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Analysis of Maternal Outcomes in Severe Pre-Eclampsia Patients under General versus Spinal Anaesthesia for Caesarean Delivery.

Pacharla Indira [1] , Rajola Raghu[1] , Kota Raju[2] ,M.ChandraShekar[3]
Assistant Professor[1] , Post graduate[2], Professor[3] ,
Department of Anaesthesiology , Osmania Medical College , Hyderabad ,Telangana State,India.

***Abstract**: Pre - eclampsia is a potentially fatal disorder and a major cause of morbidity and mortality in developing nations , anaesthetic management in these patients is challenging . Maternal outcomes of severe preeclamptics posted for caesarean under general anaesthesia and spinal anaesthesia were studied and analysed.Sixty parturients with severe pre-eclampsia posted for caesarean section under spinal or general anaesthesia were randomised into two groups of 30 each. Demographic data including age, weight , gravida , gestational age were recorded . Blood pressure and Heart rate were monitored in the ward before induction, after intubation and at 5 min intervals till completion of the operation and after spinal anaesthesia at 5 min intervals. The incidence of maternal morbidity , mortality and admissions in ICU were analysed . Spinal anesthesia for caesarean delivery has better maternal outcome in terms of hemodynamic stability and postoperative recovery when compared to general anesthesia. Spinal anesthesia is a safe alternative to general anaesthesia in severe preeclampsia patients.*

***Key words**: Caesarean , General anaesthesia , Severe Preeclampsia, Spinal anaesthesia.*

I. Introduction

Pre-eclampsia is a multi-system disorder unique to human pregnancy complicating 5-8% of pregnancies[1, 2](Saftlas et al., 1990). It is an integral part of spectrum known as hypertensive diseases of pregnancy characterized by hypertension after 20 weeks gestation and proteinuria.

CLASSIFICATION OF HYPERTENSION IN PRENANCY [24]

Classification	Gestational age (weeks)	Maternal blood pressure (mmHg)	Proteinuria	Seizures
Gestational hypertension	>20	>140/90	No	No
Mild preeclampsia	>20	>140/90	< 5g/24h	No
Severe preeclampsia	>20	> 160 /110	> 5g/24h	No
Eclampsia	>20	> 160 /110	> 5g/24h	Present
Chronic hypertension	<20 and prior to conception	>140/90	No	No
Superimposed preeclampsia.	<20	>140/90	New onset	No

Diagnostic Criteria for Severe Preeclampsia (American Congress of Obstreticians and Gynecologists (ACOG) Criteria[4] :

Severe Pre-eclampsia

i. BP is ≥160 mmHg Systolic and/or ≥110 mmHg Diastolic; Proteinuria is 300 mg/24 hours; or ≥1+ (on 2 random urine samples, collected at 4 hrs apart) ; or protein:creatinine ratio is ≥0.3 mg/dl.
ii. BP is ≥160 mmHg systolic and/or ≥110 mmHg diastolic,without proteinuria, any one of following is present:

- Thrombocytopenia, platelets count <100,000/uL
- Serum creatinine ≥1.1 mg/L or a doubling of serum creatinine concentration in absence of other renal disease.
- Impaired liver function, elevated blood concentrations of liver transaminases to twice normal concentration.
- Pulmonary oedema.
- Cerebral or Visual Disturbances.

(Blood pressures are recorded at 2 occasions 6 hrs apart with patient at bed rest).
HELLP syndrome is a subtype of severe pre-eclampsia characterised by Hemolysis (H),elevated liver enzymes (EL), and low platelets (LP).[27]

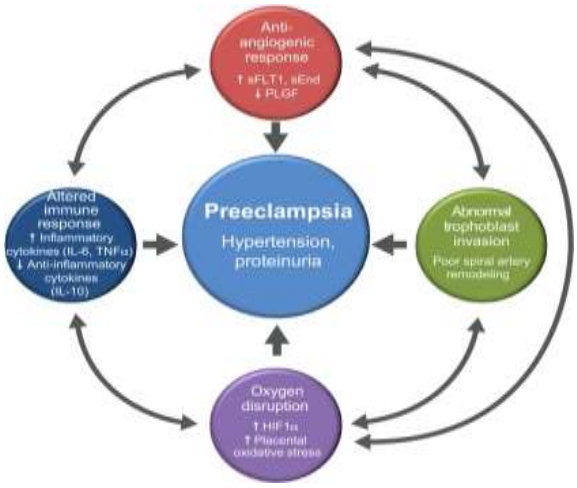


Fig.: Factors influencing pathophysiology of preeclampsia

Pre eclampsia is commonly referred as "disease of theories" , pathophysiology is complex [1] with multi organ involvement making its prevention and management an ongoing challenge. Endothelial cell dysfunction due to abnormal genetic and immunological mechanisms is the crux of multitude of pathophysiologic effects resulting in compromised uteroplacental circulation[6].

Table: Pathophysiology: Potential signs and symptoms of pre-eclampsia . [6, 9]	
Central nervous system:	Headaches, Visual changes, Hyperexcitability, Hyperreflexia and Seizures (eclampsia).
Cardiovascular system:	↑sensitivity to Endogenou controls (hormonal/ autacoid); an early Hyperdynamic state may change to a low-output, high total vascular resistance; intravascular volume depletion.
Respiratory system	Pharyngolaryngeal edema; ↑ risk of pulmonary edema due to lower colloid oncotic pressure and ↑ vascular permeability.
Hematologic system	Hypercoagulability, Platelet activation with microvascular consumption; activation of Fibrinolytic system.
Renal system	↓ Glomerular filtration rate; ↑ proteinuria; ↑ uric acid; ↑urine protein:creatinine ratio; Oliguria.
Hepatic system	↑ serum transaminases , Right upper quadrant abdominal pain; Rupture of Glisson's capsule with Hemorrhage.
Endocrine system	Imbalance of Prostacyclin relative to Thromboxane; upregulation of systemic renin angiotensin aldosterone system[31]
Uteroplacental system	Persistence of a high-resistance circuit with ↓ blood flow ; IUGR & Oligohydramnios.

Platelet dysfunction also has been implicated in pre-eclampsia, with surface-mediated platelet activation, decreased sensitivity to prostacyclin, and increased release of thromboxane and serotonin, leading to further platelet aggregation and upregulation of uteroplacental renin-angiotensin aldosterone system. Triad of physiological derangements in preeclampsia include: 1.Vasospasm , 2.Plasmavolume contraction and 3.Local or disseminated intravascular coagulation.

Cardiovascular changes in severe untreated preeclampsia (Cotton and colleagues[18,19]) are : 1.Hyperdynamic circulation ,high cardiac output with N to ↑SVR , N or slightly ↓ blood volume and filling pressures.

2. Normal cardiac output and lower filling pressures, but ↑ SVR.

3. Highly elevated SVR, but reduced blood volume and ↓ LV function.

Management of pre - eclampsia involves a multi-disciplinary approach with the anesthesiologist playing a significant role for a positive outcome . Women with a first-degree relatives are more likely to develop preeclampsia. Familial patterns of pre - eclampsia are associated with more severe disease.

Pre-eclampsia may be classified as mild or severe. Severe pre-eclampsia can occur in preterm, term and postpartum periods. Onset of pre-eclampsia at ≥ 34 weeks' gestation is associated with a less severe form of the disease while onset before that time is associated with more severe disease and greater maternal and fetal morbidity[5] . It is misleading to assume a smooth progression from mild disease to severe preeclampsia to eclampsia, because 25% - 40% of patients will have normal blood pressure at the time of their first eclamptic seizure.[20] . Other forms of severe hepatic dysfunction in pregnancy need to be differentiated from pre- eclampsia for peri-operative management. General anaesthesia can be safe in severe preeclampsia , currently, safety of spinal anaesthesia is well established with better maternal outcomes[3] .

II. Materials And Methods

After Institutional Ethics committee approvala prospective randomised study was conducted in sixty parturients with severe pre-eclampsia candidated for elective / emergency caesarean section during march 2013 to march2014 at Government Maternity Hospital, Hyderabad. All the patients were in the age group of 18 yrs to 40 yrs and randomised into two groups Group G and Group S. An informed written consent was taken from all the patients.

Inclusion criteria: Parturients with severe preeclampsia

Exclusion criteria : Cardio vascular and pulmonary disease, Diabetes, HELLP syndrome, Gestational age <34 weeks , Fetal bradycardia and any contraindications of regional anaesthesia including patients refusal, severe hemorrrhage, coagulopathy and sepsis. All patients received magnesium sulphate as anti-seizure prophylaxis and in operation theatre after securing an i.v.cannula , patients received 10 ml kg $^{-1}$ of crystalloid Ringer's lactate before anaesthesia and baseline vitals (NIBP and HR) were recorded. Monitoring included ECG , HR , NIBP ,SpO_2. Group S – Spinal anesthesia group (n=30) received 10 mg of 0.5% hyperbaric bupivacaine intrathecally between L_3-L_4 interspinous space in sitting or left lateral position with 26 G Quincke spinal needle and oxygen @ 6 ltrsmin^{-1} oxygen with Hudson's face mask was supplemented throughout surgery. Group G – General Anesthesia (n=30) - Rapid sequence induction and intubation with Thiopental 4-5 mg/kg , succinyl choline 1mg/kg, lidocaine 1 mg/kg, fentanyl 1 mcg/kg . Maintenance : 50% N_2O in 50% O_2, 0.5 to 0.75% sevoflurane and 0.10 mg/kg atracurium. Patients were extubated after fulfilling extubation criteria. Demographic data including age, weight, gravida, gestational age were recorded. Blood pressure (systolic, mean, diastolic), Heart rate, Oxygen saturation were recorded immediately after general anaesthesia, every minute for first 10mins, then every 5mins till completion of operation. Vitals were monitored post-operatively for the first 24hrs. After spinal anaesthesia BP & HR were monitored at 5 min interval till end of operation. A ± 20% change in Blood Pressure & HR from baseline, is considered as hypertension or hypotension and tachycardia or bradycardia respectively. Parturients were observed for incidence of morbidity , mortality and ICU admissions. Morbidity parameters observed were incidence of peri-operative hypertension and hypotension, changes in heart rate, post operative complications like convulsions, pulmonary edema, acute renal failure, aspiration pneumonitis and delayed recovery . An unpaired Student's t-test was used to test the significance of means of all parameters.

III. Results And Observations

(I)DEMOGRAPHICDATA:

In both study groups demographic data did not differ statistically with parturients in the age group of 23 – 29 yrs weighing 56.58 ± 5 kgs , height of 160 ± 8.40cms and mean gestational age of 33.85 weeks .

(II) HEMODYNAMIC PARAMETERS:

TABLE I : HEMODYNAMICS DATA IN GROUP G AND GROUP S

HEMODYNAMIC PARAMETERS	GROUP G (n = 30)		GROUP S (n = 30)		p value Unpaired 't' test
	MEAN	S.D	MEAN	S.D	
Highest SBP (mm Hg)	161.07	7.55	137.93	6.05	<0.0001
Lowest SBP (mm Hg)	117.80	7.93	102.80	12.60	<0.0001
Mean SBP (mm Hg)	131.27	8.84	99.17	4.89	<0.0001
Highest DBP (mm Hg)	99.83	5.85	96.10	6.35	<0.0213
Lowest DBP (mm Hg)	78.93	7.68	62.80	10.04	<0.0001
Mean DBP (mm Hg)	78.23	7.78	69.13	3.09	<0.0001
Mean MAP (mm Hg)	93.57	5.15	84.53	4.20	<0.0001
Change in Heart rate	26.77	7.973	6.57	2.55	<0.0001

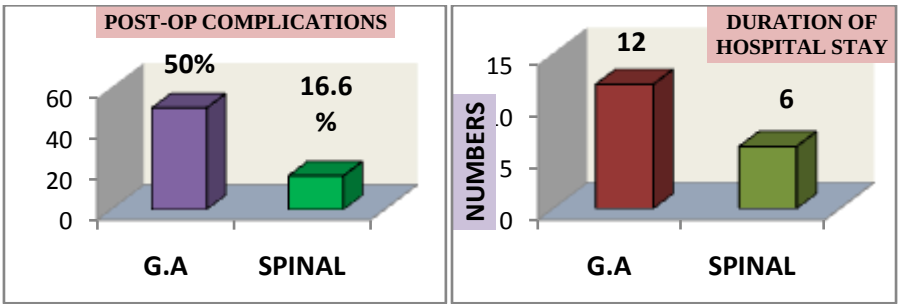
Hemodynamic monitoring included Systolic , Diastolic , Mean arterial Blood Pressure and Heart rate. The highest and lowest systolic, diastolic and mean arterial blood pressure are compared between both groups from the time of induction till end of the surgery. The difference between two groups were extremely significant statistically ($p < 0.0001$) with better control of blood pressure in the spinal anaesthesia group.

(III) MORBIDITY AND MORTALITY

TABLE II : INCIDENCE OF MORBIDITY & MORTALITY IN Group G & Group S

S.No.	PARAMETER	Group G(n 30)	Group S(n 30)	P value
1.	Intraoperative Hypertension	22 (73.3%)	2 (6.6%)	0.000006
2.	Tachycardia	22 (73.3%)	10 (33.3%)	0.0022

3.	Postoperative Complications	15 (50%)	5 (16.6%)	0.0068
4.	Admission in ICU	15 (50%)	5 (16.6%)	0.0068
5.	Hospital Stay (No. of Days)	12 (7-15)	6 (4-10)	0.045
6..	Intraoperative Hypotension	5(16.6%)	10 (33.3%)	0.1521
7.	Postoperative Hypertension	5 (16.6%)	Nil	0.030
8.	Postoperative Hypotension	2 (6.6%)	4(13.3%)	0.3326
9.	Bradycardia	5 (16.6%)	10 (33.3%)	0.1168

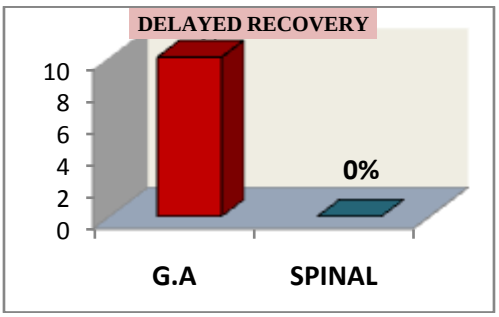


Incidence of morbidity and mortality in both groups were analysed statistically most common cause of morbidity is intra-operative hypertension with higher incidence in Group G , difference between both the groups is extremely significant statistically (p value 0.000006) , other causes of morbidity are tachycardia followed by postoperative complications.

TABLE IV : INDICATIONS FOR ADMISSION IN ICU.

S.No.	**Indications**	**Group G**	**Group S**	**P value**
1.	Postoperative Hypertension	5 (16.6%)	Nil	0.000006
2.	Post operative Hypotension	2 (6.6%)	3(10%)	0.3326
3.	Convulsions	2 (6.6%)	1(3.3%)	0.999
4.	Pulmonary Edema	1 (3.3%)	Nil	0.999
5.	Acute Renal Failure	2 (6.6%)	1(3.3%)	0.999
6.	Delayed Recovery	3 (10%)	Nil	0.2373
	TOTAL	15 (50%)	5(16.6%)	0.0068

ICU admissions in the postoperative period are more common in general anaesthesia group and statistically significant (p value 0.000006) cause of ICU admission was post-operative hypertension .Delayed recovery is another indication with an incidence of 10 %.



IV. Discussion

Women with severe pre-eclampsia have an increased rate of cesarean section consequent upon high incidence of IUGR , fetal distress and prematurity [2] and anesthesia remains a challenge as parturients may present to labor and delivery unit with or without a prior diagnosis of preeclampsia. Cesarean section in these patients is increasingly emergency in nature with high risk of cardiopulmonary morbidity [3] [4] . In severe preeclampsia, there is a significant chronic placental hypoperfusion , further decreases in perfusion is poorly tolerated by the fetus. It is essential to understand the various medical and surgical conditions, which mimic pre eclampsia. Similarly, preeclampsia can also be superimposed on one of these pathologies making diagnosis more difficult.

TABLE: Differential diagnosis of pre-eclampsia and anesthetic implications.[17]

Clinical Features	Preeclampsia	HELLP syndrome	AFLP	TTP	HUS	SLE excacerbation.
Hypertension%	Present	85	50	20=75	80-90	80+nephritis

Proteinuria %	Present	90-95	30-50	Hematuria	80-90	100+ nephritis
Jaundice	Absent	Present	Present	Rare	Rare	Absent
Fever	Absent	Absent	Present	Present	Present	During flare
Hypoglycemia	Absent	Present	Absent	Absent	Absent	Absent
Abdominal pain	Absent	Present	Present	Present	Present	Present
Neurological features	Absent	Present	Present	Present	Less common	Present
Laboratory findings						
Hemolysis	Absent	Present	Less common	Present	Present	Less common
Liver enzyme	Mild Elevation	Gross Elevation	Gross Elevation	Mild Elevation	Mild Elevation	Mild Elevation
Platelet count	> 100000	<20000	> 50000	<20000	> 20000	> 20000
Renal dysfunction	Absent	Present	Less common	Present	Present	Less common
ADAMTS13 Enzyme level <5%	Absent	Absent	Absent	Present	Rare	Rare
vWF multimers	Absent	Absent	Absent	Increased	Increased	Increased
Anaesthesia technique	RA	GA	GA	GA	GA	GA

AFLP-Acute fatty liver of pregnancy , TTP – Thrombotic thrombocytopenic purpura , SLE – Systemic lupus errythematous,VWF=Von Wiiliebrandsfactor,RA-Regional anesthesia , GA-General anesthesia,ADAMTS – A disintegrin and metalloproteinase with thromboplastin-I-like domains,HELLP=Hemolytic anemia elevated liver enzymes and low platelets.

Primary peripartum goals in the severely pre-eclamptic parturient are optimization of maternal blood pressure, cardiac output, uteroplacental perfusion , prevention of seizures and stroke.The advantages and disadvantages of spinal versus general anaesthesia will have to be carefully considered for each patient.[22,23] Neuraxial anesthetic techniques are preferable to GA for cesarean delivery in the absence of HELLP syndrome[28].

Anesthetic management of pre eclamptic patients for Emergency Caesarean Delivery depends on severity of preeclampsia and maternal/fetal status. Parturients are classified into four categories depending on urgency of delivery, maternal and fetal status during delivery [11,12].

Category	**Lucas classification[12]**	Clinical features	**Kinsella classification[11]**	Anesthetic technique
1	Immediate threat to life of mother or fetus	Maternal or fetal compromise	Cord prolapsed,significant placental abruption , Maternal cardiorespiratory distress	General Anesthesia
2	No immediate threat to life of mother or fetus		Late FHR decelerations CS prebooked to avoid vaginal delivery but presents in advanced labor Bleeding placenta praevia without hypovolemic shock Failed instrumental delivery with no fetal compromise	Regional anesthesia / General Anesthesia
3.	Requires early delivery	No maternal or fetal compromise	Deteriorating but compensated maternal medical condition	Regional anesthesia
4.	At a time to suit the woman and maternity services		Operation at short notice but no clinical	Regional anesthesia
GA-General anesthesia ,FHR-Fetal heart rate,RA-Regional anesthesia ,CS-Caesarean delivery .				

Spinal Anaesthesia Advantages :

(i) Relatively simple, rapid onset and superior quality of anaesthesia .
(ii) No effect on Apgar scores and umbilical artery pH.10
(iv) Low doses of local anaesthetic will reduce the risks of systemic toxicity
(v) Early breast feeding can be initiated.
(vi) Shorter duration of hospital stay .

Spinal anesthesia precludes the risk of aspiration, difficult and failed intubations, laryngoscopic response of intubation.

General anesthesia Advantages and Disadvantages :

General anesthesia with rapid sequence intubation is considered over RA when there is an immediate threat to the mother or fetus .

Risks of GA:

(i) Potentially Difficult ventilation and Endotracheal Intubation.
(ii) Exaggerated hemodynamic responses to laryngoscopy , intubation and extubation.
(iii) Risk of acid aspiration.
(iv) Potentiation of effects of neuromuscular blocking drugs due to $MgSO_4$.
(v) Uterine atony and coagulopathy cause considerable intrapartum blood loss.
(vi) Impaired villous blood supply[21].
(vii) Prone for rapid Desaturation during Induction of anaesthesia.
(viii) Post operative Airway management can be difficult due to laryngeal edema.
(ix) Babies born to mothers receiving general anesthesia required advanced resuscitation in the form of supplemental oxygen and bag mask ventilation .

Spinal anaesthesia is preferred over general anaesthesia for caesarean section in severe preeclampsia without coagulation abnormalities. There is always a chance that a preeclamptic patient may suddenly have a convulsion and anticonvulsant drugs (midazolam or thiopentone sodium) must be immediately available.

On the other hand, spinal anaesthesia conveys significant advantage and is now considered the method of choice for Caesarean section. Preliminary studies indicate that spinal anaesthesia may be safely performed in patients with severe preeclampsia.

Our study showed that the incidence of complications following GA (66.67%) were significantly ($P < 0.05$) higher than SA (16.67%). Commonest complication following GA was intra-operative hypertension (73.3%) , patients showed exaggerated cardiovascular responses to laryngoscopy. Blood pressure (73.3%) as well as Heart rate (73.3%) were significantly high after intubation , administration of IV lignocaine hydrochloride did not effectively reduce the response in pre-eclamptic parturients. While intraoperative hypotension following SA was 33.3% in our study and difference among GA versus SA group , was significant ($p<0.05$).

Incidence of Bradycardia in both groups were comparable ,under spinal anaesthesia bradycardia was followed by hypotension(33.3%) which responded to atropine and IV fluid therapy . Under general anaesthesia bradycardia episodes were relatively less (16.6%) . Hypotension was treated with conventional treatment using ephedrine and IV fluid therapy and hypertension was controlled with labetolol and nitroglycerine infusion.

Since the criteria for major morbidity differ among institutions, the need for transferring patients to intensive care unit (ICU) is used as an indicator for severity of illness. We observed that 50% patients from GA group, were admitted in ICU as compared to 16.6% from SA group. Indications for ICU admission were (in order of frequency) post operative hypertension, delayed recovery, postoperative hypotension ,convulsions , acute renal failure and pulmonary edema.

Similarly hospital stay in GA group was more (12 days) as compared to SA group (6 days). Difference in both the parameters between two groups is significant ($p<0.05$).

Regional anaesthetic techniques are equally acceptable for caesarean delivery in pregnancies complicated by severe preeclampsia if steps are taken to ensure a careful approach as postoperative morbidity and mortality is more after general anaesthesia. The shorter duration of hospital stay is an added advantage for the mother and newborn. Safety of spinal anesthesia has been studied in eclamptics by Razzaque et al. [13] who concluded that spinal is safer than GA for LSCS in eclamptics. A thorough evaluation to detect underlying coagulopathy or thrombocytopenia is essential prior to spinal anaesthesia. Haemodynamic changes , post operative morbidity, admissions in ICU and mortality are more common after general anaesthesia. It is therefore concluded that spinal anaesthesia could be considered as first choice for severe pre eclamptic patients. Ajuzieogu et al.[14] found significant birth asphyxia in babies of severe pre-eclamptic mothers who received general anesthesia.

A review by Dyer et al [7,8] , found that pre-eclampsia patients had a lower susceptibility to hypotension and probably less impairment of cardiac output than healthy parturients after spinal anaesthesia for CS. Ahsan-ul-Haq[16] also found lower 1-minute Apgar score with general anaesthesia.

Dasgupta et al.[15] in his study concluded that neonatal umbilical artery base deficit was significantly higher in GA group and neonates required more resuscitative efforts, a finding similar to our studies.

V. Conclusion

Single shot spinal anaesthesia is a safe choice for Caesarean delivery when compared to general anaesthesia in severe preeclampsia . Careful selection of patients is however, important. Spinal anaesthesia is safe and provides better maternal l outcome and has fewer intra operative and postoperative complications.

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