

## ORIGINAL ARTICLE

# Comparison of low dose spinal anesthesia with general anesthesia in pre-eclamptic parturients undergoing emergency cesarean section

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## ABSTRACT

**Objectives:** Both spinal (SA) and general anesthesia (GA) are commonly used for operative management of pre-eclampsia parturients. Low dose SA is practical with faster onset and with fewer complications. This study aims to compare the effect of low dose SA or GA on neonatal wellbeing for preeclamptic parturients undergoing emergency cesarean section

**Methodology:** This prospective randomized study was carried out at University Clinic of Anesthesiology and University Clinic of Gynecology and Obstetrics at UCIM, Skopje, Republic of Macedonia. Sixty (n=60) pre-eclamptic parturients undergoing emergency cesarean section were divided in two groups receiving low dose spinal (SA) or general anesthesia (GA). Intra operatively we monitored and evaluated parturients' ECG, heart rate, noninvasive blood pressure, ephedrine requirement's, as well as neonatal umbilical artery (UA) blood gas samples and Apgar scores.

Main outcome measure was a comparison of the influence of two different anesthesia methods (low dose SA vs. GA) on neonatal wellbeing, measured by umbilical artery (UA) blood gases, Apgar score and markers of fetal hypoxemia with non-invasive hemodynamic status in 60 pre-eclampsia parturients undergoing non-elective (emergency) cesarean section (CS).

**Results:** There was no statistical difference in the mean arterial blood pressure between the groups ( $90.6 \pm 12.9$  vs.  $96 \pm 8.9$  mm Hg), as well as in the neonatal acid-base status and BE ( $p > 0.05$ ). Spinal anesthesia patients required more ephedrine (8,5 vs. 1.7 mg,  $p < 0.05$ ). The Apgar score was  $\geq 7$  in 96% of newborns delivered after spinal anesthesia, while 75% after general anesthesia ( $p < 0.05$ ).

**Conclusion** We conclude that low dose spinal anesthesia can be safely used in pre-eclamptic parturients for emergency cesarean section.

**Key words:** Cesarean section; Spinal anesthesia; Apgar score; General anesthesia

**Citation:** Sivevski AG, Sholjakova MV, Kartalov AB, Biljana KK, Durnev VM. Low dose spinal anesthesia results in better neonatal outcome in non-elective preeclamptic parturients as compared to general anesthesia. *Anaesth Pain & Intensive Care* 2015;19(1)37-43

## INTRODUCTION

General (GA) and epidural anesthesia (EA) are both recommended as anesthetic technique's for

cesarean delivery in the pre-eclamptic parturients. In pre-eclamptic pregnant patients GA is risky due to difficult airway and hemodynamic consequences of laryngoscopy and tracheal intubation.<sup>1</sup>

Recently, spinal anesthesia (SA) has been recognized to have a place in operative management in pre-eclampsia parturients because it is more practical, has faster onset and with fewer complications.<sup>2</sup> There is also evidence that its use in pre-eclampsia is increasing.<sup>3</sup> A concern has been raised that SA might be unsuitable for pre-eclamptic patients as there is a potential for profound hypotension that could further compromise an already potentially compromised newborn and worsen neonatal outcome. On the other hand, there are reports stating that patients with severe pre-eclampsia experience less hypotension during SA than healthy parturients.<sup>4</sup> Minimal hemodynamic effects from spinal anesthesia in healthy pregnancy have been demonstrated when using a low dose of bupivacaine (under 10 mg bupivacaine) but this has not been sufficiently investigated in pre-eclamptic toxemia. Pre-eclampsia has an incidence of around 8% of pregnancies and is a major cause of maternal morbidity and mortality (National statistics). Over the last few years we have established a protocol for use of low dose bupivacaine spinal anesthesia for our pre-eclampsia parturients.<sup>5</sup> There are only few studies that have addressed this problem in terms of different anesthetic methods influencing fetal outcome.<sup>5-8</sup>

The aim of this study was to compare the end-point outcome of the two anesthesia modes (GA vs. SA) over the neonate outcome. We also tested the hypothesis whether the mode of anesthesia influenced the newborn short-term markers of hypoxia.

## METHODOLOGY

This prospective randomized study was conducted at in the University Clinic of Gynecology and Obstetrics at UCIM, Skopje, Republic of Macedonia, after receiving our institutional ethics committee's approval.

We enrolled 60 preeclamptic patients who were randomly allocated to receive GA or low dose SA and were undergoing emergency Cesarean delivery. Inclusion criteria in the study were: clinical signs for preeclampsia (blood pressure more than 140/90 and proteinuria >0.3 gr over 24 h, more than 1+), and one of the following indications for Cesarean Section (CS): the presence of pathological CTG trace, severe pregnancy induced hypertension (PIH) with headache, danger of HELLP syndrome, oligohydramnion with AFI < 5. Severe preeclampsia

was defined as systolic blood pressure (SBP) exceeding 160 mm Hg or diastolic blood pressure (DBP) exceeding 110 mmHg, or both<sup>9</sup> with proteinuria  $\geq$  5 gm in 24 h, with or without evidence of clinical or laboratory end organ damage.

The following type of patients were excluded from the study: patients who refused regional anesthesia, morbidly obese parturients (BMI >35 kg/m<sup>2</sup>), patients with abruptio placenta or placenta previa, as well as those with chronic hypertension, multiple gestation, diabetes and coagulopathy. Parturients with severe headache, elevated liver enzymes, low urine output (<400 ml /24h), pulmonary edema, cyanosis and those given tocolytic drugs were also not included in the study. A signed informed consent was obtained from all patients.

If the mean blood pressure (BP) of the patient exceeded 140/90 mm Hg (two occasions 6 hours apart), with or without symptoms of end-organ involvement pharmacological treatment of hypertension was initiated. Regardless of the drug used (methyldopa and/or nifedipine), the goal of acute treatment was to reduce the mean BP by at least 20%.<sup>10</sup> Seizure prophylaxis in patients with neuromuscular hyper excitability, intravenous MgSO<sub>4</sub> (4.0 g initial loading dose over 20–30 min followed by a 1 g/hr continuous maintenance infusion) was given.<sup>11,12</sup>

A protocol list for all enrolled patients (total n=60) was maintained. Demographic data of age, weight, height, parity and gestational age was noted. Data on preoperative therapy, preinduction mean BP, active/ induced labor, proteinuria was documented as well. Baseline BP and HR were obtained as the mean of three consecutive measurements taken two minutes apart. During the procedure arterial blood pressure (BP) and heart rate (HR) and O<sub>2</sub> Saturation (SpO<sub>2</sub>) were monitored continuously. The weight of the newborn was estimated as well.

All enrolled patients (n=60) received IV infusion of 500 ml of lactated Ringer's solution prior to procedure. The volume of fluids administered to severe patients with preeclampsia was not decreased because of expected intra vascular volume contraction.<sup>13</sup> During CS, all patients were in the supine and 15°–20° left uterine displacement position.

Spinal anesthesia was administered in sitting position using 26-27G Braun™ Pencan<sup>®</sup> needle. An isobaric solution of 0.5% bupivacaine (6–8 mg) and

fentanyl 20 microgram was injected intrathecally (L2-3 or L3-4). The upper sensory level was checked at 5 min, using loss of cold sensation to ice.

In the group for GA (n=30), a standardized induction of general anesthesia was performed (2 mg/kg propofol and 1.5 mg/kg succinylcholine for rapid-sequence intubation). Maintenance of anesthesia was with 50% nitrous oxide in oxygen and 0.75–1.5% end-tidal isoflurane. Patients were ventilated to a target end-tidal carbon dioxide concentration of 30–34 mmHg, using a circle system with fresh gas flows of 4 L/min until delivery. Neuromuscular blockade was maintained with rocuronium 0.6 mg/kg. Oxytocin 5 IU intravenously as well as 25 mcg/kg of fentanyl intravenously, were administered at delivery. Thereafter, a continuous infusion of oxytocin was administered (20 IU/l, at 60– 100 ml /h).

Blood pressure for all enrolled patients was recorded 15 times, starting from the time zero [3 min before induction (GA) or before puncture (SA)], until 60 minutes after induction/puncture. During the procedure (cesarean section), maternal BP and HR were recorded after the induction/puncture as follow: at 2.5 min intervals from the spinal injection for the first 10 min and then at 5 min intervals until the end of the surgery.

Hypotension was treated with IV ephedrine (5 mg every 2 min if needed). Hypotension was defined as 20-30 % decrease in SBP from the baseline value or absolute value lower than 95 mm Hg.

After delivery, all newborns were weighted, and UA acid–base status and Apgar scores was measured at 1<sup>st</sup> and 5<sup>th</sup> min.

The following variables were noted: demographic data; gestational age; upper sensory level at 5 min after spinal injection; neonatal weight; UA acid–base status and 1and 5 min Apgar scores, these are presented as number, median and range, mean  $\pm$  SD, or percentage, as appropriate. Fisher's exact test was used for intergroup comparison of upper sensory level, and incidence of hypotension. Mean values of quantitative variables were compared by using unpaired Student's *t*-test. In addition, the largest and smallest values of BP and HR were compared with corresponding baseline values in each study group by using the paired Student's *t*-test. Mann Whitney U test was used as additional statistics. A *p* value of < 0.05 was considered as statistically significant.

## RESULTS

Demographic characteristics of the patients are presented in Table 1 No statistical difference was observed between groups. Twenty three of the females were in active labour whereas 15 had their labor induced. There was no difference between groups (Table 1).

**Table 1: Demographic and preoperative data of the preeclampsia parturients and the newborn**

Parameters	GA (n=30)	SA low dose (n=30)
Age (years)	26 $\pm$ 6	25 $\pm$ 7
Weight (kg)	76 $\pm$ 12	77 $\pm$ 14
Height (cm)	154 $\pm$ 10	155 $\pm$ 9
Preinduction mean BP mmHg (mean $\pm$ SD)	117.4 $\pm$ 24	120.4 $\pm$ 22
Parity, median (range)	0.5 (0 - 3)	1 (0 - 5)
Active labor	11	12
Induced labor	7	8
Antihypertensives /P.O.	28	29
MgSO <sub>4</sub> therapy	24	22
Proteinuria 1–2	12	18
Proteinuria 3–4	10	6
Gestational age (weeks)	34.9	34.8
Neonatal weight (kg)	1.5	1.4

The mean arterial blood pressure (MAP) in both groups is shown in Table 2. MAP between GA and SA, showed a statistically significance difference in the 5<sup>th</sup> minute after induction / puncture and at 40 minutes (*p*<0.05) with pressures being lower in the SA group. In general, the results indicated perioperative hemodynamic stability, without significant hypotension in both groups.

The effects of the anesthetic techniques on the value of blood gases are shown in Table 3. This did not show any statistical significance (*p*>0.05).

The Apgar scores were estimated at one and five minutes. The results are presented in Table 4. It shows significantly higher values of Apgar scores (7.6) at one minute in SA group (*p*<0.005).

comparison of low dose spinal anesthesia with general anesthesia

**Table 2: Variations in mean arterial blood pressure (mmHg) in the groups (mean±SD)**

Time Min	GA	SA	t-value	p-value
0	117,4	120,4	-0,6	0.54
2.5	114,4	109,1	1,76	0.08
5	120,0	107,3	3,26	* 0.01
7.5	116,2	108,4	2,64	0.08
10	114,6	111,3		0.24
15	115,5	112,3	0,99	0.32
20	116,2	109,8	1,66	0.09
25	119,2	108,7	3,56	0.05
30	120,3	110,9	2,96	0.05
35	119,8	112,2	2,27	0.02
40	118,7	110,2	2,69	*0.01
45	118,0	109,5	2,60	0.09
50	118,9	110,4	2,72	*0.03
55	120,3	111,8	2,59	*0.03
60	118,9	112,7		0.07

\*significant difference (p<0,05)

**Table 3: Mean values of blood gas analysis in neonates delivered with general and spinal anesthesia**

	GA	SA low dose	t-value	p-value
pH	7.24 ± 0,03	7.22 ± 0.08	1.717	0.08
pO2 (mm Hg)	23.69 ± 3,57	21.42 ± 4.4	1.927	0.04
pCO2(mm Hg)	50.80 ± 5,31	53.06 ± 8.14	-1.499	0.13
BE (mEq/ml )	- 4.35 ± 1,91	- 5.492 ± 2.4	-2.652	0.04
HCO3 (mmol/l)	20.94 ± 2,43	21.21 ± 1.6	0.297	0.76

**Table 4: Comparison of mean Apgar scores**

Parameter	GA	SA low dose	Mann-Whitney U Test	p-value
Apgar 1 min	6.8	7.6	- 3.165	0.001
Apgar 5 min	8.9	8.9	0.00	1.00

The dosage of ephedrine (in milligram) used during the cesarean section was  $1.7 \pm 2,58$  vs.  $8.5 \pm 8.55$  (p 0.03) in GA and SA low dose groups respectively. The spinal anesthesia group needed a significantly higher dose of ephedrine than GA (p<0.05).

Table 5 presents the markers for fetal hypoxia (Apgar scores < 7, pH of neonates < 7.1, UA Base deficit < -8, resuscitative measures), expressed as number of neonates developing hypoxia. A significant difference was not observed between groups. In SA group, the number of neonates born with pH between 7.1 – 7.2 was slightly higher than in GA group, but this was not statistically significant. Apgar score was statistically higher in SA group.

## DISCUSSION

It is postulated that the main cause of development of preeclampsia is a functional imbalance between the endogenous vasodilators (prostacyclins PG I<sub>2</sub>) and vasoconstrictors (thromboxane A<sub>2</sub>) leading to arteriolar vasospasm and hypoperfusion of vital organs.<sup>13</sup> Anesthesia for C section can worsen the maternal circulation further and can influence the outcome of the new born.<sup>14</sup> Spinal anesthesia can result in hypotension. There is lack auto regulation in the utero-placental blood flow (UPBF) which is directly dependent on arterial blood pressure (BP) of the mother. A decrease in maternal BP will lead to changes in variability of fetal heartrate, pathological

**Table 5: The number of newborns with signs of fetal hypoxia (Values given as mean)**

Parameter	GA (n=30)	SA low dose (n=30)	p-value
Apgar 1 min < 7	12	5	0.02*
Apgar 5 min < 7	1	2	1.00
<b>Neonatal acidosis</b>			
pH < 7,2	6	10	0.04*
pH < 7,1	2	5	0,08
<b>UA Base deficit</b>			
- (5-7.9) mEq/l	5	11	0.02*
- (8-10) mEq/l	4	4	1.00
< - 10 mEq/l	2	3	0.4
<b>Number of neonates requiring CPR</b>			
Facemask oxygen	19	9	0.04*
Intubation	4	2	1.00
CPR + drugs	1	1	1.00

\*Significant difference between groups

hypoxic bradycardia and changes in acid-base status of the fetus (low pH).<sup>15</sup> A 65% reduction in uteroplacental blood flow for 10 minutes produces fetal acidosis with pH < 7.2 in experimental animals.<sup>16</sup> A delay in treating hypotension can lead to serious fetal complications.<sup>17</sup>

Pregnancy induced hypertension (PIH) could react differently to sudden sympathetic blockade compared to the healthy parturients and these patients could be at a higher risk from profound spinal hypotension. This is specially so if the circulatory volume is low and the treatment with fluids (crystalloids) is limited to avoid pulmonary edema. Many authors have reported that hypotension following spinal anesthesia is dependent on dosage of local anesthetic drugs and doses used in healthy women could lead to hemodynamic disturbances in preeclamptic patients.<sup>18</sup> For this reasons, GA or epidural anesthesia (EA) was preferable in these patients. The complications and risks of using GA in preeclampsia patients are well documented. EA is also less practical especially in the emergent settings when timing is a key factor for successful outcome.<sup>19,20</sup>

In recent years new studies have appeared which have confirmed that SA used in preeclampsia is more practical and avoids hemodynamic disturbance.<sup>4</sup> Low bupivacaine dosage in SA in healthy parturitions produces less fall in BP and more circulatory stability. In our study we used a dose of (6-8 mg) of 0.5% isobaric bupivacaine

supplemented with fentanyl 20 micrograms during the surgery.<sup>21</sup> In 26 out of 30 parturitions a stable circulation was noted, without any serious fall in BP (less than 25% from the starting BP). Intergroup comparison of the BP did not show any clinical and statistical difference ( $p > 0.05$ ), except at 5 and 40 min. The slight decrease of the BP (less than 25%) 25 minute is of no clinical importance because at this time the delivery had occurred and the circulation of the neonate was independent from the mother.

The slight hemodynamic changes found in both groups in this study provided stable utero - placental perfusion without any disturbance. The primary outcome measure in our study was mean neonatal umbilical arterial pH and primarily base deficit (BE). These parameter are independent from maternal ventilation variation. Lower values of base deficit were seen ( $-5,492 \pm 2.4$  vs.  $-4,35 \pm 1,91$  mEq/ml) in GA group. In general, the base excess (BE) is known as a more specific index of metabolic component in acid-base surrounding in comparison with the other parameters because it is independent from the maternal ventilation.<sup>16,22</sup> Use of ephedrine could have affected these results. There are several references that show the correlation between the use of ephedrine and lower values of pH and BE compared with phenylephrine.<sup>23,24</sup> Riley and his colleagues provided evidence that ephedrine in doses required to maintain a solid maternal BP lead to increased metabolic activity of the fetus with a reduction of the values of UA pH and BE, but also an increased accumulation of the  $pCO_2$ .<sup>25</sup>

The difference in concentration of the accumulated  $pCO_2$  between the groups (GA vs SA) was similar ( $50, 80 \pm 5.31$ ;  $53, 06 \pm 8.14$ ;  $p < 0,13$ ). In general, the  $pCO_2$  production is mainly connected with maternal ventilation, but it can be a result of increased fetal adrenergic metabolism. This indirectly shows the state of fetal metabolism and metabolic production of  $CO_2$ . In this study ephedrine was used in the range of  $8.5 \pm 8.55$ , which was insufficient to induce stimulation of fetal metabolism and thus influencing  $pCO_2$ . We speculate that the obtained results of  $pCO_2$  in this study are more related to the ventilation effect of the parturients (mechanically or spontaneously breathing) than the neonate (depression with 20  $\mu g$  intrathecal fentanyl is rare).<sup>25</sup>

This finding was supported by the values of the markers of hypoxia, where the total number of neonates with pH < 7.1 was equal in both groups, even though the number of neonates of SA group with the pH < 7.2 was slightly higher than those in

### GA group.

A larger number of neonates had base deficit (BE) between -5 to -7.9 in SA group, but there was no difference in BE (BE < -9 < -10). The other markers for acidosis (pH < 7.1 and BE < -8-10 and < -10 mEq/L) and the number of episodes for resuscitations did not show a differences between groups. This data has no clinical implications because the Apgar scores at one minute in SA group were better than those in GA, which in general accounts for lower SA affection on the babies.

Several factors are responsible for hemodynamic stability and for development of lesser degree of hypotension in patients with preeclampsia.<sup>26,27</sup> Firstly Cesarean delivery in preeclampsia patients occurs at lesser gestational maturity compared with healthy parturitions leading to lower weight of the newborns. The patients have lesser risk for aortocaval obstruction and consecutive hypotension; in addition, the same reason produces less dilatation of the epidural venous plexuses in vertebral channel, resulting in lesser cephalic spread of spinal anesthetic. Secondly, in preeclampsia, the mechanism of vasodilatation is impaired, which

produces lesser response to sympathetic blockade of SA. Ephedrine requirements are reduced during spinal anesthesia for caesarean section in preeclampsia.<sup>24</sup> These phenomena produce vasospasm in patients with preeclampsia resistant to sympathetic blockade following SA.

### CONCLUSION

In conclusion the low dose spinal anesthesia was found safe for preeclamptic parturients, was associated with hemodynamic stability and a better outcome for the newborns. It enabled the same acid-base environments (UA pH) for the newborn as with general anesthesia, but resulted in superior general conditions of the newborns.

**Acknowledgment:** Author and coauthors express their thanks to the collaborating technicians from Clinic of Gynecology and Obstetrics at UCIM in Skopje, for technical and material support during the study. Many thanks to the secretary for their technical help.

**Conflict of interest:** There was no conflict of interest during the study.

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