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A Prospective Multicenter Trial to Determine the Incidence of Transient Neurologic Symptoms after Spinal Anesthesia with Phenylephrine Added to 0.5% Tetracaine

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ABSTRACT

The addition of vasoconstrictors for spinal anesthesia is controversial, since an increase in the incidence of transient neurologic symptoms (TNS) has been reported. A multicenter, randomized, double-blind study was conducted to assess the effectiveness of spinal anesthesia with phenylephrine in addition to tetracaine as well as the incidence of neurological complications. We studied 64 patients with comparable demographic characteristics who were scheduled for elective surgery for a lower limb, or a gynecological or urological procedure. The patients were allocated randomly into 2 groups. Group P (n = 34) received 0.5% tetracaine in 10% glucose with 0.025% phenylephrine, while group C (n = 30) received 0.5% tetracaine in 10% glucose.

Our results showed that only 2 patients (6.7%) in group C experienced TNS, and their symptoms disappeared within 72 hr after anesthesia, while none of the patients (0%) in group P complained of symptoms. The incidence of TNS was thus not significantly different between the two groups. Six hours after the sensory block, group P patients demonstrated sensory disturbance, with the median spinal dermatome corresponding to the L1 segment. Moreover, systolic blood pressure in group P was significantly higher than that in group C, 5 min, 15 min, and 20 min after injection.

The incidence of TNS in the present study does not seem to be greater after surgery with spinal anesthesia using 0.5% hyperbaric tetracaine and 0.5 mg phenylephrine than without phenylephrine. Randomized, double-blind, cross-over trials with a larger sample size would be required in the future to obtain more reliable results.

Key words: *Spinal anesthesia, Phenylephrine, Transient neurologic symptoms*

Vasoconstriction drugs have been added to local anesthetic agents and used for spinal anesthesia to prolong its duration since the 1950s[2]. More recently, Concepcion et al[3] demonstrated the usefulness of vasoconstrictor agents with spinal anesthesia by a double-blind method. Since anesthesiologists are concerned about the quality of anesthesia, the incidence of anesthetic complications is assessed for each anesthetic procedure. In 1997 Sakura et al reported[14] that the addition of phenylephrine to tetracaine increases the potential risk of transient neurologic symptoms (TNS), and they warned that phenylephrine should not be used for spinal anesthesia.

We have added phenylephrine to tetracaine for spinal anesthesia for many years, and have no evidence of severe neurological complications in our patients. Thus, we consider that the addition of vasoconstrictor agents is quite safe and useful for prolongation of the effect. In order to confirm our past experience, the current multicenter, randomized, double-blind study was conducted to assess

the effectiveness of spinal anesthesia with phenylephrine added to tetracaine as well as the incidence of neurological complications.

MATERIALS AND MEHODS

With prior institutional review board approval and written informed consent, we studied 64 patients classified as American Society of Anesthesiologists physical status I or II who were scheduled for elective surgery for a lower limb, or a gynecological or urological procedure. Patients with a history of back pain, coagulation abnormality, or neurologic diseases were excluded. They were allocated randomly into 2 groups. For spinal anesthesia, group P received 0.5% tetracaine in 10% glucose with 0.025% phenylephrine-, and group C received 0.5% tetracaine in 10% glucose alone.

Atropine (0.01 mg/kg) for premedication was given intramuscularly approximately 30 min before anesthesia to both groups. After an intravenous infusion of acetated or lactated Ringer's solution was administered, each patient was placed in the lateral decubitus position, the lumbar area was cleansed, and local anesthesia was applied to the skin and subcutaneous tissue. Under sterile conditions, an epidural catheter was then placed in the L1-L2 interspace with an 18-gauge needle for rescue analgesia. Spinal anesthesia was performed in the L3-L4 interspace with a 25-gauge Quincke type needle (Top Corporation, Tokyo, Japan) using the midline approach.

After obtaining a free reflux of cerebrospinal fluid, the solution (approximately 2 ml, calculated according to patient height) was administered at a rate of 0.1 ml/sec with the bevel of the needle oriented toward the nondependent side. The solution was prepared just before injection by dissolving 20 mg of crystalline tetracaine hydrochloride in a combined solution as the allocated group. Patients were immediately placed in a supine position thereafter and remained level for at least 20 min following the injection, after which the surgery was started.

Noninvasive blood pressure and heart rate, along with electrocardiography and pulse oximetry were monitored continuously during the patient's stay in the operating theater. Hypotension was occasionally treated by intravenous administration of ephedrine on the judgement of the anesthesiologist. The extent of sensory blockade was evaluated by examination using ice. These measurements were taken by an investigator blinded to the type of local anesthetic solution injected, at 5-min intervals for a total of 20 min and then 6 hr after the injection. Twenty-four hours after the injection, on postoperative day 1, each patient was interviewed concerning TNS and other side effects, though they were unaware of the local anesthetic solution injected. When a symptom was noted, neurological examinations for sensory and motor disturbances were performed, and then repeated on a daily basis until the symptoms resolved.

Results are expressed as means ± SD. Continuous variables were compared using one-way analysis of variance and paired or unpaired t test for post-hoc analysis. Chi-squared analysis with Bonferroni correction was used to compare the incidence of side effects and TNS between the groups. The value $p < 0.05$ was considered significant.

RESULTS

1. Demographic data

Thirty patients were allocated to group C and 34 to group P. They were comparable in age, gender, weight, height, and volume of tetracaine solution injected (Table 1).

2. Side effects and TNS

Nine patients in group C (30.0%) and 3 in group P (8.8%) experienced adverse effects, which included: 4 cases complaining of a postdural puncture headache and floating sensation, 4 cases of pain at the injection site, and 1 of transient bradycardia. Only 2 patients in group C (6.7%) complained of pain or dysesthesia in the legs, and the symptoms disappeared within 72 hr after the injection (Table 2).

Table 1. Demographics

	Group C (n=30)	Group P (n=34)	
Male/Female	19 / 11	22 / 12	ns
Age (year)	60.7 ± 19.2	64.2 ± 14.5	ns
Height(cm)	161 ± 11.3	158 ± 9.5	ns
Weight(kg)	57.8 ± 11.0	57.6 ± 10.3	ns
Vol.of sol(ml)	1.9 ± 0.2	1.9 ± 0.2	ns

Values are mean ± SD. ns: not significantly different between two groups.
Vol. of sol = Volume of solution which was administered for spinal anesthesia.

Table 2. Complications

Group C (n=30)		Group P (n=34)	
Pain at injection site	3	Pain at injection site	1
Postdural puncture headache	2	Postdural puncture headache	2
TNS in leg	2		
Floating sensation	1		
Bradycardia	1		

The two cases with TNS are described briefly. The first case was a 24 year-old male who underwent plastic surgery on a right toe under spinal anesthesia uneventfully. After surgery, he received a cast on right leg. Twenty-four hours after the spinal anesthesia, he complained of dysesthesia in the gastrocnemius region, though it disappeared after the cast was removed the next day. The other was a 68 year-old male who underwent a transurethral resection of bladder cancer under spinal anesthesia without any complication. Sensory loss in both feet continued more than 24 hr, but gradually disappeared until complete recovery on the third postoperative day. These symptoms were diagnosed as TNS. No patient (0%) in group P complained of pain or dysesthesia in the region of the block. The incidence of adverse effects or TNS was thus not significantly different between the two groups.

3. Level of sensory block (Fig. 1)

To compare the grade of sensory block, the number of dermal segments were counted from S3 to the sensitive point. Twenty min after injection, the median level of sensory block was T6 on both sides in the two groups. Although the sensory block disappeared in most group C patients 6 hr after injection, patients in group P demonstrated a sensory disturbance including slight dysesthesia and/or slight motor block, with the median level at the L1 segment. There was a significant difference between the two groups.

4. Heart rate and blood pressure (Fig. 2)

Heart rate did not change significantly in either group during the observation time. Systolic pressure in group P was significantly less hypotensive than in group C, 5, 15, or 20 min after injection. As noted above, transient bradycardia occurred in

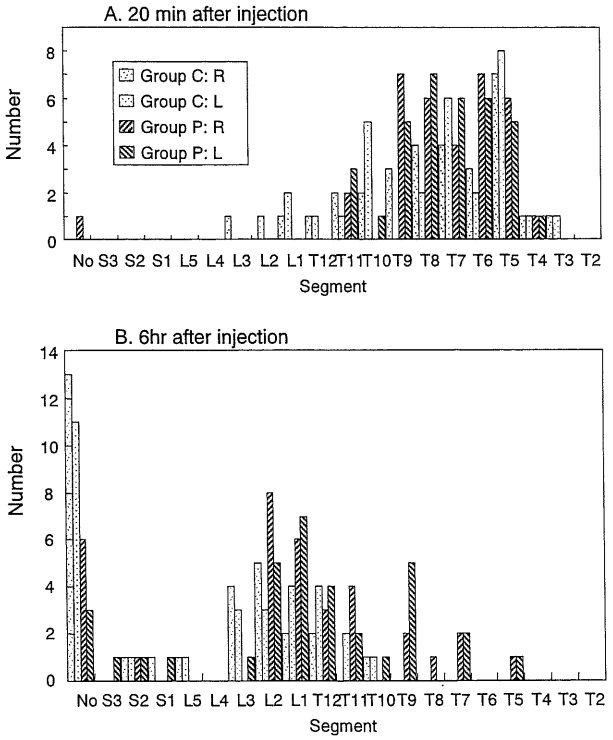

Fig. 1. Sensory block level examined with ice.
(A) Results obtained 20 min after the intrathecal injection. (B) Results obtained 6 hr after the intrathecal injection. Dermal segments (from S3 to T2) are shown on horizontal axis. No on horizontal axis means no sensory block.

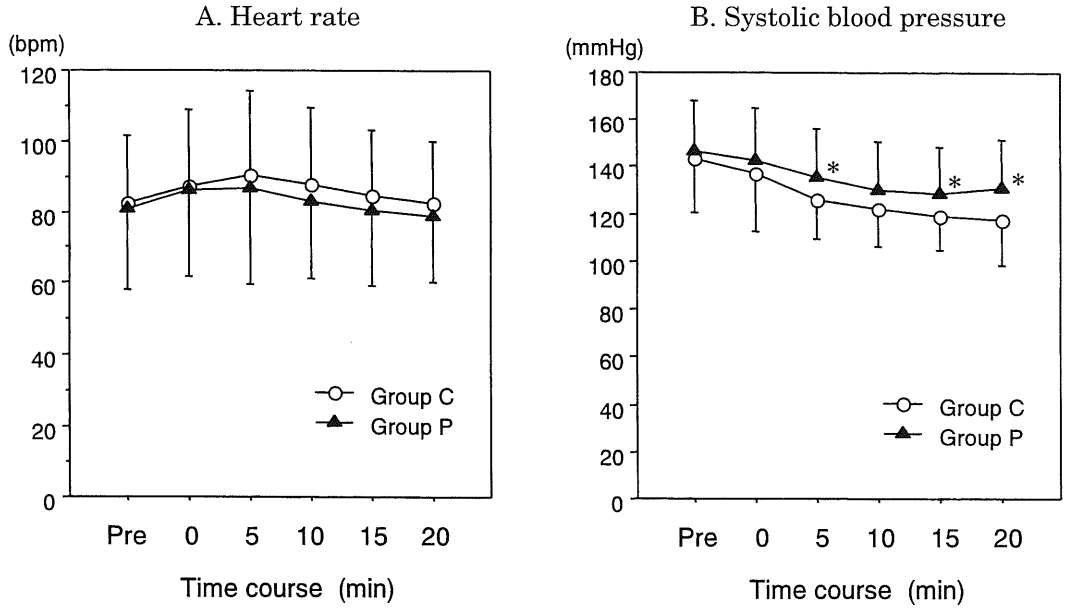

Fig. 2. Time course of hemodynamics between two groups, (A) heart rate, (B) systolic blood pressure.
Data are preinduction (Pre), 0, 5, 10, 15, and 20 min after intrathecal administration of anesthetic solution. The open circle represents group C and the filled triangle represents group P. Results are represented as mean ± SD.
*: statistical difference ($p < 0.05$) between two groups.

one group C patient, an 81 year-old male undergoing a urological procedure. He showed transient bradycardia (HR 40 bpm) just after surgery, and recovered his normal heart rate without medication within a few minutes.

DISCUSSION

The incidence of TNS in the present study was 6.7% in group C, 0% in group P, and 3.1% on average. In recent years, several reports[6,13,14] of TNS incidence in patients who underwent spinal anesthesia have shown results much higher than those reported by Phillips[12], with some exceeding 30%[6,7,15]. Possible reasons for these discrepancies include differences in the local anesthetics used, the addition of vasoconstrictors, baricity or osmolarity of the solutions, surgical procedures, and patient position during surgery.

Most anesthesiologists who have reported higher incidences of TNS used lidocaine, while many noted a low incidence of TNS in the case of bupivacaine. Sakura et al[14] used tetracaine with 2.5 mg phenylephrine for spinal anesthesia and reported the incidence of TNS as 12.5%. In the present study, we found that the incidence of TNS was 6.7% in group C and 0% in group P. Probably, tetracaine has an advantage over lidocaine, though bupivacaine is more useful for spinal anesthetics[6,7,14,15].

We were unable to confirm the result that the addition of phenylephrine to tetracaine for spinal anesthesia increased the potential risk for TNS, as described by Sakura et al[14], possibly because the dose of phenylephrine added was one fifth in our study. They suggested that the addition of phenylephrine to tetracaine for spinal anesthesia increased the potential risk of TNS, whereas it is controversial whether adding vasoconstrictors for spinal anesthesia increases the incidence of TNS. Pollock et al[13] studied 159 patients who received spinal anesthesia with lidocaine or bupivacaine along with epinephrine, using a double-blind method. They reported no difference in the incidence of transient neurologic irritation (TRI) between 5% lidocaine with epinephrine and 2% lidocaine without epinephrine.

Concepcion et al[3] compared the differences between 1 mg and 2 mg of the vasoconstrictor phenylephrine added to hyperbaric tetracaine, and did not find a significant difference in the duration of sensory recovery after anesthesia. Kito et al[9] studied the effects of various doses of epinephrine on the duration of spinal anesthesia, and could not demonstrate that recovery time at the T12 or L3 level was prolonged as the dose of added epinephrine increased. In the present study, the residual sensory block 6 hr after injection in group P was significantly greater than in group C. Thus, we consider that 0.5 mg phenylephrine (0.025%, 2 ml) is sufficient for prolonging the duration of spinal anesthesia when using a hyperbaric tetracaine solution.

The vasoconstrictors epinephrine and phenylephrine are often added to local anesthetics to prolong the duration of spinal anesthesia. Denson et al[4] reported that there was no clinically significant difference between these two drugs when added for spinal anesthesia in rhesus monkey. Although the block-prolonging effect of a vasoconstrictor presumably results from a decrease in local blood flow, these two medications may have different mechanisms for causing the effect. Epinephrine is an α_2-adrenergic agonist, known as a possible agent to prolong the duration of local anesthetics[5,11]. However, Bernards et al[1] demonstrated that epinephrine caused a prolonged sensory block by decreasing local blood flow and slowing clearance, but could not obtain evidence of the pharmacodynamic effect.

The glucose concentrations used for the anesthesia solutions were different between our study (a 10% solution) and that by Sakura[14] (7.5% and 0.75% solutions). They concluded that glucose concentration did not affect TNS occurrence. Hampl et al[7] also compared the incidence of TRI among three glucose concentrations, 7.5%, 8.25%, and 2.7%. TRI did not result from the marked hyperosmolarity of the hyperbaric solution. Although we used a 10% glucose solution, the highest concentration among these reports, we did not observe a high incidence of TNS, which coincides with the data of Hampl[7].

The present study revealed that systolic blood pressure in group P patients decreased less than in group C. Sakura et al[14] could not exhibit significant hemodynamic characteristic changes between a phenylephrine and control group. Iselin-Chaves et al[8] also found no significant difference in the maximum decrease of systolic blood pressure between patients with and without epinephrine for spinal anesthesia. In contrast, the number of patients who required vasopressors for the treatment of hypotension was significantly greater in a group which received 0.3 mg epinephrine than in a group which received 2 mg phenylephrine[3]. Kozody et al[10] studied the effect of a subarachnoid administration of lidocaine with or without epinephrine in dogs, and reported that the mean arterial pressure in the epinephrine group had a greater decrease. Therefore, the effect of added vasoconstrictors on general hemodynamic characteristics remains controversial. These reports imply that phenylephrine might affect systemic blood pressure less markedly than epinephrine when used as an added vasoconstrictor for spinal anesthesia, due to its pharmacological properties as a stimulator on the sympathetic receptors of phenylephrine and epinephrine.

The present study has limitations. First, the sample size was small. Although TNS occurred in

6.7% of the patients with hyperbaric tetracaine alone and in 0% of those with 0.5 mg of phenylephrine added, no significant difference between the two groups could be obtained. This could be the result of the insufficient statistical power of the study. Second, the surgical procedures in this study were varied and performed in different positions, which may have had an effect on vulnerability.

In summary, the present multicenter, randomized, double-blind study showed that the incidence of transient neurologic symptoms was not greater after spinal anesthesia using 0.5% hyperbaric tetracaine with 0.5 mg of phenylephrine than when using tetracaine alone. In order to obtain more reliable results, randomized, double-blind, cross-over trials with a larger sample size would be required in future.

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