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*Original Research*

# A Comparison of the Injection Rate of Local Anesthetic during Spinal Anesthesia on the Onset of Sensory Block and Incidence of Hypotension in Caesarean Section

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**Abstract**

**Objective**: The injection rate of the local anesthetic may affect the level and the time of onset of sensory block. The aim of this prospective study was to investigate the effects of two different injection rates of local anesthetic solution (0.5% heavy bupivacaine) on the onset of sensory block, and the incidence and the onset of hypotension in pregnant women undergoing spinal anesthesia for elective Cesarean delivery. **Methods**: A total of 67 patients were randomized into two groups: 120-second injection time (Group Slow; n = 33) and 15-second injection time (Group Fast; n = 34). Maximum level of sensory and motor block, time to sensory block at the level of T6, hemodynamic parameters, use of ephedrine and incidence of side effects were recorded at measurement time points. **Results**: Maximum level of the sensory block was similar in both groups. The time to achieve adequate and maximum sensory block level was shorter in Group Slow(S) ($p$ = 0.004 and 0.037, respectively). Incidence of hypotension was similar, but hypotension occurred earlier in Group Fast(F) ($p$ = 0.011). Requirement for ephedrine and incidence of nausea and vomiting was similar. **Conclusions**: This study reveals that 120-second injection duration during spinal anesthesia is associated with shorter time to achieve the maximum sensory block level and slower onset of hypotension. It means that prolonging the duration of local anesthetic injection to 120-seconds is advantageous compared with 15-seconds in caesarean section.

**Keywords:** spinal anesthesia; injection rate; sensory block; hypotension; pregnant

## 1. Introduction

Today, spinal anesthesia is the most common anesthesia for caesarean section due to the lower exposure of the fetus to drugs, creating fast, profound sensory and motor block as well as low risk of pulmonary maternal aspiration [1,2]. It is quite difficult to predict the level of the sensory block after spinal anesthesia during a caesarean section. The level of sensory block is important for preventing the development of complications from high-level spinal anesthesia and for a painless, comfortable intraoperative period. Many factors (such as the type of local anesthetic, dose, injection site, volume of the subarachonoid space, patient's position and demographic characteristics) play a role for adequate sensory block level in cesarean section with spinal block [3–6]. In addition, the injection rate of the local anesthetic affects the level and the time of onset of sensory block [7,8].

Hypotension is the most common complication during spinal anesthesia. The most feared effect of hypotension in obstetric anesthesia is that it may lead to fetal hypoxia and acidosis by reducing uteroplacental perfusion if not treated in a timely or well [9,10]. These effects are associated with the depth and duration of hypotension [11]. It is also important to prevent as well as to treat hypotension in pregnant women because of its negative effects on both mother and fetus. In the literature, techniques such as preoperative fluid replacement, different positioning techniques, leg wrapping with elastic bandages, and administration of prophylactic parenteral vasopressors have been used to prevent the development of hypotension during spinal anesthesia [12–15]. Adjusting the rate and dose of intrathecal local anesthetic injection is may be a practical way to prevent maternal hypotension due to spinal anesthesia [4,16,17]. However, there are very few studies in the literature on what the injection speed of local anesthetic should be.

In the present study, we hypothesized that there may be a delay in reaching the level of sensory block with the turbulent flow caused by rapid local anesthetic injection. We thought that this delay in sensory block might have an effect on the development of maternal hypotension. For this reason, we aimed to investigate the effects of 2 injection times that not close the each other on the time to achieve a sensory block level and intraoperative maternal hypotension using height and weight-adjusted doses of local anesthetic in elective caesarean section operations.

## 2. Materials and Methods

### *2.1 Patients*

This study is a prospective, randomized (computer-aided), double-blind study conducted after obtaining the

approval of the institutional ethics committee at a tertiary health center. The trial has been registered at clinicaltrials.gov on 10/24/2021. Written informed consent was obtained from all participants. The first participant was recruited on 16 July 2020, and the anticipated completion date was January 2021. The study included a total of 76 female patients with American Society of Anesthesiologists risk score (ASA) II risk and singleton pregnancy aged between 18–40 years status undergoing elective Cesarean delivery. Pregnant women with contraindications for spinal anesthesia; placental anomaly; hypertensive, cardiac, metabolic, vascular, hepatic, renal disease; hemodynamic instability and spinal deformity; severe mental retardation; weight $<$50 kg or $>$110 kg; height $<$140 cm or $>$180 cm; those who were on medications that may cause metabolic and acid-base balance disorders; and emergency patients were excluded from the study.

Before spinal anesthesia, ECG, peripheral oxygen saturation, non-invasive blood pressure monitoring were performed as routine monitoring in all patients, and baseline values were recorded. Basal blood pressure measured automatically and non-invasively from upper right arm with air filled occluding cuff. All of the patients were given a mixture of intravenous Ringer's lactate and hydroxyethyl starch (HES) solution at a dose of 10 mL/kg with the aid of a 22 G intravenous cannula and were premedicated with 1 mg/kg ranitidine and 0.1 mg/kg ondansentron IV before the induction of spinal anesthesia. The injection site of all of the patients was disinfected using povidone iodine in the sitting position. The patients' $L_2$–$L_3$ level was determined by an independent anesthesiologist using ultrasound (FUJIFILM Sonosite, Inc. Bothell, WA, USA). After placing a 5 MHz curved probe of the ultrasound in the sagittal paramedian plane, the sacrum was determined, and five vertebrae were estimated, with the intervertebral spaces counted cranially. During spinal anesthesia, the patients were randomized according to the time when the drug was administered intrathecally and were divided into two groups: 120-second injection time (Group Slow; $n = 33$) and 15-second injection time (Group Fast; $n = 34$). A consort diagram of the study is shown in Fig. 1. Spinal anesthesia was performed by pointing the orifice of a 25 G Quincke needle to the cephalad. A hyperbaric dose of 0.5% bupivacaine was intrathecally administered to all patients, in accordance with the weight and height-adjusted dose regime [18]. During injection, the injection time was followed with the smartphone app Pro Metronome for iOS, by Xiao.

### *2.2 Study Protocol*

The anesthetist was blinded to the groups after the intrathecal administration of anesthesia and followed up with the patients and collected the data. All spinal blocks were performed by one anesthesiologist. The other anesthesiologist responsible for data collection after local anesthesic injection was unaware of patient group allocation. After blocking was achieved, the patients were placed in the supine position, and the uterus was transported to the left by tilting the table 15° to the left. The level of the sensory block was evaluated by bilateral pinprick test, and the level of motor block was evaluated with the Modified Bromage Scale at 2-minute intervals in the first 15 minutes and at 5-minute intervals in the next 30 minutes after the spinal injection. When the level of the sensory block reached an adequate level ($T_6$) the surgery was allowed to start. The patients whose block level did not reach $T_6$ within 10 minutes were excluded from the study.

Considering the moment when the subarachnoid injection began as the onset time, the time to reach the $T_6$ level, maximum sensory block level and motor block (Modified Bromage Scale 3) level were recorded in each patient. Motor block of the lower limbs was assessed using the

Modified Bromage Scale (0 = ability to raise and extended the leg; 1 = inability to raise and extended the leg, ability to flex the knee; 2 = inability to flex the knee, ability to flex the ankle; 3 = inability to flex the knee and ankle).

The peak heart rate (HR) and systolic blood pressure (SBP) values of all patients were recorded before the procedure; immediately after spinal anesthesia; and at 1, 3, 5, 7, 9, 11, 13, 15, 20, 25, 30, 35, 40, and 45 minutes after the procedure. A decrease of systolic blood pressure (SBP) below 90 mmHg and more than a 20% decline in baseline blood pressure were considered as hypotension [11]. Any hypotension was treated with boluses of 5 mg ephedrine each time until the systolic arterial pressure returned to normal ranges ($>$90 mmHg and $>$80% baseline value). In the patients who received ephedrine, the time of first ephedrine administration was considered as the time of first hypotension, and the total amount of ephedrine used was recorded. In addition, the local anesthetic injection rate (mL/s) for each patient was calculated as the ratio of local anesthetic injection volume (mL) to local anesthetic injection times(s) and recorded. As the primary outcome, the earliest local anesthetic injection time to reach the level of sensory block was determined. Secondary outcomes were determined as time to onset of maternal hypotension, frequency of development of maternal hypotension, and amount of ephedrine use.

The sample size was calculated based on a pilot study (n = 12) which demonstrated that with a standard deviation of 1.7 min the time to onset of sensory block $T_6$ levels. After setting the alpha error level at 0.05, beta error level at 0.20, and difference in time at 1.5 min, the required sample size was determined as 26 for each group (slow and fast). By considering the potential data loss, we averaged the total sample size as at least 60 (30 patients for each group), and so the power went over 80%.

### *2.3 Statistical Analysis*

Statistical analyses were performed with SPSS version 17.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive

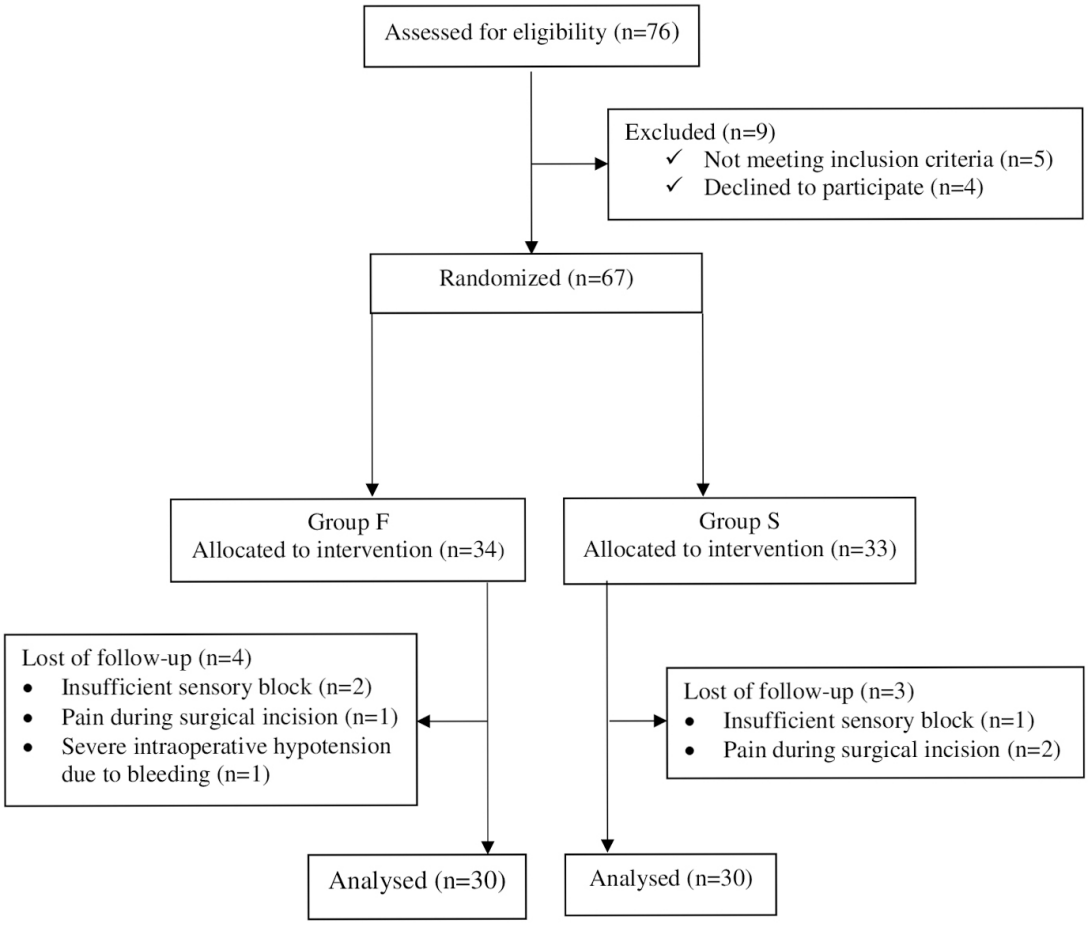


**Fig. 1. Consort flow diagram.**

statistics were given as median frequencies (ASA, nausea and vomiting, and presence of maternal hypotension) and mean ± SD (age, height, weight, body mass index, gestational age, bupivacaine dose, injection rate, baseline SBP, baseline HR, time to onset of hypotension, time to onset of sensory block at $T_6$, and time to onset of maximum level of sensory and motor block) or interquartile range (ephedrine dose requirements and maximum level of the sensory block). The normality of the data was tested with the Shapiro–Wilk test. Independent samples *t*-test was used to compare age, height, weight and body mass index, injection rate, baseline SBP, and baseline HR. Mann-Whitney U test was used to compare maximum level of sensory block, gestational age, bupivacaine dose, ephedrine dose requirements, time to onset of hypotension, time to reach the $T_6$ level of sensory block, and time to reach maximum level of sensory and motor block. Chi-square test was used to compare ASA, incidence of hypotension, incidence of nausea and vomiting. The level of significance was set at $p < 0.05$.

## 3. Results

The study included a total of 67 patients in Group F ($n = 34$) and Group S ($n = 33$). The level of sensory block was below $T_6$ in two patients in Group F and 1 patient in Group S. One patient in Group F and two patients in Group S had severe pain during the surgical incision, which did not respond to IV fentanyl. These patients received general anesthesia and were excluded from the study. Also, one patient in Group F had severe hypotension due to intraoperative bleeding and was excluded from the analysis. Thus, data from a total of 60 patients were analyzed.

The demographic data of all patients included in the final analysis are summarized in Table 1. Briefly, patient characteristics were similar (Table 1).

The time to reach the $T_6$ level of sensory block and maximum level of sensory block was significantly shorter in Group S ($p = 0.004$ and 0.037, respectively, Table 2).

Incidence of hypotension was similar ($p > 0.05$). However, the time to onset of hypotension was significantly shorter in Group F ($p = 0.011$). Requirement for ephedrine and incidence of nausea and vomiting was similar ($p > 0.05$, Table 2).

**Table 1. Patient demographic data and clinic characteristics.**

| Group | Slow (n = 30) | Fast (n = 30) | *p* value |
|---|---|---|---|
| Age (year) | 31.1 ± 4.8 | 31.1 ± 5.9 | 0.981 |
| Weight (kg) | 78.3 ± 3.1 | 79.2 ± 11.8 | 0.782 |
| Height (cm) | 161.4 ± 6.3 | 162.4 ± 7.2 | 0.572 |
| BMI (kg/m$^2$) | 30 ± 4.8 | 29.1 ± 6.3 | 0.535 |
| Gestation week | 38.1 ± 0.8 | 38.4 ± 1.1 | 0.726 |
| Bupivacaine dose (mg) | 1.8 ± 0.1 | 1.8 ± 0.1 | 0.988 |
| Injection rate (mL/seconds) | 0.015 ± 0.001 | 0.131 ± 0.018 | <0.001 |
| Baseline sBP (mmHg) | 124.4 ± 12.3 | 125.3 ± 8.72 | 0.745 |
| Baseline HR (batt/min) | 93.8 ± 12.1 | 93.2 ± 9.8 | 0.840 |

BMI, Body Mass Index; ASA, American Society of Anesthesiologist.

All values are presented as mean and standard deviation, number of cases.

**Table 2. Characteristics of sensory, motor block and hemodynamic variation associated with spinal Anesthesia.**

| Group | Slow (n = 30) | Fast (n = 30) | *p* value |
|---|---|---|---|
| Time to onset of sensory block $T_6$ level (min) [a] | 6.17 ± 1.7 | 7.7 ± 2.1 | 0.004 |
| Max thoracal sensory block level [b] | 2 | 2.25 | 0.064 |
| Time to onset of max. sensory block (min) [a] | 9 ± 0.4 | 11 ± 0.4 | 0.037 |
| Max .motor block starting time (min) [a] | 4.3 ± 0.9 | 4.8 ± 0.8 | 0.087 |
| Maternal hypotension (number) [c] | 11 (36.7%) | 15 (50%) | 0.297 |
| Time to onset of hypotension (min) [a] | 6.7 ± 1.6 | 4.7 ± 1.9 | 0.011 |
| Ephedrine dose requirements (mg) [b] | 4.3 ± 6.2 | 6 ± 6.8 | 0.34 |
| Nausea and vomiting [c] | 9 (30%) | 11 (36.7%) | 0.584 |

Values are presented; [a] mean and standard deviation, [b] interquartile range and [c] number of cases (percentage).

## 4. Discussion

In this prospective, double-blind, randomized study, we found that pregnant women undergoing spinal anesthesia with slow injection rate had an adequate level of sensory block, and the maximum level of sensory block occurred earlier. Although the incidence of hypotension was similar, hypotension occurred later with the slow injection rate.

*In-vitro* studies investigating the effect of local anesthetic injection rate on the spread of local anesthetic solution proposed various mechanisms. Bourke showed that a local anesthetic injection rate above 0.017 mL/sec may cause a turbulent flow [19]. Serpell and Holman showed that in case of slower injection rates, the local anesthetic solution tends to move more cephalad or in the direction of the injection, in contrast to fast injection rates, which tend to cause a disturbed and turbulent flow [20,21]. Similarly, we observed that the time to the level of sensory block at the level of $T_6$ dermatome and the maximum sensory block level was significantly shorter in patients who received a slower injection. However, unlike our study, they did not find a significant difference in terms of the time to reach sufficient sensory block level between slow and fast injection rates in a clinical study [8]. The reasons for this could be the injection rates which were very close to each other and the injection rates in the fast group was not fast enough to generate turbulent flow. Also, in our study the maximum level of the sensory block was not negatively affected. As patients in both groups are of similar height and weight, we used approximately equal amounts of local anesthetic. Standardization was achieved by performing spinal block with heavy bupivacaine in the same direction with the same gauge and length needle in all patients. Thus, the difference in local anesthetic injection speed and block level between the fast and slow groups was prevented in our study.

Studies to date comparing the injection rates of the local anesthetic solution for spinal anesthesia during caesarean sections, determined the appropriate intervertebral space for injection via palpation. The correct identification rate with this method varies between 29–41% [22]. It was also shown that the intervertebral space determined by palpation is 1–2 spaces higher than the level desired to be injected [23]. This may affect the distribution of local anesthetic and the time to onset of the sensory block. Therefore, in our study, we performed all injections at the same ($L_2$–$L_3$) intervertebral space under the guidance of ultrasound, to eliminate differences due to this bias.

There are controversial results in studies on the effects of local anesthetic injection times on maternal hypotension in pregnant women undergoing spinal anesthesia. While some authors have shown that maternal hypotension develops more frequently in patients receiving fast injections [4,16,24], some authors have shown that the injection times have no effect on maternal hypotension [8,25,26]. How-

**Table 3. Summary of the literature investigating the effect of different injection rates of local anesthetics on incidence of hypotension and onset of sensory block.**

| | Injection rate (mL/s) | | | Results | |
|---|---|---|---|---|---|
| Author | Slow | Fast | Volume of local anesthetic (mL) | Incidence of hypotension | Onset of adequate level of sensory block |
| Tugcugil | 0.015 ± 0.001 | 0.13 ± 0.014 | 1.8 ± 0.1 | No difference | Slow is better |
| Chiang [26] | 0.04 | 0.15 | 2.3 | No difference | - |
| Bouchna [4] | 0.06 | 0.18 | 3.5 | Slow is better | - |
| Badheka [25] | - | - | 2.2 (2–2.6) | Slow is better | No difference |
| Singh [8] | 0.06 | 0.55 | 2.2 | No difference | No difference |
| Simon [16] | 0.03 | 0.27 | 4 | Slow is better | No difference |
| Nugroho [24] | 0.027 | 0.2 | 2.5 | No difference | - |

All values are presented as mean and Standard deviation, median value (minimum–maximum).

ever, unlike our study, injection rates were not considered in these studies (Table 3, Ref. [4,8,16,24–26]). We attributed the reason for the different results in these studies comparing slow and fast injection rates to the fact that the injection rates they used were above the rate (0.017 mL/s) that causes turbulent flow in *in-vitro* studies. In our study, we have shown that using an injection rate that does not cause turbulent flow in the slow injection group resulted in the delay of maternal hypotension. Although the exact reason for this is unknown, we conclude that the fast, turbulent flow reached the sympathetic efferent fibers originating from the anterior motor neurons that provide vasoconstriction, thus preventing the local anesthetic from spreading cephalad. We also thought that the patients in the fast injection group did not have time to compensate for the hemodynamic change that occurred after the sudden-onset sympathetic block. Contrary to the theory [27], which states that high block level is associated with high incidence of hypotension, hypotension has occurred later in the slow injection period, which reached the level of early sensory block in our study. This situation is more in line with the theory that hypotension after spinal block in pregnant women related to decrease in systhemic vascular rsistance secondary to artery vasodilation [28,29] with a modest degree of venodilation [30].

## 5. Limitations

Our study has some limitations. First, the injection rate may not have been uniform because we performed the injection manually, rather than with an electronic pump. To facilitate slow and fast injection we used a 2.5 mL syringe (divided into 0.1 mL section). Secondly, we could not identify or change some factors (such as volume of subarachnoid space and intraabdominal pressure) in the development of sensory block level and maternal hypotension, which made it difficult for us to standardize these variables. Finally, only elective cesarean sections were included in our study. Because pregnant women in emergency cesarean section may not have taken enough fluid and adequate preoperative optimization may not have been provided, which may affect the hypotension and sensory block occurrence due to spinal block. We must also indicate that our study was registered in clinicaltrials.gov retrospectively. This was due to the limitation of forgetting to get registiration our study.

## 6. Conclusions

Slow injection rate of local anesthetic may allow the surgery to start earlier with the earlier onset of adequate level of sensory block. In addition, it may help to prevent potential complications by delaying the onset of hypotension.

## Author Contributions

ET—data collection, data analysis, manuscript writing, consultation, protocol development AB—data collection, data analysis, manuscript writing, consultation. All authors have been personally and actively involved in substantive work leading to the manuscript, and will hold themselves jointly and individually responsible for its content.

## Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board of Karadeniz Technical University Medicine Faculty (Trabzon, Turkey; approval on January 2020, 2019/357) and the clinical registration number of the trial is NCT05091294.


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## Conflict of Interest

The authors declare no conflict of interest.

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