

Anesthetic Considerations in Preeclampsia

Jayavelan Ramkumar¹ and Nidhi Sharma^{2*}

¹Department of Cardiothoracic Vascular Surgery, Sri Ramachandra Medical College, Sri Ramachandra University, Chennai, Tamil Nadu, India

²Department of Obstetrics and Gynaecology, Saveetha Medical College, Saveetha University, Chennai, Tamil Nadu, India

*Corresponding author: Sharma N, Department of Obstetrics and Gynaecology, Saveetha Medical College, Saveetha University, Chennai, Tamil Nadu, India, Tel: + 919445560392; E-mail: drbonuramkumar@yahoo.co.in

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Abstract

Background: Preeclampsia is prevalent in 3%-7% of pregnant women globally. The etiology is multifactorial. A pregnant women with preeclampsia presenting with an indication of caesarean section, is an anesthetic challenge. There is an increase in blood volume by 40% after 20 weeks of pregnancy. This can result in severe hypertension in a non-pregnant individual but still blood pressure decreases in second trimester of pregnancy. This happens because of decreased peripheral vascular resistance and increased venous capacitance. If the vascular system is non-resilient and the vessel walls still maintain their stiffness and elastic recoil; pregnancy induced hypertension can result. There is general organ hypo perfusion in severe preeclampsia. The anesthetic challenges are an edematous airway, cardio circulatory dysfunction, dysfunction of cerebro-vascular system and the exaggerated coagulopathy.

Aims and objectives: Preeclampsia is a common cause of maternal mortality and morbidity. The etiology is unknown though a lot is known about its pathophysiology. The cardiovascular, pulmonary and cerebral change of severe preeclampsia needs to consider while administering spinal, epidural or general anesthesia. Hypotensive drugs and anesthetic monitoring need special care in severe preeclampsia. This study was designed to assess the effectiveness and safety of epidural and spinal anesthesia in pregnant women with preeclampsia.

Methods: It is an ex post facto quasi experimental study to evaluate the effectiveness of spinal anesthesia, epidural anesthesia and general anesthesia in reducing pain severity in cesarean section in preeclampsia. (G1=30, G2=32, G3=31). Pregnant women at term with preeclampsia with chronic hypertension, diabetes, renal disease, anemia and coagulopathy were excluded from the study after a detailed pre-anesthetic assessment.

Observations and results: There was a significant improvement in pain scores in epidural anesthesia group as compared with spinal anesthesia group and general anesthesia group.

Conclusion: In pregnant women with preeclampsia spinal and epidural anesthesia can be useful during caesarean section. Epidural anesthesia in properly indicated cases provides safe and effective pain relief.

Keywords: Anesthesia; Caesarean Section; Hypertension; Preeclampsia; Pregnancy

Introduction

The word "Preeclampsia" is derived from the Greek word *Eklampsis* meaning "lightening" or "convulsions". In a woman with term pregnancy and preeclampsia there is contracted plasma volume, normal or increased cardiac output, vasoconstriction, and hyper dynamic left ventricular function. There may also be a coexisting left ventricular dysfunction in systole and diastole. Other problems are increased airway edema, decreased glomerular filtration and platelet dysfunction superimposed on the exaggerated hypercoagulable state of pregnancy.

In severe preeclampsia there is chronic placental hypo perfusion [1]. The uteroplacental circulation is not auto regulated and the fetus may poorly tolerate any further decline in perfusion. Thus the primary peripartum aim in the management of a severely preeclampsia parturient is the optimization of maternal blood pressure, cardiac output and uteroplacental perfusion. There should also be a

monitoring to detect cerebral edema in order to prevent of seizures and stroke. The main concerns to the anaesthetist are an edematous airway, cardio circulatory dysfunction, dysfunction of cerebro-vascular system and the exaggerated coagulopathy [2].

Materials and Methods

Participants

Anesthesia for caesarean section for various obstetrical indications was given in 93 preeclampsia pregnancies.

This prospective study involved pain scoring by visual analogue scoring within 24 hours of caesarean section at term gestation in women with singleton pregnancies with preeclampsia. All women preeclampsia hypertension were asked to fill the VAS (Visual Analogue Score) questionnaire of spinal anesthesia, epidural anesthesia or general anesthesia. An initial preanesthetic assessment according to ASA was done for all pregnant women. This study was approved by the ethical and research board (002/001/2016/SU/IEC). Written consent was obtained in all cases in local language.

Study was carried out on 93 pregnancies in the Department of Anesthesiology and Department of Obstetrics and Gynecology at Saveetha Medical College and Hospital (Chennai, India) between 1 Jan 2016 and 31 December 2016. Preeclampsia was defined according to the guidelines of the International Society for the Study of Hypertension in Pregnancy. This requires two recordings of diastolic blood pressure of ≥ 90 mmHg at least 4 h apart in previously normotensive women, and proteinuria of 300 mg or more in 24 h. or two readings of at least ++ on dipstick analysis of midstream or catheter urine specimens were taken (if no 24 h. collection was available). Blood pressure was measured in the right arm in the sitting posture and Koratkov 5 sounds were taken as the diastolic blood pressure. Urine albumin was measured at each visit.

Multiple pregnancies, pregnancies with anemia, diabetes, chronic hypertension, renal disease, abnormal coagulation profile and uncontrolled hypertension were excluded. Detailed maternal factors like age, gestational age, parity, pre pregnancy body mass index, previous surgery and anesthesia, hemoglobin levels, chronic hypertension, gestational diabetes and pregnancies with previous preeclampsia were recorded. Problems with endotracheal intubation like laryngeal spasm, retro placental calcifications, small placenta, and premature separation were noted. Problems with spinal and epidural anesthesia like difficulties in positioning, catheter insertion bleeding from injection site were noted.

Measurement of pain score

The patients were asked to indicate on a scale of 1 to 10 about how bad there pain was and their overall impression of intensity of pain and

ability to bear the pain on a line. The left of the line meant no pain at all (Score 1) and the right side of the line meant severe, intolerable pain (Score 10).

Statistical analysis

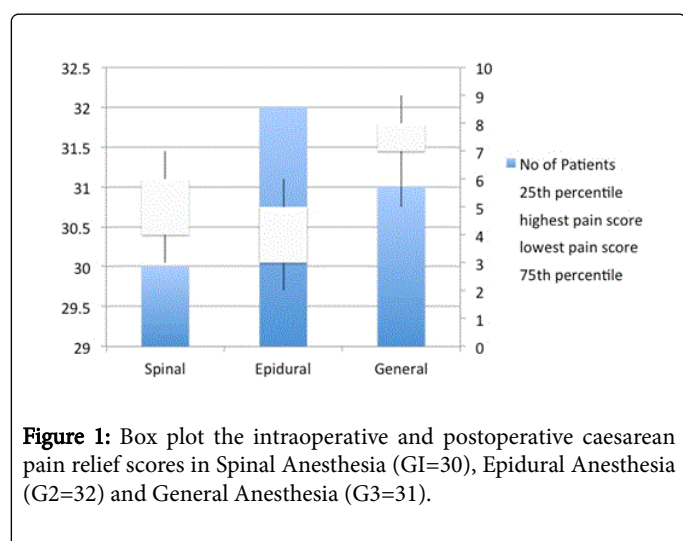
The pain scores were plotted on a box plot. Mean pain scores was calculated and expressed as mean \pm standard deviation. One-way ANCOVA (one way analysis of covariance) was used to analyze variables using MEDCALC. This online calculator was used to generate a complete one-way analysis of variance (ANOVA) table for the groups, including sums of squares, degrees of freedom, mean squares, and F and p-values, the mean and standard deviation. Differences were considered significant when $p < 0.0001$ (CI). Statistical analysis was done using MEDCALC version 18 (Medcalc is a statistical software designed for biomedical science at Aalcialaan 22, 8400, Ostend, Belgium).

Observations

The mean age of the 93 patients was 28 years (range 18-37). Cases were comparable in age and indications of Caesarean section. Epidural anesthesia showed a significantly better patient tolerance (3.59 ± 0.94) as compared to spinal anesthesia group (5.067 ± 1.20) and general anesthesia group (7.77 ± 1.11). This was statistically significant reduction (p value < 0.0001 , F value = 118.650) (Table 1).

Group	Anesthesia	Post Caesarean Pain scores (Mean \pm SD)	One way ANOVA	Sum of squares	Degree freedom	Mean Squares	F value	p-value
G1 (30)	Spinal	5.06667+1.20153	Between group	282.135	2		118.650	<0.0001
G2 (32)	Epidural	3.59375+0.9455	Within the groups	107.004	90	141.067		
G3 (31)	General	7.7777+1.116831	Total	389.139	92	1.189		

Table 1: Spinal anesthesia (G1=30), Epidural Anesthesia (G2=32) and General Anesthesia (G3=31) groups: post caesarean pain scores.



Box plot for all the group frequencies showed the maximum significant pain relief in the epidural anesthesia group (Figure 1).

Results

There were no cases of bleeding from the catheter insertion site in our patients. Box plots were plotted for spinal, epidural and general anesthesia group. There is a significant improvement in Pain scores in epidural and 2 patients were completely pain free following post operative epidural top up infusions therapy. Our study had the maximum pain relief in the epidural group, thereby showing safety and efficacy of epidural anesthesia during caesarean section in preeclampsia pregnancies. Epidural anesthesia with catheter in epidural space for 24 hours post caesarean has maximum efficacy. The ideal catheterization technique and exact position of catheters is to be ensured.

Discussion

Pathophysiology of preeclampsia

Preeclampsia is characterized by widespread endothelial dysfunction, in which placenta-derived mediators cause multisystem organ dysfunction. The endothelium is a biologically active biophysical barrier that controls the movement between the intra-vascular and extra-cellular compartments. It is also secretes active metabolites. The amount of synthesis of vasodilators like nitric oxide (NO) and prostacyclin (PGI₂) is decreased compared to the amount of synthesis of vasoconstrictors. There is also an altered expression of receptors. This alters the vascular smooth muscle reactivity and platelet adhesiveness.

Vasodilators

Vasoactive drugs during pregnancy affect the utero-placental blood flow to the fetus and placenta. The aim of vasodilator treatment in the first 20 weeks of pregnancy is to regulate the blood flow to the placenta as ischemic placenta releases sFLT and sENG. sFLT binds to VEGF and PLGF while sENG binds to TGF. Deprived of VEGF and TGF the vessel smooth muscle will decay and fray. In the preclinical stage of preeclampsia low dose aspirin, heparin and dipyridamol can minimize placental ischemia. After 20 weeks of pregnancy the aim of vasodilator is to maintain uteroplacental blood flow and minimize organ damage to maternal organs like liver, brain, kidneys and lungs. Vasodilators used are alpha and beta-blockers like labetalol, calcium channel blockers, and NO donors like L-arginine and sodium nitropruside. ACE inhibitors and angiotensin receptor antagonist are contraindicated in pregnancy. Diuretics also cannot be used as they reduce the already shrunken intravascular compartment and thereby further compromising the uteroplacental blood flow.

Magnesium sulphate

MgSO₄ can be used safely in its therapeutic range of 4-7 meq/dL in pregnancy. It acts on the neuromuscular junctional transmission of impulses and also lowers the vascular smooth muscle tone. The hypotensive effect of MgSO₄ during regional anesthesia has to be remembered. MgSO₄ can also blunt the response to vasoconstrictors. Treatment of overdose is (1 gm) intravenous calcium following the rule of 10 (e.g., Calcium gluconate 10 mL of 10% over 10 minutes). Magnesium therapy should be continued every 4 hourly for 24 h post-partum or last convulsion whichever occurs later.

Monitoring of magnesium toxicity is done by checking tendon reflexes and respiratory rate. If the pregnant woman is on continuous ECG monitoring, ECG changes can also be recorded. There is prolongation of P-Q interval and widening of QRS complex. This may progress to conduction defects and cardiac arrest. The risks of toxicity increase in the presence of decreased renal blood flow and glomerular filtration rate and oliguria in preeclampsia. This is because magnesium depends on the kidneys for excretion so urine output should be maintained above 30 mL/h. by giving intravenous fluids (normal saline or ringer lactate 500 mL over 8 h).

Choice of anesthesia

Regional anesthesia in caesarean section has several advantages. Regional anesthesia obviates the need of laryngoscopy required in general anesthesia. Additional advantage of spinal anesthesia is lesser

blunting of the neuro-endocrine response to surgery, which is more profound after general anesthesia. Another advantage of regional anesthesia is that there are no cases of neonatal depression associated with general anesthesia.

Spinal anesthesia is fast acting, effective and involves less potential trauma in the epidural space. Nevertheless, it carries a theoretical risk of sudden hypotension in a patient who may be relatively hypovolemic and thereby further reducing the downstream blood flow to the placenta and intrauterine fetus. The risk is more theoretical as recent randomized controlled trials have proved the safety of spinal anesthesia in preeclampsia [3-5]. Another option is to combine the epidural anesthesia with spinal anesthesia. This can be done by placing an epidural catheter in the subarachnoid space and injecting a small dose of local anesthetic like bupivacaine in the sub arachnoid space. The epidural catheter can also be utilized to inject analgesics in the immediate postoperative period to provide adequate pain relief. Providing pain relief post operatively encourages the patient to take deep breaths as patient restricts diaphragmatic movement during abdominal pain. This increases the tidal volume and tissue oxygenation.

Spinal anesthesia requires patient positioning and cooperation and so general anesthesia is inevitable in a comatose eclampsia patient and so preparations must be made for difficult intubation. In a preeclampsia woman there may be laryngeal mucosal edema of the upper airway and the hypertensive autonomic responses to laryngoscopy and surgery is pronounced. So it is mandatory that the anesthetic intubation carts have endotracheal tubes ranging in sizes till 5.5 mm internal diameters and external diameters. Laryngoscopes with adequate light source, masks and ventilation apparatus should be pre checked before attempting to intubate a preeclampsia pregnant woman.

Magnesium sulphate, labetalol, nitrates, nitropruside, lidocaine and/or potent parenteral opioids have been used to prevent the intense hypertensive crises in preeclampsia during intubation. For general anesthesia it is pertinent that equipment is available to manage a difficult airway and medication to blunt the hemodynamic response to laryngoscopy is provided (e.g., via a bolus of an antihypertensive drug or remifentanyl) [6]. Preeclampsia women on magnesium sulphate may be very sensitive to the effects of non-depolarizing neuromuscular blocking drugs like vecuronium used during general anesthesia and strict monitoring is required.

Cerebral hemorrhage

Cerebral hemorrhage is the single most common cause of maternal death in preeclampsia and the second most common cause is pulmonary edema. Cerebral edema deaths are much more common than pulmonary edema deaths in preeclampsia. Earlier studies on preeclampsia pointed out that the rise in diastolic pressure was the most important cause of eclampsia but recently the concept of rise in systolic blood pressure is also being considered. Some studies are highlighting the concept of "Delta Hypertension" i.e., the rise in blood pressure above the prepregnant values.

The current recommendations of the National Enquiries into Maternal Death are to treat systolic blood pressures above 160 mmHg to prevent intracranial bleeding [7-9]. Noninvasive monitoring techniques such as pulse wave analysis of middle cerebral artery and T2 weighted FLAIR sequence MRI have helped to decipher the cause

of vasogenic and cytotoxic cerebral edema in preeclampsia [10] (Figure 2: PRES syndrome in T2 weighted FLAIR sequence of MRI).

Pulmonary edema

Placing a pulmonary arterial wedge catheter can be used to measure and treat blood pressure changes, especially in patients with severe or volatile hypertension. Echocardiography can provide information about volume status and cardiac function. However in preeclampsia, due to generalized vasoconstriction the central venous pressure may not be the same as pulmonary capillary wedge pressure. Left ventricular end diastolic volume and stroke work also may not correlate. Additionally, pulmonary artery and central venous catheter placement are invasive procedures and carry a 4% reported risk of complications in preeclampsia. Noninvasive measures that can be used to measure stroke volume are arterial waveform analysis and impedance cardiography. There is a proven benefit to risk ratio when noninvasive measures like thermo dilution-based measurements are used monitor the preeclampsia during caesarean section and in the immediate postpartum period. Figure 3a-3c outline the pathophysiology behind the development of pulmonary edema in preeclampsia.

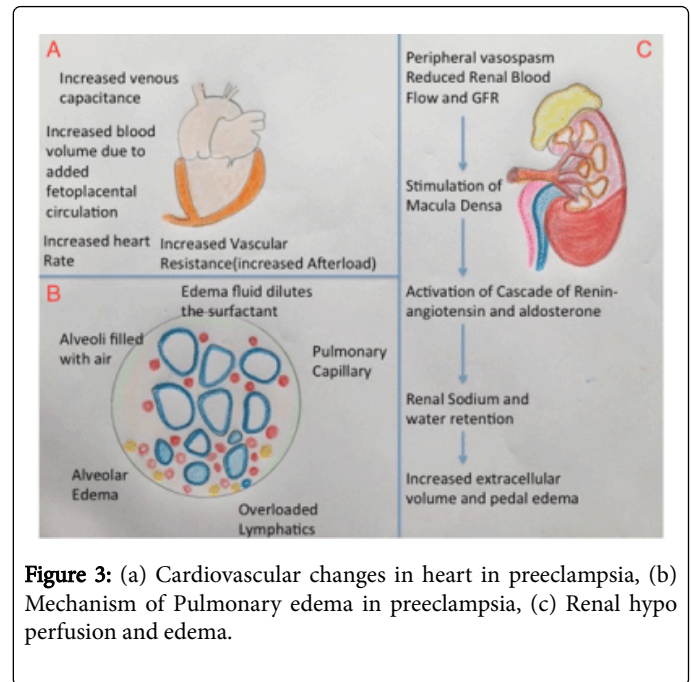


Figure 3: (a) Cardiovascular changes in heart in preeclampsia, (b) Mechanism of Pulmonary edema in preeclampsia, (c) Renal hypo perfusion and edema.

Conclusion

Preeclampsia pregnancy is primarily a disease of non-resilient cardiovascular system and the frequent hemodynamic findings are low filling pressures, low cardiac output and vasoconstriction. Traditionally it was believed that giving spinal anesthesia for caesarean section in preeclampsia pregnancy could lead to severe hypotension and thereby compromise the uteroplacental perfusion. Thus spinal anesthesia was not used in these patients. However, this clinical study in women severe preeclampsia has revealed this concern is mainly theoretical because of the increased vascular wall tone in these women. Furthermore, this hypotension is transient and easily treated.

Risk-benefit analysis studies strongly favor neuraxial regional techniques like spinal over general anesthesia for cesarean delivery in the setting of severe preeclampsia when the contraindications to spinal and epidural anesthesia are ruled out.

To conclude, epidural and spinal anesthesia is a reasonable anesthetic option in severe preeclampsia when cesarean delivery is indicated, when there is no contraindication like coagulation disorders.

Author Research ID: P-2293-2016; [Orcid.org/0000-0003-1468-8996](https://orcid.org/0000-0003-1468-8996)

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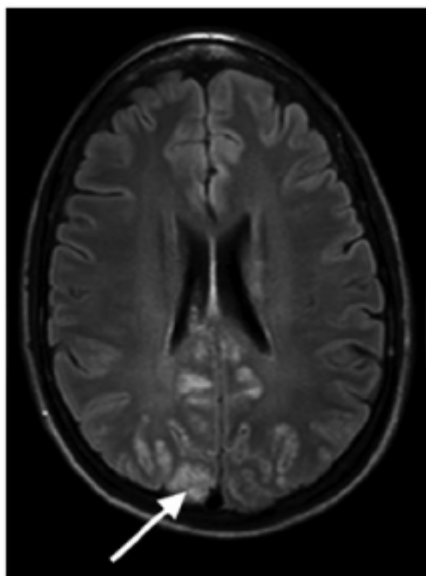


Figure 2: Magnetic Resonance image of axial section brain showing foci of FLAIR increased intensity in bilateral parietal and occipital regions.

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