Original contribution

Injection speed of spinal anaesthesia for Caesarean delivery in Asian women and the incidence of hypotension: A randomised controlled trial

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Abstract

Study objective: The purpose of this investigation was to determine if a slower speed of spinal anaesthesia injection would reduce the incidence of hypotension.

Study design: Randomised controlled trial.

Setting: Tertiary level hospital in Malaysia.

Patients: 77 patients undergoing elective Caesarean delivery.

Intervention: Differing speeds of spinal injection.

Measurements: Systolic blood pressure was assessed every minute for the first 10 min and incidence of hypotension (reduction in blood pressure of >30% of baseline) was recorded. The use of vasopressor and occurrence of nausea/vomiting were also recorded.

Main results: 36 patients in SLOW group and 41 patients in FAST group were recruited into the study. There was no significant difference in blood pressure drop of >30% (p = 0.497) between the two groups. There was no difference in the amount of vasopressor used and incidence of nausea/vomiting in both groups.

Conclusion: In our study population, there was no difference in incidence of hypotension and nausea/vomiting when spinal injection time is prolonged beyond 15 s to 60 s.

Trial registration: ClinicalTrials.gov NCT02275897. Registered on 15 October 2014.

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1. Introduction

Spinal anaesthesia for patients undergoing Caesarean delivery is now the preferred technique as compared to general anaesthesia [1]. One of the reasons for this is due to the increased risk in securing an airway for pregnant mothers [1]. It also allows the mother to be awake and participate in the birthing experience. A common side effect of spinal anaesthesia is hypotension [2]. This can lead to other problems including nausea and retching. Severe hypotension threatens the well-being of the mother and the foetus due to impaired blood flow.

Finding the balance between achieving adequate block height for surgery and maintaining blood pressure can be a challenge in obstetric patients. It has been postulated that the speed of injection should play a role. Previous studies attempted to answer this [3–5]. However, while some studies showed a correlation between speed and block height, another did not. Furthermore, the type of anaesthetic, volume, and patient height in the sample population of the previous studies limited its application as patients in our setting are generally shorter.

In this study, we hypothesize that a slower injection speed would result in less incidence of hypotension. We also analysed the vasopressor utilization and incidence of nausea/vomiting.

2. Methods

This clinical study was registered at clinicaltrials.gov (ID no. NCT 02275897). After obtaining approval from the Medical Research and Ethics Committee of the Ministry of Health, Malaysia (Chairperson Dato’ Dr. Chang Kian Meng; NMRR-13-608-16854 dated 25 November 2013), patients aged above 18 with singleton pregnancy at term and American Society of Anaesthesiologists (ASA) physical status I to II, scheduled for elective (non-emergent) Caesarean delivery at Hospital Tengku Ampuan Rahimah, Klang, Selangor, Malaysia were evaluated for eligibility to be enrolled in the study from November 2013 to November 2014. Patients were excluded if their height was <150 cm or >180 cm, weight of >100 kg, had a history of severe pre-eclampsia,
baseline systolic blood pressure (sBP) of < 90 mmHg or > 150 mmHg, or any contraindication to spinal anaesthesia which include inability to give consent, or refusal to participate.

A statistician was consulted to determine the sample size. Calculations based on a study by Simon L et al. showed that 42 patients per group were needed to detect a statistically significant difference between the groups with \( \alpha = 0.05 \) and a power of 80%.

Using a concealed allocation method, a computer generated block randomization was used to allocate patients into 2 groups, SLOW and FAST. Upon obtaining written informed consent, patients were randomly assigned to either the SLOW or FAST group. Group allocations were concealed in a sealed opaque envelope and were opened by an anaesthesiologist who later administered the spinal anaesthetic. A second anaesthesiologist or assistant who was blinded to group allocation was tasked to collect data.

Prior to the spinal anaesthetic, application of routine monitoring i.e. ECG, SpO2, NIBP was done and values recorded. All patients received co-administration of intravenous Ringer’s lactate solution (B Braun, Melsungen, Germany) 500 mL via an 18G intravenous cannula. Patient was placed in sitting position and the skin area was disinfected using povidone iodine and draped. After infiltration of the skin with local anaesthetic 2% lignocaine, spinal anaesthesia was performed using a 27G pencil-tipped needle (Pencan®, B Braun, Melsungen, Germany) at the L3-L4 level. All patients received 9.5 mg of 0.5% heavy bupivacaine, 15 μg of fentanyl and 100 μg of morphine with a total volume of 2.3 mL. (The dose being reflective of local practices.)

The speed of injection was timed by use of a Smartphone app: Pro Metronom, iOS, by Xiao. The software was first tested for its accuracy by determining if the amount of beats corresponded to the time as determined by a stopwatch. For the SLOW group, the injection time to complete 2.3 mL was 60 s. The metronome was set with a beat count of 4 at 92 bpm (total 23 beats of 4 over 1 min i.e. 0.1 mL was injected every 4th beat). For the FAST group, the injection time to complete 2.3 mL was 15 s. The metronome was set with a beat count of 2 at 184 bpm (total 23 beats of 2 over 15 s, i.e 0.1 mL was injected every 2nd beat). The actual injection time for both groups was also recorded. The syringes used have increments of 0.1 mL.

After spinal injection had been completed, the patients were placed supine with a left lateral tilt. Non-invasive blood pressure and heart rate was measured at 1-minute intervals for the first 10 min, and at 5-minute intervals until 30 min after spinal injection. Block height was determined by loss of cold sensation 3 min later just prior to skin incision. Surgery was allowed to proceed if it achieved thoracic T6 level and above.

A patient was considered to have hypotension when systolic blood pressure decreased to < 90 mm Hg or decreased > 30% of baseline. Hypotension was managed by the administration of a vasopressor, which was either intravenous phenylephrine 100 μg or ephedrine 6 mg by the attending anaesthesiologist.

The amount of vasopressor used and time of administration and incidence of nausea/vomiting was recorded. In cases of a failed spinal anaesthesia or inadequate anaesthesia, the patient was converted to a general anaesthetic and withdrawn from the study.

Simon L et al. in their study indicated that the probability of hypotension among patients receiving a fast injection speed was 0.92 and those receiving a slow injection speed was 0.68. Calculations based on this study showed that 42 patients per group were needed to detect a statistically significant difference between the groups with \( \alpha = 0.05 \) and a power of 80%.

Data analysis was done using SPSS version 21 (SPSS Inc., Chicago, Illinois, U.S.A). We determined if there was any significant association between each group and the severity of hypotension using the Chi-square test. We also analysed the relationship between absolute injection time and the amount of blood pressure drop, using a Pearson correlation test. Means were compared using the t-test.

### 3. Results

A total of 94 subjects were evaluated for eligibility for the study, from which 17 were rejected due to various reasons (short height, high body weight, high baseline blood pressure). None were due to patient withdrawal from the study. There was a single block failure, which had to be converted to general anaesthesia. All the others had satisfactory block until the completion of surgery. A total of 77 patients were randomised, of which 36 patients were recruited as part of the SLOW group, while 41 were recruited for the FAST group. While the number of patients recruited was slightly fewer, it was not far from the calculated sample size.

There was no difference in the demographics and baseline systolic blood pressure between the two groups. The mean injection time for the FAST group was 19.5 ± 4.0 s and 60.6 ± 4.3 s for the SLOW group (refer Table 1).

We calculated the percentage drop in blood pressure between the baseline systolic blood pressure and the lowest systolic blood pressure in the first 10 min after administering the spinal anaesthetic (Fig. 1). Comparing the two groups, there was no significant difference in the incidence of blood pressure drop of >30% (\( p = 0.497 \)) using the Pearson Chi-Squared test (refer Table 2). There was also no significant correlation between absolute injection times versus percentage drop in blood pressure (Pearson correlation of 0.06, \( p = 0.604 \)) (refer Fig. 2). We found no difference in terms of mean drop in systolic blood pressure and the time to lowest systolic blood pressure between the two groups.

Regarding the use of vasopressors between the 2 groups, analysis did not reveal any significant difference (\( p = 0.56 \)). For simplification during analysis, 1 unit of vasopressor was equal to every 100 μg of phenylephrine, or 6 mg of ephedrine. This was done to account for the fact that some patients required the use of both agents while some required only one. There were 33 patients who were given vasopressors, 18 belonged to the FAST group which required 1.9 ± 1.1 units, while 15 belonged to the SLOW group which received 1.8 ± 1.4 units.

We also analysed the relationship between percentage drop in blood pressure before the first dose of vasopressor was used. Analysis showed no significant difference between the two groups (\( p = 0.14 \)) (refer Table 3). Only 2 patients had nausea/vomiting. One patient was from the SLOW group and the other was from the FAST group.

### 4. Discussion

Hypotension is a known side effect of spinal anaesthesia and the goal of this study was to investigate if reducing the speed of injection would cause less hypotension to a parturient undergoing spinal anaesthesia for Caesarean section. From the results, it would appear that FAST injection speeds and SLOW injection speeds had similar incidence of hypotension. Thus, prolonging the injection time did not reduce this side effect. It is conceivable however, that giving a bolus push would unnecessarily increase the spread of anaesthesia causing dangerous side effects. Therefore, changing the rate should theoretically have an effect in the extremes of cases, i.e. giving a bolus push versus injecting over 5 min. However, 15 s would seem to be a “slow enough” speed to administer

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient Demographics and baseline systolic blood pressure.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td><strong>FAST (n = 41)</strong></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>31.7 ± 5.3</td>
</tr>
<tr>
<td>Gestation (week)</td>
<td>37.8 ± 0.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.3 ± 9.7</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.55 ± 0.05</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.5 ± 4.5</td>
</tr>
<tr>
<td>Injection time (seconds)</td>
<td>19.5 ± 4</td>
</tr>
<tr>
<td>Baseline sBP (mmHg)</td>
<td>127 ± 13</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD. BMI - body mass index, sBP - systolic blood pressure.
a spinal anaesthetic safely. Note however, that the mean injection time for the FAST group was 19.5 s. This was due to the fact that during the injection, some of the beats from the metronome could have been missed, and therefore causing a slight delay. In spite of this, we felt it was within practical limits for this study, and that the mean time taken in the SLOW group was still at least twice as long as the FAST group. Visual inspection of the scatter plot included should allay concerns of whether they were “different enough” increase.

We chose the time of 10 min for two reasons: First was based on previous observations, whereby hypotension would be at the lowest within the first 10 min. The second reason was that beyond 10 min, we would not have been able to account for hypotension caused by surgical blood loss. Therefore, we wanted to confine it to hypotension attributable to the spinal anaesthetic.

The criteria for classifying hypotension were done after discussion with local consultants. Firstly, a systolic BP of <90 mm Hg is usually defined as hypotension. As to the reduction of 30%, we wanted to have a margin of safety for the patients who had a high normal blood pressure, and that point was set to trigger the administration of a vasopressor in order to avoid circulatory compromise to the patients and foetus.

We also decided that instead of a more detailed analysis of block characteristics, it was more important and practical for us to determine if the final block height was similar and adequate for surgery. Furthermore, previous studies have not shown any increased risk of inadequate block height even when the injection was given over twice as long. On the issue of the direction of the spinal needle orifice; although it was not standardised in this study, we would normally insert all spinal needles with the needle orifice pointing cephalad.

Table 2
Blood pressure characteristics.

<table>
<thead>
<tr>
<th>Group</th>
<th>FAST (n = 41)</th>
<th>SLOW (n = 36)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>sBP drop at least 20% (n)</td>
<td>29</td>
<td>22</td>
<td>0.173</td>
</tr>
<tr>
<td>sBP drop at least 30% (n)</td>
<td>14</td>
<td>15</td>
<td>0.497</td>
</tr>
<tr>
<td>Time to lowest sBP drop (min)</td>
<td>5 ± 3</td>
<td>5 ± 3</td>
<td>0.155</td>
</tr>
<tr>
<td>Mean drop in sBP (mmHg)</td>
<td>33.2 ± 16.5</td>
<td>35.6 ± 22.4</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD or as number. sBP = systolic blood pressure.

Fig. 1. CONSORT flow chart [13].

Fig. 2. Scatter plot showing the relationship between absolute injection time and the percentage systolic blood pressure drop.
We did not expect injection speed to have an impact on neonatal outcomes based on previous studies. As such this data was not collected. However, none of the neonates delivered to the patients recruited had been highlighted to have low Apgar scores.

This leads one to presume a potential benefit, in that anaesthetists would no longer have to try to increase the time of injection beyond what is reasonable. Previous studies that have shown conflicting results were of limited use in our current setting for several reasons. One study had demonstrated significant reduction in the incidence of hypotension but the volume administered was large (4 mL) and the injection time was long (120 s) [3]. It may be that in cases of large volume, the injection time plays a more significant role. Also it would seem impractical to hold on to a spinal needle steadily for 2 min while administering the injection. (based on our observations - most practitioners complete the injection in under 30 s).

Another study compared two injection times of 20 s and 60 s, but the total volume was larger (2.6 mL) [4]. Local practice protocols have tended away from large volume spinal anaesthetics as it has the potential to cause high spinal blocks and hence more side effects. Its study population was also different from ours in that the average height of the subjects was approximately 10 cm taller.

A third study also attempted to answer this question, however the speed of injection used for both groups could still be considered as ‘fast’ because they compared 4 s versus 40 s [5]. The incidence of hypotension was higher (almost 80%) in both groups compared to our study population. This study also defined hypotension at a systolic blood pressure of <100 mm Hg, while in our experience patients can still tolerate a systolic pressure of >90 mm Hg.

Another method that has been postulated to reduce the incidence of hypotension is to administer an intravenous bolus of fluid, either crystalloid or colloid before spinal anaesthesia. This is termed ‘preloading’ a patient. However, a meta-analysis did not show any benefit in preloading, and concluded that the timing of fluid loading does not have an impact on the incidence of hypotension [6]. Furthermore, evidence suggests that there was no advantage of using colloid over crystalloid, and that co-loading (giving intravenous fluids during and after spinal anaesthesia) may have some benefit over preloading [7,8]. It was also common in our practice to administer 500 mL crystalloid by rapid infusion. Therefore, as part of our regimen, we chose to administer a fluid co-load of 500 mL crystalloid.

One patient did suffer a failed spinal anaesthetic. It is impossible to determine if a slow injection speed was the cause. However, we believe it could have been the result of other factors other than the slow injection speed for several reasons. Firstly, failure of spinal anaesthetics have been known to happen, ranging from < 1% to as high as 17% [9-11]. Secondly, it is not uncommon for patients to be left in the sitting position for longer than 60 s, as in the case of combined spinal-epidural anaesthesia. The incidence of failed spinal is low for these patients [12]. Thirdly, previous studies have not shown any increased risk of inadequate block height even when the injection was given over twice as long [3-5].

One possible limitation was the use of vasopressors, which could have falsely reduced the incidence of hypotension in a particular group. However, analysis indicated there was no significant difference with regards to the percentage of blood pressure drop before administration of a vasopressor.

Another possible limitation was that the 1-minute interval measurements were limited to only the first 10 min, with subsequent 5-minute interval measurements. This may not have accounted for blood pressure drops that occurred beyond the 10-minute mark. However, almost all patients developed the ‘lowest systolic blood pressure’ within the first 10 min. Also, the time of 10 min was chosen in order to rule out blood loss (due to ongoing surgery) as a cause of hypotension.

The incidence of hypotension was almost equally distributed between the two groups. Also, the percentage drop in blood pressure, absolute drop in blood pressure, and the amount of vasopressors used also appeared to be similarly distributed among the two groups.

5. Conclusion

From the results of this study, we can conclude that administering a spinal injection over 15–20 s versus 60 s does not increase the rate of hypotension or vasopressor use in ASA class I-II, term singleton parturients undergoing Caesarean delivery. This however is limited to Asian women with a similar height and who receives a similar volume of anaesthetic as the study population. In other words, there is no benefit in increasing the time taken for injection to beyond 15–60 s.

### Table 3

<table>
<thead>
<tr>
<th>Author</th>
<th>SLOW (mL/s)</th>
<th>FAST (mL/s)</th>
<th>Vol (mL)</th>
<th>LA used</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chiang</td>
<td>0.04</td>
<td>0.15</td>
<td>2.3</td>
<td>Heavy bupivacaine 0.5% 9.5 mg Fentanyl 15 μg Morphine 0.1 mg</td>
<td>No difference</td>
</tr>
<tr>
<td>Simon</td>
<td>0.03</td>
<td>0.27</td>
<td>4</td>
<td>Heavy bupivacaine 0.5% 10 mg Sufentanil 2 μg Morphine 0.2 mg</td>
<td>Slow is better</td>
</tr>
<tr>
<td>Bouchnak</td>
<td>0.06</td>
<td>0.18</td>
<td>3.5</td>
<td>Heavy bupivacaine 0.5% 10 mg Fentanyl 2.5 μg Morphine 0.1 mg</td>
<td>Slow is better</td>
</tr>
<tr>
<td>Singh</td>
<td>0.06</td>
<td>0.55</td>
<td>2.2</td>
<td>Heavy bupivacaine 0.75% 12 mg Morphine 200 μg</td>
<td>No difference</td>
</tr>
</tbody>
</table>

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### References


