□ Clinical Research Article □

Spinal anesthesia with 3.75 mg of 0.25% hyperbaric bupivacaine for diabetic foot surgery

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Background: Spinal anesthesia in the sitting position with low-dose local anesthetics usually provides satisfactory anesthesia for diabetic foot surgery because most operations do not require tourniquet application. This study was designed to investigate the influence of different sitting periods after subarachnoid injection of low dose bupivacaine on the spread of analgesia.

Methods: In this randomized, controlled clinical trial, 60 patients undergoing diabetic foot surgery under spinal anesthesia without a tourniquet were randomized to three groups. Patients remained sitting for 2 (Group D2, n = 20), 5 (Group D5, n = 20), or 10 (Group D10, n = 20) min after the completion of subarachnoid administration of 3.75 mg of 0.25% hyperbaric bupivacaine solution. They were then placed in the supine position. Analgesia levels were assessed bilaterally using pinpricks. Blood pressure and heart rate were also recorded.

Results: The maximal sensory block level [median (range)] was higher in Group D2 [L3 (L2-L3)] compared with Group D10 [L4 (L3-L4)] (P = 0.002). The highest sensory block levels were T12, T11, and L2 in Group D2, 5 and 10, respectively. There were no hemodynamic differences among the three groups and none of the patients showed hemodynamic instability except for one patient in Group D10.

Conclusions: Although spinal anesthesia using a minimal dose of 0.25% hyperbaric bupivacaine provides adequate anesthesia for diabetic foot surgery without profound hypotension, regardless of the time spent in the sitting position, maintaining the position for 10 min required to confine the sensory blockade on the lower level. **(Korean J Anesthesiol 2009; 56: 273~9)**

Key Words: Bupivacaine, Diabetic foot, Spinal anesthesia.

INTRODUCTION

A diabetic foot ulcer is a serious complication of long-term diabetes. Surgery for the diabetic foot is a relatively minor operation with negligible blood loss, but providing anesthesia for these patients is a frequent challenge because of serious co-morbidities. Cardiovascular autonomic neuropathy is associated with increased morbidity and mortality [1], and hemodynamic instability is common in patients with autonomic dysfunction during anesthesia induction and maintenance [2,3]. It is important to maintain anesthesia as stable as possible including

adequate analgesia.

Although there is no clear evidence that one type of anesthetic is superior for patients with diabetes, the stress response to surgery may be reduced with combinations of local or regional anesthesia and the administration of opioids [4]. Regional anesthesia is a reasonable choice for lower extremity operations in diabetic patients [5]. When spinal anesthesia is planned, high sensory block levels are not required, especially when a tourniquet is not used. Limiting the block to lower dermatomal levels and avoiding the occurrence of hypotension is important because fluid loading and vasopressor administration may not be ideal methods to prevent or treat hypotension since end-stage renal disease and coronary artery occlusive disease are common in these patients. A peak level of sensory block of only L4 or even L5 provides sufficient anesthesia, and spinal anesthesia with a low dose of local anesthetics with the patient in the sitting position is one method to minimize analgesic level and the occurrence of hypotension. It

has been suggested that when compared with the general population, patients with preexisting sensorimotor neuropathy or diabetic polyneuropathy may be at increased risk of further neurologic sequelae after neuraxial anesthesia or analgesia [6,7]. Diabetic nerve fibers may be more susceptible to the toxic effects of local anesthetics [7]. Minimizing the concentration of local anesthetics can be safe for patients undergoing diabetic foot surgery.

This study was designed to investigate the influence of different sitting periods after subarachnoid injection of a small dose (3.75 mg) of hyperbaric 0.25% bupivacaine on the spread of analgesia.

MATERIALS AND METHODS

After obtaining approval from the Hospital Ethics Committee and written informed consent from the subjects, sixty adult patients undergoing diabetic foot surgery without tourniquet were enrolled in this study. All patients were admitted prior to the surgical procedure for daily dressing and control of infection of diabetic foot. Patients were checked for sensory dysfunction in the dermatomes of the lower extremities to exclude pre-existing sensory loss from diabetic neuropathy. Patients were excluded from the study if they had coagulopathy, infection at the site of injection, or refusal to spinal anesthesia as well as pre-existing sensory loss. Subjects were randomly assigned to one of three study groups that differed with respect to the duration that patients remained in the sitting position after injection of an anesthetic agent. Group assignment was randomized using computer-generated randomization.

Premedication was not given to patients. When patients arrived at the operating theatre, routine monitoring, including electrocardiogram, pulse-oximetry and non-invasive automated blood pressure were established. Heart rate (HR) and mean arterial pressure (MAP) were recorded in the supine position as a baseline. Patients were slowly placed into a sitting position to prevent orthostatic hypotension. When patients were seated comfortably, HR and MAP were recorded every 5 min until the end of the operation. Before spinal anesthesia, no fluid loading was performed and normal saline was infused intravenously for maintenance. Dural puncture was performed in the sitting position with a standard midline approach using a 22-gauge Quincke spinal needle at the L4-5 interspace. When a free flow of clear cerebrospinal fluid was confirmed, 1.5 ml of 0.25% bupivacaine (3.75 mg) was injected over 15 seconds

with the spinal needle bevel toward the caudad direction. The hyperbaric 0.25% bupivacaine solution was made by mixing 0.5% bupivacaine in 8% dextrose (Marcaine® Spinal heavy, AstraZeneca, Södertälje, Sweden) with the same volume of 0.9% saline. Patients remained seated for 2 min (Group D2), 5 min (Group D5), or 10 min (Group D10) after subarachnoid injection of the anesthetic agent and then were returned to the supine position.

Sensory block level was assessed bilaterally at the midclavicular line by a pinprick test using a 24-gauge hypodermic needle. Assessments were made every 5 min during the first 30 min after the injection and every 10 min thereafter until there was a 2-segment regression of sensory level. The maximal sensory block level (MSBL), the time at which MSBL was attained, increased sensory block levels after supine positioning, and the time to the 2-segment regression of sensory level were recorded. During the first 10 min, all assessments were made by the anesthesiologist who had performed the lumbar puncture. Thereafter, assessments were made by another anesthesiologist who was blinded to the patients' group assignment.

No additional sedatives were given during the operation unless requested by the patient. When the patient complained of pain or discomfort, remifentanil was continuously infused intravenously at a rate of 0.1 to 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The blinded anesthesiologist was allowed to convert to general anesthesia if an inadequate amount of anesthesia was continuously detected in spite of the infusion of remifentanil. Hypotension (defined as a systolic blood pressure of < 90 mmHg or a decrease of mean arterial pressure by more than 25% of the pre-anesthetic baseline value) and bradycardia (defined as heart rate < 50 beats/min) were treated by an intravenous bolus of ephedrine, phenylephrine, or atropine sulfate as deemed appropriate. Follow up was performed 1 day postoperatively by a blinded investigator who inquired about headaches (positional headache was considered to be a postdural puncture headache), backaches, urinary retention, and transient neurological symptoms (TNS), which are defined as pain radiating to the buttocks or legs and sensory disturbances in areas not related to the surgery.

For the purpose of statistical analyses, each dermatomal level was scored in sequence starting at S5 = 1, such that S1 = 5, L1 = 10, T8 = 15, and T3 = 20. Sample size was calculated based on the pilot study, since there was no previous study about the influence of different sitting periods after sub-

arachnoid injection of low dose 3.75 mg of 0.25% bupivacaine on the spread of analgesia. Based on the results of our pilot study, more than 14 patients in each group were required in order to detect a difference of one dermatome analgesia levels to pinprick with a variability of 0.9 between with α error of 0.05 and β error of 0.2. We decided to evaluate 20 patients in each group to compensate for possible protocol violations during the study period.

Statistical analyses were performed using software packages (SigmaStat 3.1 for Windows, Systat Software, Inc., CA., USA). Data are expressed as mean (SD), median (interquartile ratio [range]), or number of patients, as appropriate. MSBL, time to MSBL, and increased level of sensory block after supine positioning were analyzed by Kruskal-Wallis test followed by Tukey test. Changes in MAP and HR were analyzed by re-peated measures of analysis of variance (ANOVA) corrected by the Bonferroni method. P value less than 0.05 was considered to be statistically significant.

RESULTS

Sixty patients were enrolled from whom data were obtained between March 2006 and December 2007. Characteristics of the patients are summarized in Table 1. There were no differences among the groups. Hypertension, coronary artery occlusive disease, and end-stage renal disease were found in 76.7%, 38.3%, and 41.7% of all patients, respectively.

The characteristics of sensory block are presented in Table 2. The individual times to MSBL revealed that sensory block level was fixed within 5 min in 28 out of 60 patients and the

**Table 1.** Characteristics of Patients and Duration of Surgery

	Group D2 (n = 20)	Group D5 (n = 20)	Group D10 (n = 20)
Age (yr)	63.2 ± 8.0	61.8 ± 10.6	64.5 ± 8.8
Height (cm)	167.0 ± 7.5	164.3 ± 9.1	163.6 ± 9.0
Weight (kg)	66.7 ± 10.6	65.3 ± 9.9	60.9 ± 8.8
Sex (M : F)	17 : 3	15 : 5	15 : 5
ASA physical status (II : III)	9 : 11	6 : 14	5 : 15
Duration of surgery (min)	49.2 ± 20.1	45.9 ± 16.1	40.0 ± 14.6
Coexisting diseases			
Hypertension	14 (70.0%)	16 (80.0%)	16 (80.0%)
Coronary artery occlusive disease	7 (35.0%)	7 (35.0%)	9 (45.0%)
End stage renal disease	7 (35.0%)	8 (40.0%)	10 (50.0%)
Peripheral artery occlusive disease	2 (10.0%)	1 (5.0%)	2 (10.0%)
Name of operation			
Debridement	10 (50.0%)	9 (45.0%)	7 (35.0%)
Toe amputation	5 (25.0%)	8 (40.0%)	10 (50.0%)
Ray amputation	4 (20.0%)	3 (15.0%)	1 (5.0%)
Resection arthroplasty	1 (5.0%)	0 (0.0%)	2 (10.0%)

Values are mean ± SD or numbers. Patients in groups D2, D5 and D10 remained sitting for 2, 5 or 10 min after completion of the sub-arachnoid injection.

Table 2. Sensory Block Characteristics

	Group D2 (n = 20)	Group D5 (n = 20)	Group D10 (n = 20)
MSBL (dermatome)	L3 (L2-L3 [T12-L4])[b]	L3.5 (L2-L3 [T11-L5])	L4 (L3-L4 [L2-L5])
Increase after supine positioning (dermatomes)	1 (0-2 [0-4])[a]	0 (0-1 [0-4])	0 (0-1 [0-2])
T-MSBL (min)	9.8 ± 5.7	10.5 ± 5.4	9.3 ± 5.2
TSRT (min)	95.0 ± 22.3	103.2 ± 32.6	114.5 ± 32.6

Values are median (interquartile ratio [range]), mean ± SD, or numbers. Groups D2, D5 and D10 = patients who remained sitting for 2, 5 or 10 min after completion of the subarachnoid injection. MSBL: maximal sensory block level, T-MSBL: time to maximal sensory block level, TSRT: 2-segment regression time. [a]Data in Group D2 are increased sensory block level after 5 min (analgesia levels were not assessed at 2 min), [b]Significantly different compared to Group D10 (P = 0.002).
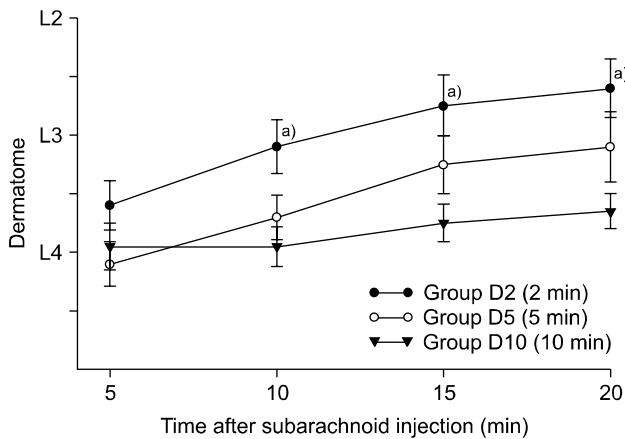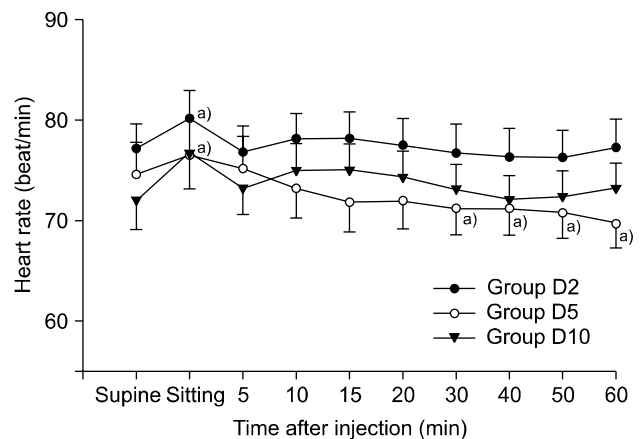
Fig. 1. Segmental spread of sensory analgesia after subarachnoid injection of 3.75 mg of 0.25% bupivacaine for diabetic foot surgery. Medians are corrected for tied observations. Groups D2, D5 and D10 = patients who remained sitting for 2, 5 or 10 min after completion of the subarachnoid injection. [a]Significantly different compared to Group D2 and D10 (P < 0.008).
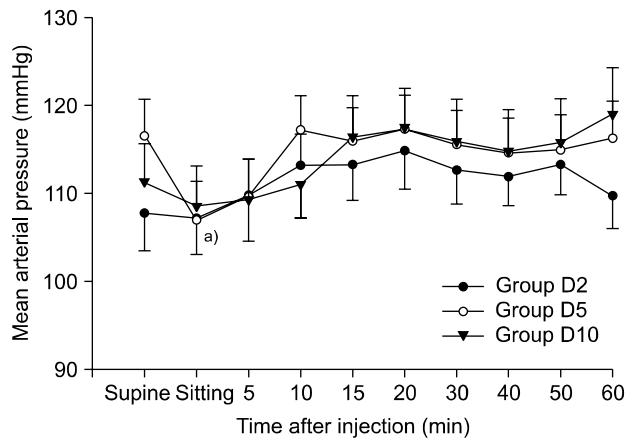
Fig. 2. Changes in mean arterial pressure (MAP) during the 60 min after subarachnoid injection. Values are mean ± SE. Groups D2, D5 and D10 = patients who remained sitting for 2, 5 or 10 min after completion of the subarachnoid injection. There were no significant differences among groups. [a]P < 0.05 compared with supine position value in each group.

Fig. 3. Changes in Heart rate (HR) during the 60 min after subarachnoid injection. Values are mean ± SE. Groups D2, D5 and D10 = patients who remained sitting for 2, 5 or 10 min after completion of the subarachnoid injection. There were no significant differences among groups. [a]P < 0.05 compared with supine position value in each group.

Analgesia was adequate during the whole period of surgery except for one patient in Group D2. Although the initial sensory block was adequate, this patient required additional infusion of intravenous remifentanil due to prolonged operation time (85 min after the induction of anesthesia).

Changes in mean arterial pressure and heart rate were comparable among the groups (Fig. 2, 3). Only one patient in Group D10 received a single dose of 6 mg ephedrine. The blood pressure of that patient was 99/62 mmHg in the supine position, 90/64 mmHg in the sitting position, and 82/56 mmHg at 5 min after subarachnoid injection. Neither atropine nor phenylephrine was used to treatment of bradycardia or hypotension in this study. Postoperative follow up revealed no headache, backache, urinary retention, or TNS.

DISCUSSION

In this study, spinal anesthesia using 3.75 mg of hyperbaric 0.25% bupivacaine in the sitting position ensured adequate anesthesia and maintained stable hemodynamics regardless of the duration of sitting. Although there was only one segment difference in MSBL between Group D2 and D10 statistically (P = 0.002), we found that the 10 min sitting period was required to confine the sensory blockade on the lower level. The highest MSBL was confined to L2 in Group D10, whereas the highest MSBL in Group D2 and D5 were T12 and T11, respectively, even with small dose of bupivacaine.

longest time for fixation was 20 min in each group. The highest sensory block levels were T12, T11, and L2 in Group D2, 5, and 10, respectively. MSBL of Group D2 was 1 dermatome higher than that of Group D10 (P = 0.002) (Table 2) (Fig. 1). MSBL of Group D10 showed the limited distribution of the local anesthetics (Table 2) (Fig. 1). There were no differences in the time to MSBL or increased levels of sensory block after supine positioning among the groups or two segment regression time.
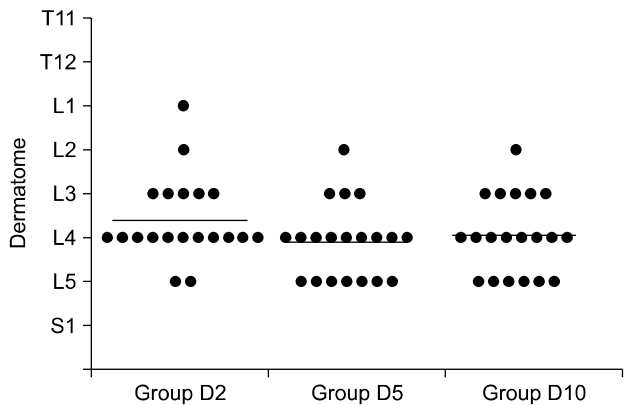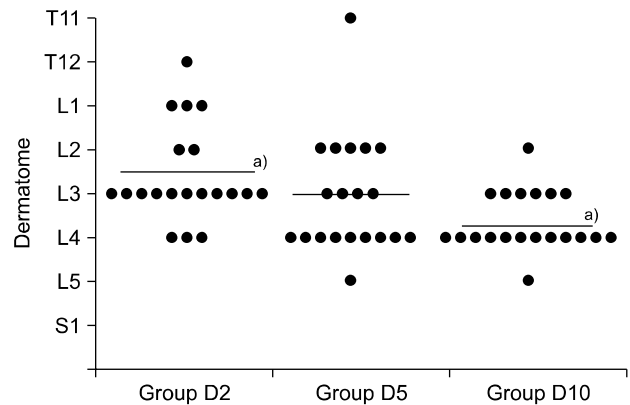
Fig. 4. Individual analgesia levels 5 min after the injection. Horizontal lines represent median levels. Medians are corrected for tied observations. Groups D2, D5 and D10 = patients who remained sitting for 2, 5 or 10 min after completion of the subarachnoid injection.

Fig. 5. Individual maximal sensory block level of analgesia. Horizontal lines represent median levels. Medians are corrected for tied observations. Groups D2, D5 and D10 = patients who remained sitting for 2, 5 or 10 min after completion of the subarachnoid injection. [a]Significantly different compared to Group D2 and D10 (P = 0.002).

There are three reasons to use 0.25% bupivacaine solution instead of 0.5%. First, when using the undiluted 0.5% bupivacaine solution in the sitting position, there is a high risk of localized anesthesia within the S-dermatome region. Secondly, it is highly probable that patients with DM foot disease also have nerve fiber neuropathies. It has been previously reported that DM patients are at a high risk of developing toxicity due to local anesthetics when used in high concentrations [6,7], and concentrations as low as 0.25% can induce sufficient sensory and motor block in these patients. Finally, because 0.25% bupivacaine is weakly hyperbaric and thus settles at a slow rate at the injection site, we can anticipate effective analgesia at the desired dermatomes (below L3) than with high concentration local anesthetics such as 0.5% bupivacaine.

Among many factors that affect the intrathecal spread of local anesthetics, the major factors are the baricity of the injected solution and the posture of the patient [8]. Although it is generally believed that injection of hyperbaric local anesthetic solution in the sitting position would limit MSBL to lower levels, earlier studies on the time that the patient is kept in the sitting position after the subarachnoid injection of high doses (15−20 mg) of hyperbaric bupivacaine have demonstrated that the time in the sitting position has little or no influence on the maximum cephalad spread of sensory analgesia [9-12]. The results were mainly determined by the final position of the patients. When a larger volume (4 ml) of 0.5% bupivacaine was injected, even a sitting period of 60 min was not enough for the fixation of analgesic levels [12]. We used

a small-dose (3.75 mg) of 0.25% hyperbaric bupivacaine unlike previous investigations [9-12].

We did not measure sensory block level at 2 min when patients were moved into the supine position in Group D2, but there is a possibility that there was 1 segment upward progression between 2−5 min in this group compared to others because sensory block level at 5 min in Group D2 was 1 segment higher than that of Group D5 or D10 (Fig. 4). After 5 min, increased sensory block level in Group D2 was similar to increased sensory level after supine positioning in Groups D5 and D10. This would mean that when even a small dose of local anesthetic is injected into the subarachnoid space with the patient in the sitting position, a 2-min period of sitting is not sufficient enough to limit analgesic level. Although there was no statistical difference between Group D5 and D10 in regard to MSBL, a 10-min sitting period after subarachnoid injection is preferable for achieving a more consistent analgesic level because MSBL was demonstrated to have a lower inter-individual variability in Group D10 (Fig. 5). In addition, MSBL was fixed during the period when the patient was sitting in 15 patients in Group D10 (75.0%) compared to 8 patients in Group D5 (40.0%).

The presence of MSBL of L2, L1, or even T11 in this study suggests considerable inter-individual variances and the existence of many factors that determine sensory block levels we did not assess. Onset time to MSBL is determined by 2 factors; the time needed for the local anesthetic to reach the highest spinal cord segment in a sufficient amount to produce

sensory block and the latency between the presence of local anesthetics at a given spinal cord segment and the time that signs of sensory block in the corresponding dermatome become apparent [13]. Onset time to MSBL in this study was also variable as with the level of MSBL, and it should be noted that in 5 patients, MSBL increased until 20 min after subarachnoid injection. Whether this latency in onset time of MSBL is from the delayed movement of local anesthetics in the subarachnoid space or from the delayed response of the spinal cord segment is not clear from this study. The two-segment regression time (TSRT) from the MSBL showed the tendency of prolongation with the duration of sitting period although it did not statistically significant (P = 0.182) (Table 2).

A 0.25% bupivacaine solution was made with 0.5% bupivacaine with the same volumes of 8% dextrose and 0.9% normal saline. The specific gravity of 0.25% bupivacaine in 4% dextrose at 37°C was 1.010, and it was hyperbaric compared to cerebrospinal fluid density in adults at 37°C (1.00054) [14]. Diluting 0.5% intrathecal bupivacaine in 8% dextrose solution with the same volume of saline was reported to have a faster recovery time [15], but this is a controversial issue because it is generally accepted that dosage rather than volume or concentration of the solution is the main factor that determines the duration of the block [17]. This was not a primary investigation point of this study. We used 3.75 mg of 0.25% hyperbaric bupivacaine and decreasing the bupivacaine dose could be considered but it might result in inadequate analgesia for the surgery because MSBL of 2 patients were already as low as L5 with 3.75 mg. Although all patients in this study showed stable hemodynamics during the period of sitting position except one patient, ten minutes sitting for diabetic patients after subarachnoid injection can cause fainting. Careful monitoring is mandatory for these patients during the sitting period.

There are some limitations to this study. First, the measurement of analgesia level at 2 min in Group D2 was not performed. This made it impossible to investigate actual increased sensory block level after subjects in this group changed to the supine position. Second, we used a 22-gauge Quincke spinal needle because it is still the most commonly used in our department. Using the different types and gauges of spinal needle could result in different distribution of local anesthetics [16,17]. Among the different types of spinal needles, the Quincke needle can always produce an undeviated stream of anesthetics and do not form tracks at any flow rate [18].

In conclusion, this study demonstrated that spinal anesthesia using a minimal dose of 0.25% hyperbaric bupivacaine with the patient in a sitting position provided adequate anesthesia for diabetic foot surgery without profound hypotension regardless of the time spent in the sitting position (2, 5, or 10 min) after subarachnoid injection. However, even with this small dose, keeping the patient in the sitting position for 2 or 5 min after subarachnoid injection was not adequate to confine the sensory blockade on the lower dermatome.

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