Egyptian Journal of Anaesthesia (2014) **30**, 299–303

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Effect of preoperative Mg sulfate infusion on serum cardiac troponin (cTn) in moderate preeclamptic undergoing elective cesarean section under spinal anesthesia

Nashwa S. Elzayyat [a,*], **Marium H. Yacoub** [b]

[a] *Department of Anesthesia, Cairo University, Egypt*
[b] *Department of Clinical Pathology, Cairo University, Egypt*

Received 13 December 2013; revised 13 January 2014; accepted 17 January 2014
Available online 7 February 2014

KEYWORDS

Magnesium sulfate;
Preeclampsia;
Troponin

Abstract This study was designed to investigate and compare the effect of preoperative Mg sulfate infusion on serum cardiac troponin (cTn) in moderate preeclampsia undergoing elective cesarean section. A total of fifty parturients having moderate preeclampsia scheduled for elective cesarean section were included. They were randomly allocated into two equal groups 25 each, magnesium group (GMg) received preoperative magnesium sulfate infusion and control group (GC) then both received spinal anesthesia, serum troponin measured preoperative then at 6, 12 and 24 h postoperative. Mean arterial pressure and heart rate were also recorded. Baseline serum cardiac troponin was higher above normal and was comparable at the rest of times in both groups. Mean arterial pressure readings were significantly lower in GMg compared to GC at induction of spinal, skin incision and skin closure ($P < 0.05$) and were comparable at the rest of times. Serum cardiac troponin (cTn) levels were comparable in parturients received magnesium sulfate infusion preoperatively with those did not receive magnesium sulfate.

1. Introduction

Hypertensive disorders occur as a complication of approximately 5–8% of all pregnancies, and preeclampsia represents 50–60% of these disorders. All have serious effects on both maternal and fetal mortality and morbidity [1].

Pre-eclampsia is a multi-system disease and the main pathology is capillary damage and vasospasm. Moderate preeclampsia is diagnosed according to the criteria recommended by American college of Obstetrics and Gynecology (ACOG):

* Corresponding author. Address: Cairo University, Anesthesia, 12 ahmed mokhtar hegazy manial elroda, Cairo, Egypt. Tel.: +20 1222394934.
E-mail address: nanosami@yahoo.com (N.S. Elzayyat).

Peer review under responsibility of Egyptian Society of Anesthesiologists.

ELSEVIER Production and hosting by Elsevier

1110-1849 © 2014 Production and hosting by Elsevier B.V. on behalf of Egyptian Society of Anesthesiologists.
Open access under CC BY-NC-ND license. http://dx.doi.org/10.1016/j.egja.2014.01.006

Blood pressure $\geqslant$140/90 mmHg and under 160/110 mmHg measured in two opportunities 6 h apart plus proteinuria (+1 or +2 on dipstick). Proteinuria is defined as a concentration of at least 30 mg/dl (at least 1+ on dipstick) in at least two random urine samples collected at least 6 h apart. In severe preeclampsia pulmonary edema can develop due to high left ventricular filling pressure, also can progress with seizures [2].

Cardiac troponin (cTn) is an inhibitory protein complex located on the actin filament in all striated muscles and consists of three submits T, I, and C and it coordinates striated muscle contraction in response to voltage charges. Cardiac troponin I is encoded by specific genes, and blocks the formation of actin-myosin bridges and since it is not found in skeletal muscles, it is considered a highly specific indicator of myocardial injury in adults [3].

It is reported that troponin measurement has a great value in the diagnosis of diseases with myocardial damage as ischemic heart disease, hypertension, preeclampsia, cardiac trauma; congestive heart failure, hypotension, chronic renal failure, myocarditis, sepsis, amyloidosis, and pulmonary embolism. It has also been suggested that as this damage is frequently seen in practice and there is a significant relationship between cardiac troponin levels and the severity of disease, the importance of troponin tests is increased [4].

The vasodilator effect of $MgSO_4$ has been investigated both in vivo and in vitro animal studies which have shown that it is a vasodilator of large arteries as the aorta [5], as well as smaller vessels including mesenteric [6], skeletal muscle [7] uterine [8], and cerebral arteries [6].

Magnesium may act by stimulating production of prostacyclin by endothelial cells causing vasodilatation, or by inhibiting platelet aggregation [9]. In patients with pregnancy-induced hypertension, $MgSO_4$ treatment significantly decreases circulating levels of angiotensin-converting enzyme [10]. These actions may inhibit the endothelial dysfunction associated with preeclampsia [11].

Magnesium ions also suppress calcium influx so modulating cardiovascular cell function. Mg^{2+} inhibits ion channels, including voltage-dependent Ca^{2+} channels in cardiac myocytes, which leads to cardio-protection via antiarrythmic action. This action also decreases cell injury and cell death due to ischemia [12].

Aim of the study: was to compare the effect of Mg sulfate given preoperative on cardiac troponin I to parturients with moderate preeclampsia undergoing elective cesarean section.

2. Patients and methods

After the approval of institutional ethical committee and obtaining informed written consent, 50 full-term pregnant females (age group 25–40 years and gestational age 36–40 weeks) having moderate pre-eclampsia scheduled for elective cesarean section. Exclusion criteria included the following: severe preeclampsia, HELLP syndrome, chronic hypertension not pregnancy induced, diabetes mellitus, ischemic and valvular heart disease, infections at puncture site contraindicating spinal anesthesia, renal or hepatic diseases affection with preeclampsia, coagulopathies, and known allergy to any of the studied drugs. The study performed from January 2013 to July 2013 in the new obstetric and gynecology hospital-Kasr ELAini.

Parturients were randomly allocated by closed envelops to two groups.

Control group (G C) (n = 25): parturients with moderate preeclampsia did not receive Mg sulfate.

Study group (G Mg) (n = 25): parturients with moderate preeclampsia received Mg sulfate.

3. Protocol for magnesium sulfate administration in the study

Half an hour preoperatively, a loading dose of 4 g $MgSO_4$ was infused over 15–20 min. This is then followed by a continuous infusion of 1 g/h for 24 h post-operative. The target plasma concentration should be between 2 and 3.5 mol/l and magnesium sulfate toxicity was monitored by urine output, deep tendon reflexes, respiratory rate and serum magnesium levels and managed with an infusion of 10 ml of 10% calcium gluconate and cessation of magnesium infusion.

4. Preoperative preparation

Systolic and diastolic blood pressure, ECG and echocardiogram were assessed, coagulation profile including prothrombin time, activated partial thromboplastin time, platelet, serum glucose, creatinine, Na, K, Ca, ALT, AST, and total bilirubin were all reviewed. All medications were given at the time. Half an hour before entering the operating room two intravenous lines were inserted one for Mg sulfate infusion was started, and 8 ml/kg ringer acetate was given as a preload in the other iv line. On entering the operating room all parturients received the routine monitors; five leads ECG, non-invasive blood pressure monitoring and pulse oximetry.

Spinal anesthesia was performed with the parturient sitting and after complete sterilization, infiltration of the skin with 2 ml of 2% lidocaine, atraumatic spinal needle (G25) is advanced into the subarachnoid space and 0.5% heavy bupivacaine and 25 μg fentanyl (a total volume of 2.8 ml) was administered. Sensory block was assessed using cold and pinprick perception till reach T4 sensory level. Motor blockade assessed using modified Bromage scale.

After delivery of the fetus, Oxytocin 10 IU/L ringer acetate given by intravenous drip. Neonatal viability is assessed by using APGAR scoring system at 1 and 5 min post-delivery.

Hypotension is defined as a decrease in systolic blood pressure by 20% from baseline. It was treated by the administration of intravenous ephedrine in incremental doses of (5 mg). Bradycardia (Heart rate $<$60/min) was treated by 0.02 mg/kg atropine.

IM pethidine 50 mg was given for postoperative pain when needed.

5. Samples collection

Venous Blood samples were collected in EDTA tubes from all parturient before caesarian sections and magnesium sulfate infusion, then 6, 12 and 24 h postoperative. The samples were transported immediately to the clinical pathology laboratory of Kasr ELAini hospital, Cairo University, where plasma was separated by centrifugation at 2000 $\times$ g for 15 min and

the assay was performed immediately after sample collection using SIEMENS Dimension® clinical chemistry system Heterogenous Immunoassay Module, Flex® reagent cartilage, Cat. No. RF421C. Assays for cardiac troponin-I (CTNI) is a one step enzyme immunoassay based on the "sandwich" principle. Sample is incubated with chromium dioxide particles coated with a monoclonal antibody specific for the cardiac troponin-I molecules, and a conjugate reagent [alkaline phosphatase (ALP)] labeled monoclonal antibody specific for cardiac troponin-I, to form a particle/cardiac troponin-I/conjugate sandwich. Unbound conjugate is removed by magnetic separation and washing. After separation and washing, the particle/cardiac troponin I/conjugate sandwich is transferred to the cuvette where the sandwich bound ALP triggers an amplification cascade. ALP dephosphorylates synthetic flavin adenine dinucleotide phosphate (FADP) to produce FAD. FAD binds to apo D-amino acid oxidase and converts it to active holo D-amino acid oxidase. Each molecule of holo D-amino acid oxidase then produces multiple molecules of hydrogen peroxide (H_2O_2) which, in the presence of horseradish peroxidase (HRP), convert 3,5-dichloro-2-hydroxybenzenesulfonic acid (DCHBS) and 4-aminoantipyrine (4-AAP) to a colored product that absorbs at 510 nm. The color change measured is directly proportional to the concentration of cardiac troponin-I present in the patient sample.

6. Statistical analysis

Data were analyzed using SPSS (SPSS 15.0, SPSS Inc, Chicago, II, USA). Parametric data were expressed as mean and standard deviation (SD) and analyzed using the independent *t* test. Continuous data are compared by one-way ANOVA or repeated measures with two-way ANOVA as a post hoc procedure for comparisons against baseline values to further investigate any statistically significant findings. *P* values <0.05 will be considered significant.

7. Results

Parturients demographic and obstetric data were comparable (Table 1)

Preoperative mean serum troponin levels were higher than normal in both groups (0.12–0.13) ng/ml.

The mean serum cardiac troponin I (cTnI) preoperative readings were (0.12 ± 0.07 and 0.13 ± 0.08) ng/ml, slightly elevated above normal levels (0–0.05 ng/ml).

Serum levels of cardiac troponin I (cTnI) are summarized in Table 2. Serum cTnI at different sampling times were compared as regards the pre-treatment with $MgSO_4$ serum cTnI did not showed any statistically significant between-groups differences at 6, 12 and 24 h postoperative ($P > 0.05$).

As regards pre-treatment with $MgSO_4$; MAP values showed significant differences in GMg compared to GC at the time of induction, skin incision and at skin closure ($P < 0.05$) (Table 3). As regards intergroup differences between baseline and postoperative MAP readings, no statistically significant data observed in both groups.

Heart rate (HR) recordings throughout the study period are summarized in Table 4. HR recordings were comparable with no statistically significant differences between-group or intragroup variability ($P > 0.05$).

Table 1 Demographic and obstetric.

Variable	G C ($n = 25$)	G Mg ($n = 25$)	*P* value
Age (years)	30 ± 4.4	31 ± 4.8	NS
Weight (kg)	76 ± 3	75 ± 2.8	NS
Hight (cm)	158 ± 2	157 ± 4	NS
Gestation (weeks)	38 ± 1.3	37 ± 2.7	NS
Platelets	172 ± 17	177 ± 15	NS

Data expressed as mean ± SD, $P < 0.05$ considered significant.

Table 2 Serum cardiac troponin I (cTnI).

Time	G C ($n = 25$)	G Mg ($n = 25$)	*P* value
Preoperative	0.12 ± 0.07	0.13 ± 0.08	0.975
6 h postoperative	0.11 ± 0.05	0.12 ± 0.06	0.700
12 h postoperative	0.11 ± 0.03	0.11 ± 0.05	0.206
24 h postoperative	0.10 ± 0.03	0.09 ± 0.01	0.830

Data expressed as mean ± SD, $P < 0.05$ considered significant.

Table 3 Mean arterial blood pressure.

Time	G C ($n = 25$)	G Mg ($n = 25$)	*P* value
Preoperative	120.7 ± 2.9	109.2 ± 1.8	<0.001
Induction of anesthesia	112.4 ± 1.6	107.4 ± 1.7	<0.001
Skin incision	117.5 ± 1.8	111.3 ± 2.4	<0.001
Skin closure	112.2 ± 1.7	107.4 ± 1.8	<0.001
1 h Postoperative	110.4 ± 1.7	108 ± 1.6	0.027
2 h Postoperative	112.4 ± 1.7	110 ± 2.9	0.07
3 h Postoperative	113.2 ± 1.5	109.8 ± 29	0.03

Data expressed as mean ± SD, $P < 0.05$ considered significant.

Table 4 Heart rate (HR).

Time	G C ($n = 25$)	G Mg ($n = 25$)
Preoperative	95.2 ± 3.7	93.6 ± 2.6
Induction of anesthesia	97.6 ± 5.1	98.2 ± 4.2
Skin incision	104.1 ± 2.7	103.1 ± 2.1
Skin closure	103.4 ± 2.7	103.4 ± 3
1 h Postoperative	92 ± 1.7	92.2 ± 1.8
2 h Postoperative	96.8 ± 3.1	96.2 ± 3.1
3 h Postoperative	100.4 ± 4.5	101 ± 4.8

Data expressed as mean ± SD, $P < 0.05$ considered significant.

8. Discussion

The results of the current study showed mean serum troponin cardiac troponin I (cTnI) mildly elevated above normal levels in all preeclamptic parturients.

This finding was consistent with the results of the study done by Fleming and colleagues [13] who investigated serum cardiac troponin I, a sensitive marker of cardiac myocyte damage, in normal pregnancy and pregnancies complicated by

hypertension with and without significant proteinuria and was elevated in women with hypertensive disorders of pregnancy indicating some degree of cardiac myofibrillary damage in these disorders.

Patients with arterial hypertension have shown increased cardiac troponin I (cTnI) level above normal limits due to subclinical myocardial necrosis [14].

Contrary to these results another study by Atis et al. [15] investigated troponin I and homocysteine in pregnant women with severe and mild preeclampsia and concluded that Troponin I levels are not significantly increased in either mild or severe preeclampsia.

The results of the current study showed comparable levels of serum cardiac troponin at 6, 12 and 24 h postoperative in GMg (study) compared to GC (control) and although the serum troponin was lower in (GMg) compared to GC, yet did not reach significant levels.

These results were contrary to Atalay and colleagues [16] found that the serum cTnI level in the pre-eclamptic was significantly high ($P < 0.01$), and $MgSO_4$ pretreatment values of cTnI were significantly higher compared with post-treatment values ($P < 0.01$).

Also Chakraborti et al. [17] reported that hypomagnesemia leads to progressive coronary vasoconstriction and suggested that magnesium can be protective in many cardiovascular diseases, including ischemic heart disease.

Other studies by Katus et al., showed that cTnI has a consistent release pattern following myocardial injury compared to cTnT which has a biphasic pattern after cardiac surgery which prohibit its use in such population.

This can be explained pathophysiologically as the major percentage of cTnT (94%) is structurally bound to the contractile apparatus of the cardiomyocyte, and a smaller amount found as a precursor in the cytoplasm. When minor ischemic or reperfusion occurred there is disruption and leakage of cytosolic cTnT into the circulation [18].

In the current study, MAP values showed significant lower values ($P < 0.05$) in G Mg (study) compared to gG C (control). And in spite of these lower levels it was accepted and rapidly corrected with ephedrine if lowered less than 20% of baseline values.

These findings may be explained by the vasodilator effects $MgSO_4$ together with the sympatholytic effect of spinal anesthesia.

Magnesium is a unique calcium antagonist as it can act on most types of calcium channels in vascular smooth muscle and as such would be expected to decrease intracellular calcium. The decreased intracellular calcium inactivates the calmodulin-dependent myosin light chain kinase activity which decreased contractility leading to arterial relaxation and this lower peripheral and cerebral vascular resistance, relieve vasospasm, and decrease arterial blood pressure [7].

In this study spinal anesthesia was used safely in preeclamptic parturients.

These results went in agreement with Wallace and colleagues who performed a randomized trial investigating the effects of general anesthesia compared to combined epidural and spinal anesthesia in severe pre-eclampsia and found that regional anesthesia is as safe as general anesthesia on patient's hemodynamic status [19]. Also the study by Hood and Curry, who retrospectively recorded the effect of epidural and spinal anesthesia in parturients with severe pre-eclampsia who were scheduled for elective cesarean section [20].

Several meta-analyses studies investigated the effect of general anesthesia and neuroaxial (epidural, spinal) anesthesia on cardiac complications and they found that overall mortality was approximately one third less in patients in the neuroaxial anesthesia group compared to those received general anesthesia, similar benefits were seen for noncardiac complications, including thromboembolism and pneumonia [21].

9. Recommendations

It is recommended that further studies should include pregnant females with severe pre-eclampsia and the use of more indicators of myocardial injury other than serum cardiac troponin I as S–T segment analysis of ECG can be employed.

10. Conclusion

Pretreatment with $MgSO_4$ did not lower serum cardiac troponin I values in moderate pre-eclampsia undergoing elective cesarean section using spinal anesthesia. It has vaso-dilatory effect on blood vessel smooth muscles and control hypertension in pre-eclamptic parturients. Spinal anesthesia was not associated with major myocardial adverse events and was as acceptable and comparable as general anesthesia for cesarean delivery.

Conflict of interest

No conflict of interest.

References

[1] Resnick L, Barbagallo M, Bardicef M, Bardicef O, Sorokin Y, Evelhoch J, et al. Cellular-free magnesium depletion in brain and muscle of normal and preeclamptic pregnancy. Hypertension 2004;44:322–6.
[2] Davison J. Pre-eclampsia as a multi-system disease. Adv Exp Med Biol 1989;252:119–31.
[3] Sharma S, Jackson P, Makan J. Cardiac troponins. J Clin Pathol 2004;57(10):1025–6.
[4] Panteghini M. The measurement of cardiac markers: where should we focus? Am J Clin Pathol 2002;118:354–6.
[5] Longo M, Jain V, Vedernikov YP, Facchinetti F, Saade GR, Garfield RE. Endothelium dependence and gestational regulation of inhibition of vascular tone by magnesium sulfate in rat aorta. Am J Obstet Gynecol 2001;184:971–8.
[6] Euser AG, Cipolla MJ. Resistance artery vasodilation to magnesium sulfate during pregnancy and the postpartum state. Am J Physiol Heart Circ Physiol 2005;288:H1521–5.
[7] Altura BM, Altura BT, Carella A, Gebrewold A, Murakawa T, Nishio A. Mg2_–Ca2_ interaction in contractility of vascular smooth muscle: Mg2_versus organic calcium channel blockers on myogenic tone and agonist-induced responsiveness of blood vessels. Can J Physiol Pharmacol 1987;65:729–45.
[8] Nelson SH, Suresh MS. Magnesium sulfate-induced relaxation of uterine arteries from pregnant and non-pregnant patients. Am J Obstet Gynecol 1991;164:1344–50.
[9] Ravn HB, Vissinger H, Kristensen SD, Wennmalm A, Thygesen K, Husted SE. Magnesium inhibits platelet activity – an infusion study in healthy volunteers. Thromb Haemostas 1996;75:939–44.
[10] Goldkrand JW, Fuentes AM. The relation of angiotensin-converting enzyme to the pregnancy-induced hypertension–preeclampsia syndrome. Am J Obstet Gynecol 1986;154:792–800.

[11] Khan F, Belch JJF, MacLeod M, Mires G. Changes in endothelial function precedes the clinical disease in women in whom preeclampsia develops. Hypertension 2005; 46:1123–8.
[12] Scardo JA, Hogg BB, Newman RB. Favorable hemodynamic effects of magnesium sulfate in preeclampsia. Am J Obstet Gynecol 1995;173(4):1249–53.
[13] Fleming SM, O'Gorman T, Finn J, Grimes H, Daly K, Morrison JJ. Cardiac troponin I in preeclampsia and gestational hypertension. BJOG 2000;107:1417–20.
[14] Nunes J. Cardiac troponin I in systemic diseases. Rev Port Cardiol 2001;20:785–8.
[15] Atis A, Aydin Y, Başol E, Göker N. Troponin I and homocysteine levels in mild and severe preeclampsia. Clin Experiment Obstet Gynecol 2010;37(1):21–3.
[16] Atalay C, Erden G, Turhan T. The effect of magnesium sulfate treatment on serum cardiac troponin I levels in pre-eclamptic women. Acta Obstet Gynaecol Scand 2005;84:617–21.
[17] Chakraborti T, Mandal M, Mandal A, Das S, Ghosh S. Protective role of magnesium in cardiovascular disease: a review. Mol Cell Biochem 2002;238:163–79.
[18] Katus H, Schoeppenthau M, Tanzeem A, Bauer H, Saggau W, Diederich K, et al. Non-invasive assessment of perioperative myocardial cell damage by circulating cardiac troponin T. Brit Heart J 1991;65:259–64.
[19] Wallace D, Leveno K, Cunningham F. Randomized comparison of general and regional anaesthesia for caesarean delivery in pregnancies complicated by severe pre-eclampsia. Obsetet Gynecol 1995;86:193–9.
[20] Hood D, Curry R. Spinal versus epidural anaesthesia for caesarean section in severely pre-eclampsia eclamptic patients: a retrospective survey. Anaesthesiology 1999;90:1276–83.
[21] Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomized trials. BMJ 2000;321:1493.