hypertensive pregnant women by Fleming et al., the median serum cTnI level in the preeclamptic group was higher than that in the group with gestational hypertension [10].

Pasupathi et al., investigated lipids and oxidative stress markers among women and correlated them with cardiac troponin I (cTnI) and troponin T (cTnT). They had demonstrated that serum cTnI and cTnT levels are elevated in association with hypertension in pregnancy, and that preeclampsia is associated with the highest levels [11].

Magnesium sulphate has a role in protecting the myocardium and brain from the intense vasospasm that occurs in preeclamptic patients. It can also lead to reduction of cTnI level in preeclamptic patients [12].

Atalay et al., found that the serum cardiac troponin I level in the preeclamptic group was significantly high, and pretreatment values with magnesium sulphate were significantly higher compared with post-treatment values [13].

In this study, 60 parturient with severe preeclampsia undergoing cesarean section were divided into two groups. Serum cTnI at different sampling times were obtained (baseline, 6hrs, 18hrs and 24hrs postoperative). The two groups were compared as regarding the pre-treatment with MgSO4 versus labetalol.

Serum cTnI didn’t show any statistically significant differences between the two groups at different sampling times (\(p>0.05\)). Also, the results of this study showed that serial post-operative cTnI level did not show any significant rise if compared to the baseline in both groups.

Conclusion and Recommendations:

We found that Labetalol can be used as magnesium for cardioprotection in patients with severe preeclampsia as they have comparable troponin levels with magnesium sulphate during the first 24 hours following delivery by cesarean section.

The time course of cardiac troponins elevation in association with hypertension in pregnancy needs further investigations.

References


الملخص العربي

يلصاحب مرض تسمم الدم قصور يتفاقم لسنة الجسم ويستخدم عقار سلفاميساميد لدوره في حماية عضلة القلب وكذلك الوقاية من التشنجات.

الهدف من البحث هو المقارنة بين استخدام الماغنسيوم والليبتالول لوقاية عضلة القلب للمرضى تسمم الحمل الشديد.

تتم البحث ستين سيدة مصابة بتسمم الحمل الشديد، وتعتبر نسبتهم عشوائيا إلى المجموعتين. تم إعطاء المجموعة الأولى الماغنسيوم بينما تم إعطاء الآخر الليبتالول. أجريت العملية القصصية تحت تأثير المخدر الأساسي ثم قياس التروبيتين عند دخول الريفة ثم كل ست ساعات بعد اجراء العملية الجراحية.

ظهر البحث عدم وجود فروق إحصائية جوهريا في نسبة التروبيتين بين المجموعتين. كذلك لم يوجد فروق بين نسبة التروبيتين الأساسية ونسبة التروبيتين المتائلة في المجموعتين.

وحيده أنه لم بيث وجود فروق بين المجموعتين في نسبة التروبيتين إذا لم يتم استخدام عقار الليبتالول لوقاية عضلة القلب للسيدات الحوامل المصابات بتسمم الحمل الشديد.