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ABSTRACT

Hypotension associated with spinal anaesthesia for caesarean delivery can have deleterious effects on the fetus. The objective of our study was to investigate the prophylactic phenylephrine infusion for prevention of hypotension during spinal anaesthesia for caesarean delivery. 120 parturients consenting for the study, posted for elective caesarean delivery, were included in the study and randomly allocated into two groups. Immediately after intrathecal injection, phenylephrine was started at 100µg/min(n=60) until uterine incision. Systolic arterial pressure (SAP), mean arterial pressure (MAP), heart rate, ECG and SpO2 were recorded at every 3 minutes interval until uterine incision. A control group (n=60) received normal saline infusion at 1ml/min, starting immediately after intrathecal injection until uterine incision. Parturients received intravenous bolus phenylephrine when the SAP was <80% of baseline or <100 mmHg. Bradycardia was defined as heart rate < 50 beats/min. Phenylephrine decreased the incidence (0[0%] of 60 versus 31[52%] of 60) and number of episodes (0 versus 31; p<0.001) of hypotension compared with control(0.0001). Heart rate progressively decreased over time in the infusion group compared with the control.

Conclusion: Prophylactic phenylephrine infusion is a simple and effective method of maintaining blood pressure during spinal anaesthesia for caesarean delivery.

KEYWORDS: Caesarean delivery, spinal Anaesthesia, hypotension

INTRODUCTION:

Spinal anaesthesia for caesarean delivery is frequently associated with hypotension (up to 60-70%) especially without any prophylactic therapy which can have deleterious effects on the fetus [1]. The primary cause of hypotension may be sympathetic blockade leading to vasodilation and relative hypovolemia [2]. This sympathetic nerve blockade is exaggerated by the physiological changes during pregnancy [3]. Hypotension due to spinal anaesthesia is usually defined as a decrease in systolic blood pressure by more than 20% to 30% or less than 90-100 mmHg of systolic blood pressure [4],[5],[6].

Different modalities have been investigated for the prevention of hypotension including fluid loading, vasopressor or both [7],[8]. Prophylactic phenylephrine is widely considered the choice [8],[9],[10]. Phenylephrine is principally a directly acting stimulator of Alpha-1 adrenergic receptors. It primarily causes vasoconstriction rather than arterial vasoconstriction [11].

Heart rate may decrease following spinal anaesthesia, the causes may include high neuraxial block due to blockade of the cardioaccelerator fibres T1-T4, extensive peripheral sympathectomy(T5-L2) with venous pooling in lower extremity and the abdominal and pelvic viscera [12].

METHODS:

After obtaining approval from the Institutional Ethics Committee, we recruited 120 parturients belonging to ASA physical status I and II, with term singleton pregnancies scheduled to undergo elective caesarean delivery under spinal anaesthesia and divided them into group A and B. by a computer-generated random selection using block randomization with blocks of variable sizes. Concealment of allocation was done by opaque sealed envelope technique. Parturients gave written, informed consent to participate in the study. Patients with contraindications to spinal anaesthesia, pre-existing or pregnancy endocrine disorders, or known fetal abnormalities were excluded.

On the day of operation, a designated O.T technician opened the sealed envelopes, once the patients were shifted to the operation theatre. After allocation, the technician also prepared the drugs used in our study. Two identical syringes were prepared containing either phenylephrine 100µg/ml or normal saline. A designated resident, who was not involved in the pre-operative and intra-operative assessment of patient parameters as well as analysis of the study, noted the parameters of the patients and started the infusion after the induction of spinal anaesthesia.

Group 1 consisted of 60 parturients receiving prophylactic phenylephrine infusion at the rate of 1ml/min 100µg/ml immediately after induction of spinal anaesthesia till uterine incision and Group 2 consisted of 60 parturients receiving normal saline infusion at the rate of 1ml/min immediately after induction of spinal anaesthesia till uterine incision

All parturients were subjected to detailed pre-anesthetic checkup with clinical history and systemic examination with routine and specific investigations and they were explained in detail about the procedure of the study. Parturients were kept nil orally for 6 hours preoperatively. Monitoring in the form of measurement of baseline heart rate, ECG, non-invasive arterial blood pressure and peripheral oxygen saturation was done pre-operatively. Intraoperative access was secured with 18-gauge intravenous cannula in either of the forearms. Baseline systolic, diastolic, mean arterial pressure, ECG, pulse oximetry and heart rate were measured before the induction of spinal anaesthesia. Parturients were kept in the left lateral position with their back parallel to the edge of the operating table, thighs flexed onto the abdomen, with the neck flexed to allow the forehead to be as close as possible to the knees in an attempt to open up the vertebral spaces [13]. After identifying the L3-L4 interspace, spinal anaesthesia was induced with 23 G Quincke’s spinal needle and 0.5% hyperbaric bupivacaine 2.2ml and buprenorphine 0.2ml. Patients were then immediately turned supine. The level of spinal block was confirmed by evaluating the loss of sensation to pain using pin prick method bilaterally in the mid axillary line and motor block using modified Bromage scale [14].

The subarachnoid block, infusion of the study drug was started in either group and continued until uterine incision. Hemodynamic parameters of the parturient including the heart rate, ECG, peripheral oxygen saturation, systolic, diastolic and mean arterial pressure were noted at 3 minutes interval until uterine incision. Episodes of hypotension, hypertension, bradycardia and tachycardia, complications of subarachnoid block including nausea and vomiting were noted. Total rescue doses of phenylephrine used in either group were also noted.

Hypotension was defined as systolic arterial pressure < 80% of the baseline or systolic arterial pressure <100mmHg [15]. Bradycardia was defined as heart rate <50 beats per minute [15]. Injection atropine 0.6mg intravenous was to be given following episode of bradycardia.

STATISTICAL ANALYSIS

Univariate intergroup comparisons were made with the Mann-Whitney U-test. Nominal data were compared by using the X2 test and Fisher’s exact test. Serial changes in SAP and HR were compared by
using analysis of variance for repeated measures. All analyses were performed with SPSS 22.0. Values of $P < 0.05$ were considered statistically significant.

**RESULTS**

Patient characteristics, level of blockade and period of gestation were similar between groups (Table 1). There was no significant difference between the groups with respect to the level of block at the start of surgery ($p=0.6$). Majority of patients in both the groups had blockade till the level of T5. Oxygen saturation was comparable and no patient required supplemental oxygen. The total consumption of phenylephrine was considerably more in the infusion group (median, 1200 µg; interquartile range, 1000–1500 µg) compared with the control group (median, 50 µg; interquartile range, 30–75 µg; $P=0.0001$). Serial analysis of hemodynamic changes showed that Systolic arterial pressure (SAP) was significantly greater over time in the infusion group compared with the control group ($P<0.0001$; Fig. 1) and that HR was significantly slower over time in the infusion group compared with the control group ($P<0.0001$; Fig. 2). Although some patients in the infusion group had relatively slow HRs and two patients had one or more episodes of bradycardia (HR, <50 bpm), in each case this was associated with an increase in SAP to more than baseline. In all of these cases, HR increased after the phenylephrine infusion was stopped, and no patient required treatment with atropine. Overall, none of patients in the infusion group had any episode of hypotension, compared with 25 (41.7%) of 60 in the control group ($P<0.0001$), and the number of episodes of hypotension was none in the infusion group compared with the control group (31[52%]; $P<0.0001$; Table 2). 19 of the 25 patients in the control group who had hypotension had only one episode, and 6 had 2 episodes. The minimum SAP recorded was lower in the control group compared with the infusion group. In the first few minutes after intrathecal injection, SAP increased slightly more than baseline in some patients in the infusion group, whereas SAP decreased in all patients in the control group (Fig. 1). The incidence of reactive hypertension was more frequent in the infusion group compared with the control group, but no patient complained of symptoms. The maximum SAP recorded was greater in the infusion group compared with the control group (Table 2). There was a nonsignificant trend toward a less frequent incidence of nausea and vomiting in the infusion group compared with the control group (0 of 60 vs 09 [15%] of 60). All episodes of nausea or vomiting were transient, and all were related to decreases in SAP. None of the patients required antiemetic in any form for this complaint.

**Table 1** Baseline characteristics and level of blockade

<table>
<thead>
<tr>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (YEARS) MEDIAN (INTERQUARTILE RANGE)</td>
<td>25(22.7-27.2)</td>
<td>24.5(22-27)</td>
</tr>
<tr>
<td>WEIGHT (KG) MEDIAN (INTERQUARTILE RANGE)</td>
<td>58(56-59)</td>
<td>58(57-59)</td>
</tr>
<tr>
<td>HEIGHT (CM) MEDIAN (INTERQUARTILE RANGE)</td>
<td>158(157-159)</td>
<td>158(157-159)</td>
</tr>
<tr>
<td>LEVEL OF BLOCKADE (NO. OF PATIENTS)</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>T4</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>T6</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>PERIOD OF GESTATION (MONTHS) MEAN ± SD</td>
<td>271.6 ± 5.48</td>
<td>270 ± 4.38</td>
</tr>
</tbody>
</table>

**Table 2** Details of Hypotension Episodes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 60)</th>
<th>Group 2 (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of hypotensive recordings</td>
<td>0</td>
<td>50(100%)</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>19(31.0%)</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>06(10%)</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Minimum recorded systolic arterial blood pressure (mm Hg) median (IQR)</td>
<td>140(94-110)</td>
<td>98(72-92)</td>
</tr>
</tbody>
</table>

**Figure 1** Serial changes in systolic arterial blood pressure. Data are mean and SD. Changes over time were significantly different between groups ($P<0.0001$).

**Figure 2**. Serial changes in heart rate. Data are mean and SD. Changes over time were significantly different between groups ($P<0.0001$).

**Figure 3** Serial changes in mean arterial blood pressure. Data are mean and SD. Changes over time were significantly different between groups ($P<0.0001$).

**DISCUSSION**

Our study confirmed that starting a prophylactic infusion of phenylephrine immediately after the induction of spinal anaesthesia for caesarean delivery is effective at reducing the incidence, frequency, and severity of hypotension. Though different doses of phenylephrine in the form of infusion or bolus has been experimented within different studies, in this study, we decided to use phenylephrine infusion at the rate of 1ml/min (in a strength of 100µg/ml) starting immediately after giving spinal anaesthesia until uterine incision. Similar doses were also used in studies by Cooper DW et al [16], Ngan Kee et al [15], Pinto V et al [17], Kee WD et al [18], Ansari T et al [19], Liu H et al [20], Mon W et al [21]. Most other strategies for decreasing the incidence of hypotension during spinal anaesthesia for caesarean delivery have not proved to be reliable. In our study, none of the patients in group A had hypotension as compared to almost 52% patients in group 2 who had hypotension. According to Somboonviboon et al [22], the incidence of hypotension following spinal anaesthesia is reported to be as high as 52.6%. Sahoo T et al [23] reported an incidence of hypotension to be as high as 50-60 % in non-labouring patients undergoing elective caesarean section under spinal anaesthesia. In a study conducted by Ngan Kee et al [15], the incidence of hypotension in patients receiving prophylactic phenylephrine infusion at the rate of 100µg/min was 23 % and in the control group it was 88%, but none of the patients in group 1 of our study had hypotension. This was probably due to the fact that in the study conducted by Ngan Kee et al [15], the prophylactic phenylephrine infusion was continued till first 3 minutes of starting the spinal anaesthesia, after which the infusion was either stopped or continued according to a predefined protocol based on the systolic arterial pressure measurement each minute. After each minute
measurement of systolic arterial pressure, the infusion was stopped if the systolic arterial pressure was more than baseline, and it was continued or restarted if the systolic arterial pressure was less than or equal to baseline. So, hypotension in the phenylephrine infusion group occurred after the initial infusion was stopped. Although the infusion was restarted, when the systolic arterial pressure decreased to less than baseline again, transient hypotension occurred as phenylephrine has a latency for effect. But we continued phenylephrine infusion at the rate of 10 µg/min until uterine incision, so none of the patients in group I of our study experienced hypotension. We found that maternal HR was statistically significantly slower in the infusion group compared with the control group, and two patients in the infusion group had episodes of bradycardia (HR < 50 bpm). However, because these cases were not associated with hypotension, the likely mechanism was a baroreceptor reflex. There were no associated adverse clinical sequelae, and in both cases the HR increased soon after the phenylephrine infusion was stopped. Although there was a difference in the incidence of nausea and vomiting between groups, our sample size was small, and the study was not powered for determining differences in this outcome.

The limitations of our study are:
1. The study was conducted until uterine incision after which the phenylephrine infusion was stopped. Therefore, the effect of phenylephrine on further management of hemodynamics was not assessed.
2. We used only continuous infusion of phenylephrine to investigate its efficacy in preventing and reducing the incidence and episode of hypotension. The effect of different doses of phenylephrine on hemodynamic parameters could not be assessed.
3. It is a single hospital-based study for the purpose of evaluation of hemodynamic parameters. A multi hospital-based study would have been considered to be better.
4. Effect of such high total doses of phenylephrine on fetal acid-base status was not assessed.

In conclusion, these data suggest that a prophylactic phenylephrine infusion is an effective and simple method of reducing the incidence and magnitude of hypotension during spinal anaesthesia for caesarean delivery, with no adverse effect on neonatal outcome. Further work investigating more flexible regimens would be of interest and might result in the complete elimination of hypotension.

REFERENCES