Observational study of choice of anaesthesia and outcome in patients with severe pre-eclampsia who present for emergency Caesarean section

Keerath K, MBCh, DA, FCA(SA), Specialist, King Edward VIII Hospital
Honorary Lecturer, Nelson R Mandela School of Medicine
Cronje L, MBCh, FCA(SA), Principal Specialist, King Edward VIII Hospital
Department of Anaesthesiology, Nelson R Mandela School of Medicine, University of Kwazulu-Natal
Correspondence to: Kiran Keerath, e-mail: kirankee@gmail.com

Keywords: severe pre-eclampsia, emergency Caesarean section, maternal and neonatal outcomes, intraoperative haemodynamic changes

Abstract

Objectives: Recent evidence in the literature suggests that regional anaesthesia may be the preferred choice over general anaesthesia for patients with severe pre-eclampsia who present for a Caesarean section. This study was conducted to determine if this applied to our population and to assess outcomes.

Design: A retrospective comparative observational study was conducted.

Setting and subjects: The study was carried out at the King Edward VIII Hospital and included patients with severe pre-eclampsia who presented for emergency Caesarean section. Eighty-four charts were analysed.

Outcome measures: The type of anaesthetic that was administered was determined and compared for maternal intraoperative haemodynamic changes and maternal and neonatal outcomes.

Results: Sixty-nine per cent of patients received spinal anaesthesia and 25% general anaesthesia (GA). Intraoperative systolic blood pressures of < 100 mmHg were recorded in 19% of GA and in 27.6% of spinal anaesthesia cases. A > 20% fall in mean arterial pressure from baseline was noted in 66.7% of GA and in 75.9% of spinal anaesthesia cases. There was no maternal mortality and one case of morbidity (a spinal anaesthesia case). An Apgar score of < 7 was recorded in 66.7% of GA cases and in 19% of spinal anaesthesia cases. Neonatal morbidity and mortality occurred in 33.3% of GA and in 10.3% of spinal anaesthesia cases.

Conclusion: Maternal morbidity and mortality were not significantly different between the two groups. Neonatal outcomes were poorer in the GA group, but neonates in the GA group had significantly lower birthweights and gestational ages. Their mothers also had more severe disease. This study supports spinal anaesthesia as an appropriate anaesthetic choice in patients with severe pre-eclampsia.

Introduction

Pre-eclampsia complicates approximately 5-8% of pregnancies. It is associated with significant morbidity and mortality and is still listed as one of the top three causes of maternal morbidity and mortality in South Africa.1

The management of pre-eclampsia poses a challenge to the obstetrician. The risk of morbidity and mortality increases substantially in the case of severe pre-eclampsia. As a result, patients often present for an emergency Caesarean section. In this situation, there is limited time for preoperative optimisation of clinical conditions. This poses a considerable challenge to the obstetric anaesthetist. The choice of a safe anaesthetic and maintenance of intraoperative stability to ensure the delivery of a healthy neonate, and to minimise maternal morbidity and mortality, is of particular concern.

Several studies have shown that concerns about the reduction in blood pressure specifically during regional anaesthesia in patients with severe pre-eclampsia are unfounded. Most of these studies were conducted in a First World setting. In most cases, there was adequate
time for preoperative optimisation of the patients' clinical condition.\textsuperscript{2,4} This study was carried out to determine if our patient population was similar to that of the other studies, and in so doing, to make recommendations regarding clinical practice for these patients.

The primary objectives of this study were to determine the type of anaesthesia that should be administered to patients with severe pre-eclampsia who present for emergency Caesarean section, and to compare the maternal intraoperative haemodynamic changes and maternal and neonatal outcomes that were associated with each type of anaesthesia.

**Method**

After approval by the Hospital Management Committee and the University of KwaZulu-Natal Biomedical Research Ethics Committee, a retrospective comparative observational study was conducted at King Edward VIII Hospital in Durban. The medical charts of the patients who satisfied the inclusion criteria were reviewed. These were determined from the 2008 labour ward operating theatre register.

The inclusion criteria for the study were parurients with a diagnosis of severe pre-eclampsia who presented for emergency Caesarean section. Severe pre-eclampsia is defined as pre-eclampsia with one or more of the following: systolic blood pressure of $\geq 160$ mm Hg, or diastolic blood pressure of $\geq 110$ mmHg on two or more occasions, six hours apart; proteinuria, < 5 g in 24 hours, or 3+ or greater on dipstix; oliguria < 500 ml in 24 hours; pulmonary oedema; liver function impairment; visual or cerebral disturbances; epigastric or right upper quadrant pain; decreased platelet count and HELLP syndrome or intrauterine growth restriction.\textsuperscript{7}

Exclusion criteria comprised patients with antepartum haemorrhage and cardiac disease (as these would impact on haemodynamic variables), patients who had received regional anaesthesia who needed to be converted to general anaesthesia (GA) (as this would confound data interpretation), and patients whose charts did not satisfy the study objectives due to poor recordkeeping.

The charts of 95 patients were reviewed. Important data were missing from seven of the charts and these were excluded. Four cases included conversion from regional to GA and were excluded. Therefore, 84 charts were analysed and included in the study. Collected preoperative data included maternal demographics, preoperative maternal condition as assessed by maternal haemodynamics (blood pressure and heart rate on admission to the labour ward), maternal medication (antihypertensives and magnesium sulphate), maternal blood results, maternal comorbidities and indication for Caesarean section.

Intraoperative data included preinduction maternal blood pressure and heart rate; type of administered anaesthesia; maternal haemodynamic changes, namely the highest and lowest blood pressure [including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and heart rate recorded from induction of anaesthesia to the end of surgery]; amount and type of intravenous fluid used; details of vasopressor drug usage; and neonatal birthweight and outcomes as assessed by neonatal condition on delivery (live or stillbirth and Apgar scores).

Postoperative data included maternal outcomes (maternal level of postoperative care and any maternal mortality or morbidity), as well as any neonatal mortality or morbidity.

With regard to statistical analysis, analysis of variance (ANOVA) was used to determine quantitative variables. Pearson’s chi-test was used to establish categorical variables. Multivariate analysis was used to control for any confounders. Logistical regression was used to determine binary outcomes. Multiple linear regression was used to establish quantitative outcomes. Data that were not normally distributed were compared between groups using the Mann-Whitney U test. A p-value < 0.05 was considered to be statistically significant.

**Results**

Of the 84 charts reviewed, 58 patients received spinal anaesthesia (69%), 21 patients received GA (25%), four patients received epidural anaesthesia (4.8%) and one patient received combined spinal epidural (CSE) anaesthesia (1.2%).

Figure 1 shows the distribution of the various types of anaesthesia.

Because of the much smaller proportion of patients who received CSE and epidural anaesthesia, only the spinal anaesthesia and GA group of patients were statistically compared. The results from the CSE and epidural groups were included mainly for descriptive purposes.
The demographic data are listed in Table I. All of the patients in the study were of African ethnicity, except for one Asian patient in the epidural group. Primigravidae constituted 32.8% of the spinal anaesthesia group and 52.4% of the GA group.

Table II demonstrates the various maternal co-morbidities in the spinal anaesthesia and GA groups.

Table III demonstrates the maternal platelet count range.

Table IV shows the number of patients who received the relevant drug in each group and the corresponding percentage. Magnesium sulphate was administered as per Sibai regimen which is discussed later. Alpha-methyldopa, nifedipine, hydralazine and prazosin were administered orally. Labetalol was administered as an intravenous infusion and titrated to blood pressure.

All the patients received a prophylactic dose of cefoxitin preoperatively. A 5 U intravenous bolus of oxytocin was administered post-delivery, followed by an intravenous infusion of 15 U of oxytocin. Currently, our unit uses a lower bolus dose of oxytocin. There is evidence to support a bolus dose of up to 3 U of oxytocin in patients who are at low risk of acquiring uterine atony. Patients who received spinal anaesthesia received 9 mg hyperbaric bupivacaine with 10 μg of fentanyl intrathecally. Administered drugs in the GA group varied and depended on patient factors, as well as drug choice of the anaesthetist concerned.

Table V shows the various indications for Caesarean section. All patients in the study had severe pre-eclampsia. Worsening of the severe pre-eclampsia may have been an indication for a Caesarean section.

Table VI compares the various maternal haemodynamic variables between the spinal anaesthesia and GA groups. It is interesting to note that the peak intraoperative SBP was significantly higher in the GA group, compared to the spinal anaesthesia group. In general, in all of the categories in Table VI, the blood pressure was higher in the GA group. In Table VII, it can be seen that intraoperatively, the DBP reached values of ≥ 110 mmHg in 42.9% of the GA cases, as opposed to 10.3% of the spinal anaesthesia cases. This reflected a statistically significant difference. Clinically, significant maternal hypotension may occur at an SBP of
< 100 mmHg (or even higher, depending on autoregulation) or a reduction in MAP of > 20% from baseline. Intraoperative SBP of < 100 mmHg was recorded in a high proportion (19%) of GA cases and in 27.6% of spinal anaesthesia cases, but with no statistically significant difference being noted between the two groups. It is possibly more significant that there was a > 20% fall in MAP from baseline in 66.7% of GA and in 75.9% of spinal anaesthesia cases, but with no statistically significant difference. Vasopressor drugs, including ephedrine and phenylephrine, were often used intraoperatively in 14.3% of GA and in 27.6% of spinal anaesthesia cases. Intraoperative blood product usage was significantly higher in the GA group (66.7%), compared to the spinal anaesthesia group (3.4%).

Table VIII demonstrates the intraoperative vasopressor usage. Ephedrine was the only vasopressor that was used in the GA group. Phenylephrine was used in 10 out of 16 spinal anaesthesia cases, and ephedrine was used in 11 out of 16 spinal anaesthesia cases. (Ephedrine and phenylephrine were used in combination for five of the spinal anaesthesia cases.) The mean ephedrine dose used per case was 21.1 mg in the spinal anaesthesia group, and 23.3 mg in the GA group. The mean phenylephrine dose per case was 242.5 μg in the spinal anaesthesia group.

The results from Table IX should be viewed with caution, as only four patients received an epidural anaesthetic. One patient received a CSE anaesthetic. No patients in either the epidural or CSE group had an intraoperative SBP that was > 180 mmHg, or a DBP > 110 mmHg. In both groups, no intraoperative heart rates were above 120 beats per minute or < 60. There was no intraoperative colloid usage in either group.

Table X compares the maternal outcomes in the spinal anaesthesia and GA groups. 89.7% of patients in the spinal...
Table X: Maternal outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Spinal anaesthesia</th>
<th>General anaesthesia</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High care</td>
<td>52 (89.7%)</td>
<td>21 (100%)</td>
<td>0.186</td>
</tr>
<tr>
<td>Morbidity</td>
<td>1 (1.7%)</td>
<td>0</td>
<td>0.734</td>
</tr>
</tbody>
</table>

anaesthesia group, and all the patients in the GA group, were admitted to the high care unit postoperatively. The remainder of the patients in the spinal anaesthesia group were admitted to the general ward. There were no intensive care unit admissions. There was no mortality in either group, but one patient in the spinal anaesthesia group developed post partum eclampsia that resolved uneventfully with therapy.

Three patients (75%) in the epidural group and one patient in the CSE group were admitted to the high care unit postoperatively. There was no mortality in either group, but one patient in the epidural group developed postoperative pulmonary oedema that resolved with treatment.

The Apgar scores at one and five minutes in Table XI are reported as the median value (with the range in parenthesis). An Apgar score of < 7 at one or five minutes occurred in 66.7% of the GA cases. This was significantly higher than the 19% in the spinal anaesthesia group. The mean neonatal birthweight was lower in the GA group, compared to the spinal anaesthesia group. Neonatal morbidity or mortality (inclusive of stillbirths) occurred in 33.3% of GA cases. This was significantly higher than the 10.3% that occurred in the spinal anaesthesia group. Three of the six neonatal morbidity cases in the spinal anaesthesia group required ventilation post-delivery, but all of these neonates recovered uneventfully. Of the remaining three cases in the spinal anaesthesia group, one was a stillbirth and two were early neonatal deaths. Three of the seven cases in the GA group required ventilation post-delivery. All of these neonates recovered uneventfully. Of the remaining four cases in the GA group, three were stillbirths and one was an early neonatal death. There were no neonatal morbidities or mortalities in both the epidural and CSE groups.

Table XI: Neonatal outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Spinal anaesthesia</th>
<th>General anaesthesia</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillbirths</td>
<td>1 (1.7%)</td>
<td>3 (14.3%)</td>
<td>0.055</td>
</tr>
<tr>
<td>Apgar at 1 minute</td>
<td>8 (0-9)</td>
<td>5 (0-8)</td>
<td>0.004†</td>
</tr>
<tr>
<td>Apgar at 5 minutes</td>
<td>9 (0-10)</td>
<td>8 (0-9)</td>
<td>0.015†</td>
</tr>
<tr>
<td>Apgar score &lt; 7</td>
<td>11 (19%)</td>
<td>14 (66.7%)</td>
<td>0.01†</td>
</tr>
<tr>
<td>Mean birthweight (kg)</td>
<td>2.1 ± 0.7</td>
<td>1.5 ± 0.8</td>
<td>0.512</td>
</tr>
<tr>
<td>Morbidity and/or</td>
<td>6 (10.3%)</td>
<td>7 (33.3%)</td>
<td>0.03†</td>
</tr>
</tbody>
</table>

†Statistically significant value

Discussion

There has been some reservation about the use of spinal anaesthesia in patients with severe pre-eclampsia, because of concerns about a precipitous reduction in blood pressure following sympathetic tone.1 However, over the last decade, regional anaesthesia has been used with increasing frequency in this group of patients. Furthermore, there is growing evidence6,4,9,10 to support the use of regional anaesthesia. In some studies, regional anaesthesia has been shown to be both safer and superior to GA.10

Dyer et al showed that patients with severe pre-eclampsia undergoing Caesarean section were found to have clinically insignificant changes in cardiac output during spinal anaesthesia.9 Aya et al conducted an interesting study that compared the haemodynamics of spinal anaesthesia in treated and fluid-replete patients with severe pre-eclampsia and those who were normotensive, all having a Caesarean section. The results showed a greater risk of hypotension and greater vasopressor requirements in the normotensive group.2 Studies that have compared spinal anaesthesia vs. epidural anaesthesia in patients with severe pre-eclampsia have shown varying results. Some have favoured epidural anaesthesia, while others have shown similar haemodynamic changes and neonatal outcomes.3,4,5,11 Studies that compared regional and GA in patients with pre-eclampsia have also shown varying results. Some reported poorer maternal and neonatal outcomes in the general anaesthetic group, while others indicated similar maternal and neonatal outcomes when a comparison was made between the two groups.3,9,12

It can be seen that the results from these studies are variable. Also, in most of these studies, there was adequate time for preoperative optimisation. Thus, it was difficult to extrapolate the results of such studies and apply them to our local patient population. We hypothesised that our patient population was very different from the patient populations in most of the referenced studies, and also that our patients would present with a greater degree of disease severity. With this in mind, the impact of these factors on the choice of anaesthetic administered, the intraoperative haemodynamic changes and the maternal and neonatal outcomes were sought.

The majority of patients received a spinal anaesthetic (69%), and 25% received a GA. A minority of patients received an epidural or CSE anaesthesia. This may relate to the emergency setting where time may not permit the insertion of an epidural. Also, an epidural service was not always available to patients due to staffing shortages. Theoretically, there are many advantages to having a regional anaesthesia over a GA. Regional techniques avoid airway manipulation...
which can be difficult in these patients, while the analgesia offered by regional anaesthesia is excellent. Drug exposure to the foetus is limited during a regional technique, which is not the case during GA.

When comparing the haemodynamic consequences, it was noted that blood pressure (preoperative and intraoperative peaks and troughs) was higher in the GA group. Statistical significance was noted for the peak intraoperative SBP only (Table VI). Importantly, patients with pre-eclampsia are at increased risk of intracranial bleeds. High-peak intraoperative SBP further increases this risk. Therefore, limiting or preventing episodes of high-peak intraoperative SBP is of paramount importance during anaesthesia. Episodes of intraoperative DBP ≥ 110 mmHg occurred in 42.9% of GA cases. This was significantly higher than the 10.3% that occurred in the spinal anaesthesia group.

Clinically significant maternal hypotension, as depicted by SBP < 100 mmHg, occurred in 19% of GA cases and in 27.6% of spinal anaesthesia cases. A reduction of > 20% from baseline MAP was reported in 66.7% of GA cases and in 75.9% of spinal anaesthesia cases. Even though statistically significant outcome differences could not be demonstrated between the spinal anaesthesia and GA groups, these episodes of clinically significant maternal hypotension occurred at an alarmingly high rate, as well as in the few epidural and CSE cases (Table IX). This may be because of the emergency nature of the cases, where due to time constraints, patients may not have been adequately volume resuscitated, or blood pressure may not have been adequately treated. No obvious surgical causes were documented to account for these episodes of hypotension. Intraoperative vasopressor usage was not significantly different between the two groups. Ephedrine was the only vasopressor that was used in the GA group. As this was a retrospective study, it can only be speculated that the reasons for this may relate to the patients’ heart rates, or the attending anaesthetist’s personal preference or concern about the effects on uterine blood flow. However, studies have demonstrated less neonatal acidosis with phenylephrine than with ephedrine. It is unlikely that the differences in maternal haemodynamics and neonatal outcomes between the spinal anaesthesia and GA groups can be solely attributed to this vasopressor difference, but rather to a combination of factors, as discussed previously.

With regard to fluid therapy, blood product usage was significantly higher in the GA group at 66.7%, but this may relate to the large proportion (66.7%) of patients in the GA group who developed HELLP syndrome, for which platelet transfusions were administered. Although it was not of statistical significance, colloid usage was lower in the spinal anaesthesia group (Table VII). Other haemodynamic variables were similar when comparing the two groups (Table VII).

A large proportion of patients (Table X) were admitted to the high care unit postoperatively, but this correlated with the need for completion of magnesium sulphate therapy. The Sibai regimen was used, namely 6 g loading dose, followed by an infusion of 2 g/hour for 24 hours. There were no maternal intensive care unit admissions, and there was no maternal mortality in any of the groups. Maternal morbidity occurred in one spinal anaesthesia group patient (Table X). There were no significant differences between the spinal anaesthesia and GA groups with respect to maternal outcomes.

Neonatal gestational ages were almost four weeks less, and birthweights were mostly smaller, in the GA group (Table XI). Generally, the Apgar score at one minute was also lower in the GA group. An Apgar score of < 7, at one or five minutes, is an accepted criterion to identify if a neonate is at risk of hypoxia. Apgar scores of < 7 occurred in a worrisome 66.7% of GA cases. This was significantly higher than that in the spinal anaesthesia group (19%). Neonatal morbidity and mortality occurred in an alarming 33.3% of GA cases. This was significantly higher than that in the spinal anaesthesia group (10.3%). Thus, neonatal outcomes appeared to be poorer in the GA group, despite a much larger proportion of patients in the spinal anaesthesia group having been identified as having evidence of foetal distress (Table V). Other confounding factors to consider were the lower gestational age (Table I) and lower birthweight (Table XI) in the GA group, which were not significantly lower than that in the spinal anaesthesia group statistically. However, the clinical significance of this difference may have affected neonatal outcomes. Also, the greater severity of pre-eclampsia in the GA group (Tables VI and VII) may have contributed to the neonatal outcomes.

**Study limitations**

This was a retrospective study and suffered the limitations that are inherent in such studies. We could not be sure that all potential factors that influenced the outcome were controlled. Patient care may not have been consistent. The preoperative management of blood pressure was not standardised, and fluid therapy, especially crystalloid usage and volume, was poorly documented in patients’ charts. There was great variation in the use of intraoperative drugs, especially in the GA group. We were unable to verify that all the blood pressures that were recorded were correct. Despite these limitations, this study provided invaluable information.
Conclusion

In our study, the majority of patients received spinal anaesthesia. It was difficult to draw conclusions from the epidural and CSE groups, due to the small number of cases. Episodes of maternal hypotension occurred at surprisingly high rates in both the spinal anaesthesia and GA groups during Caesarean section. This may relate to the emergency nature of the cases, where patients may not have been adequately optimised preoperatively. Lack of phenylephrine usage and low colloid usage in the GA group may also have been contributing factors. Maternal morbidity and mortality were not significantly different between the spinal anaesthesia and GA groups. However, neonatal outcomes were poorer in the GA group, with smaller birthweights, lower Apgar scores (with a large proportion scoring < 7), and a significantly higher morbidity and mortality. It must be highlighted that this does not imply a causal relationship between neonatal outcomes and choice of anaesthesia. It was probably a mere association as the choice of anaesthesia was undoubtedly influenced by the more ill parturients in the GA group who produced smaller and more premature neonates. This study provides support for spinal anaesthesia as the anaesthetic of choice in patients with severe pre-eclampsia, provided there is no contraindication. However, the episodes of intraoperative maternal hypotension occurred at surprisingly high rates.

Conflict of interest

There was no conflict of interest.

References