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Epinephrine Increases the Effectiveness of Tetracaine Spinal Anesthesia

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The effect of epinephrine on the need for supplementation of spinal anesthesia produced with hyperbaric tetracaine was assessed in 60 patients undergoing transurethral resection of the prostate. Patients were randomly assigned to receive either 6 mg tetracaine alone (n = 20), 6 mg tetracaine with 0.2 mg epinephrine (n = 20), 10 mg tetracaine alone (n = 10), or 10 mg tetracaine with 0.2 mg epinephrine (n = 10). Observers were blinded to the presence or absence of epinephrine. Sensory level of anesthesia was assessed by pin prick, and surgery did not start until the level reached T_{10}. Anesthesia was considered successful if the patient had no pain at the operative site. The success rate of low-dose tetracaine (6 mg) with epinephrine was 95% compared with 65% in patients receiving low-dose tetracaine alone ($P = 0.04$). All patients receiving 10 mg had successful anesthesia. Compared with patients receiving 6 mg tetracaine, those given 10 mg had higher dermatomal levels of anesthesia ($P = 0.0001$) and a higher incidence of nausea ($P = 0.04$). Thus, epinephrine can increase the effectiveness of low-dose tetracaine. (Key words: Anesthetic techniques, Spinal: Duration; failures; quality; success rate. Anesthetics, Local: tetracaine. Vasoconstrictors: epinephrine.)

EPINEPHRINE is frequently added to local anesthetics to augment spinal anesthesia. Previous studies have focused on the ability of epinephrine to prolong the duration of neural blockade. However, the addition of epinephrine to local anesthetics may also increase the intensity of analgesia, thus increasing the effectiveness of spinal anesthesia.[1,2] This study was designed to determine whether epinephrine increases the effectiveness of spinal anesthesia produced by tetracaine and also to assess whether epinephrine produces any undesirable side effects.

Materials and Methods

Sixty patients undergoing transurethral resection of the prostate (TURP), who consented to spinal anesthesia, were studied. The initial 40 patients were randomized into two groups who received 6 mg Niphanoid® tetracaine reconstituted in 0.6 ml sterile water, combined with 0.6 ml of 10% dextrose and either 0.2 ml sterile water (group I, n = 20) or 0.2 ml of 0.1% epinephrine (group II, n = 20). To assess the efficacy and side effects of a larger dose, the subsequent 20 patients were randomized into two groups receiving 10 mg Niphanoid® tetracaine reconstituted in 1.0 ml of sterile water and combined with 1.0 ml 10% dextrose and either 0.2 ml of sterile water (group III, n = 10) or 0.2 ml of 0.1% epinephrine (group IV, n = 10). Although we use tetracaine crystals in this study, we expect our results to apply to liquid tetracaine solutions because there is no difference in onset or duration of anesthesia or in the resulting block height after subarachnoid injection of liquid or crystalline tetracaine.[3] This study was approved by the Research Advisory Committee of the Virginia Mason Medical Center.

Techniques were identical in each group. Preanesthetic medication was given in small doses, repeated if needed, but limited to a maximum of 10 mg diazepam and 50 μg fentanyl. No additional analgesics were administered during surgery. Eight patients had additional doses of diazepam (up to a total of 3 mg); however, the maximum total dose for any patient was 10 mg (including preoperative and intraoperative doses). The attending anesthetist was blinded regarding the presence or absence of epinephrine. Subarachnoid block was performed with the patient in the lateral decubitus position using a 22-G Greene point needle at the L2–3 or L3–4 interspace. A total of 0.2 ml cerebrospinal fluid was aspirated into the syringe containing the local anesthetic before the solution was injected. Local anesthetic was then injected at a rate of 0.5 ml/s. The patient was immediately turned supine and the legs were immediately placed in stirrups. Flexing the hips for this position flattens the lumbar lordosis that is usually present when a patient is supine and decreases the cephalad migration of hyperbaric solutions (peak block height should be 1.5–2 dermatomes lower than for the same dose in patients whose legs are extended).[4] This position also decreases the variability in peak block heights that result from a given dose of local anesthetic. The operating room table was maintained in the horizontal position throughout the procedure.

Sensory level was assessed by pin prick using an 18-G needle 1, 2, 3, 5, 10, 15, 20, and 30 min after injection and at 15-min intervals thereafter until there was two-segment regression from the level of highest blockade. The number of segments blocked was defined as the total number of dermatomes anesthetized to pin prick (total sacral, lumbar, thoracic, and cervical dermatomes blocked). Surgery did not start until at least a T_{10} sensory level was obtained. Anesthesia was considered successful if the patient had no painful sensations at the operative

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TABLE 1. Patient Characteristics

	6 mg Tetracaine		10 mg Tetracaine	
	Epinephrine	No Epinephrine	Epinephrine	No Epinephrine
N	20	20	10	10
Age (yr)	68.8 ± 7.3	70.5 ± 8.4	68.0 ± 8.0	72.7 ± 7.0
Height (cm)	173.7 ± 5.7	175.3 ± 7.1	179.0 ± 6.7	173.5 ± 4.4
Weight (kg)	78.6 ± 12.1	78.1 ± 9.5	83.7 ± 20.4	75.8 ± 9.0
Success rate (%)	95	65*	100	100

Results are mean ± SD.

* $P = 0.04$, Fisher's exact test.

site. If the patient complained of pain, fentanyl was administered intravenously. If the additional fentanyl was not sufficient, supplemental inhalational anesthesia was administered.

Heart rate and blood pressure were recorded every 5 min. Atropine was administered in increments of 0.2–0.4 mg when the heart rate decreased below 60 beats/min or decreased by greater than 25% from baseline. Decreases in blood pressure were initially treated with a bolus of iv fluid. Ephedrine was administered in increments of 2.5–5 mg when systolic blood pressure decreased below 90 mmHg or decreased by greater than 25% from baseline. Nausea and vomiting were also recorded and treated with atropine in increments of 0.2–0.4 mg. Differences in patient characteristics, number of segments blocked, and heart rate and blood pressure changes between groups were assessed by ANOVA. Differences in the incidence of failed anesthesia and/or nausea and vomiting was assessed by Fisher's exact test or chi-square analysis. Differences in the dosages of ephedrine and atropine and in the duration of anesthesia were assessed by unpaired *t* test.

Results

The subjects were of comparable age, height, and weight in all groups (table 1). All patients developed sensory block to a level of at least T_{10} as assessed by pin prick prior to beginning surgery.

TABLE 2. Characteristics of Patients with Failed Blocks

Patient No.	Age (yr)	Height (cm)	Weight (kg)	Block Height
1	57	170	67	T_9
2	71	188	79	T_{10}
3	64	173	96	T_2
4	78	170	91	T_4
5	69	173	77	T_6
6	51	189	80	T_9
7	68	170	90	T_3
8	61	182	100	T_{10}

All failures were in the 6-mg groups. Only patient 8 had received epinephrine.

Addition of epinephrine to the low dose of tetracaine (6 mg) significantly reduced the incidence of pain during surgery and decreased the need for supplemental anesthesia (table 1). Four patients had pain with insertion of the scope or initiation of surgery. The pain was described as burning or sharp and originated from the penis or groin. The other four patients had dull pain during surgery described as originating in the lower abdomen, groin, or rectum. The pain was not related to bladder distension and was not relieved by draining the bladder of irrigation fluid. None of these painful episodes occurred when the block was wearing off (the block height was stable or increasing in all patients when pain occurred). The pain was relieved in seven patients by iv fentanyl; one patient required supplementation with isoflurane. The eight patients with failed blocks were younger than those with successful blocks ($P < 0.03$), but they did not differ in height, weight, or number of segments blocked (tables 2 and 3).

All patients receiving 10 mg tetracaine had successful anesthesia (table 1). The 10-mg dose resulted in significantly higher dermatomal levels of anesthesia, T_3 *versus* T_6 (table 4). The incidence of nausea was significantly greater in the groups receiving 10 mg (table 4). In addition, two patients who received 10 mg tetracaine had emesis. Patients who received 10 mg tetracaine had a tendency to require greater doses of ephedrine to maintain their blood pressure, but this difference was not statistically significant ($P = 0.09$, table 4).

TABLE 3. Comparison of Groups with Successful and Failed Spinal Anesthesia

	Failed	Successful
Age (yr)	64.8 ± 8.5*	70.7 ± 7.4*
Height (cm)	176.9 ± 8.2	174.8 ± 6.1
Weight (kg)	85.0 ± 11.1	77.9 ± 12.6
No. of segments blocked	16 ± 3	17 ± 2

Results are mean ± SD. Failure is defined as pain at the operative site. All failures were in the 6-mg groups.

* $P = 0.05$, ANOVA.

Duration of anesthesia, as assessed by two-segment regression from the highest level of anesthesia, was similar for the groups receiving 6 and 10 mg doses of tetracaine (64.2 ± 35.5 and 62.0 ± 24.3 min, respectively; mean ± SD). Epinephrine prolonged the duration of anesthesia by approximately 40% ($P < 0.05$) for either dose compared with that following the plain solution. The duration was 87.0 ± 28.5 min for the 6-mg dose with epinephrine and 89.0 ± 32.7 min for the 10-mg dose with epinephrine. The duration of surgery was 59 ± 22 min (range, 25–105 min).

TABLE 4. Comparison of Block Height, Maximum Hemodynamic Effects, and Interventions during Spinal Anesthesia

	6 mg Tetracaine	10 mg Tetracaine
No. of segments blocked	17 ± 3*	20 ± 3*
Mean block level	T_6	T_3
% nauseated	12.5†	35.0†
% requiring ephedrine	22.5	50.0
Ephedrine dose (mg)	8 ± 3‡	13 ± 7‡
% requiring atropine	37.5	50.0
Atropine dose (mg)	0.5 ± 0.2	0.6 ± 0.2
BP decrease (%)	21.0 ± 11.2	22.8 ± 15.1
HR decrease (beats/min)	16.4 ± 3.3	16.9 ± 2.4
Lowest HR (beats/min)	56 ± 11	56 ± 9

Results are mean or mean ± SD.
* $P = 0.0001$, one-way ANOVA.
† $P = 0.04$, chi-square.
‡ $P = 0.09$, t test.

Discussion

The addition of epinephrine to tetracaine (6 mg) decreased the incidence of pain during surgery, thus increasing tetracaine's effectiveness as a spinal anesthetic. Our results are consistent with those from a similar study, which assessed the effectiveness of bupivacaine spinal anesthesia for cesarean section.[2] In that study patients who received bupivacaine plus epinephrine required lower doses of narcotic supplementation during their surgery. There are several possible mechanisms to explain this effect. Epinephrine produces vasoconstriction, potentially decreasing vascular absorption of local anesthetic and increasing the concentration of local anesthetic in the spinal cord. This explanation is supported by some studies but not by others.[5–7]

Considerable data exist to suggest that epinephrine directly produces analgesia. For example, subarachnoid injection of 0.2–1.0 mg epinephrine in dextrose alone has been reported to produce effective analgesia for labor and delivery.[8] Similarly, epinephrine is reported to potentiate the effects of intrathecal tetracaine. Patients receiving subarachnoid injection of tetracaine alone have complete recovery from sensory anesthesia when the average concentration of tetracaine in the cerebrospinal fluid decreases to 0.8 mg/100 ml.[9] In contrast, a tetracaine concentration of 0.25 mg/100 ml is sufficient to produce sensory anesthesia to the level of the fifth thoracic dermatome when epinephrine is added.

Furthermore, intrathecally administered epinephrine and other alpha-adrenergic agonists have been found to produce analgesia.[10,11] In theory, epinephrine stimulates alpha-adrenergic receptors in descending pathways of the spinal cord, which then inhibit transmission of pain signals. In light of this evidence, the ability of epinephrine to increase the intensity of spinal anesthesia seems more likely due to a direct analgesic action at the level of the spinal cord than to local vasoconstriction, although both mechanisms may play a role.

Near 100% successful anesthesia for TURP can be achieved using either 6 mg tetracaine with epinephrine or 10 mg tetracaine without epinephrine. However, the 10-mg dose produced a significantly higher level of sensory blockade (mean = T_3) than that resulting from the 6-mg dose (mean = T_6) (table 4). A sensory level of T_3 would be expected to produce a greater blockade of cardioaccelerator fibers. However, we detected no difference in heart rate or blood pressure. The increased incidence of nausea and vomiting in the 10-mg group likely resulted from the higher dermatomal level of anesthesia associated with more complete blockade of sympathetic activity and relatively unopposed vagal output to the gastrointestinal tract (table 4).

Our study could be criticized because the 10-mg dose of tetracaine was administered in a larger volume than the 6-mg dose, and this difference in volume may have contributed to the differences we observed in block height or block intensity.[12] Although the effect of volume changes on block height or intensity of spinal anesthesia have not been conclusively identified, the best information indicates that volume is not a major factor determining the spread of analgesia for hyperbaric solutions.[13] Regardless of the effect of volume, our methodology is consistent with the clinical practice of most anesthesiologists. We increased the dose by increasing the volume of local anesthetic solution while keeping the concentration constant. Thus, we believe these results are clinically relevant.

Our finding that epinephrine significantly prolongs the duration of tetracaine spinal anesthesia is consistent with previous studies that have found an increase in duration ranging from 12% to 60%.[14] The time for two-segment regression was similar for each dose. However, after two-segment regression in the 10-mg group, the average block height was still higher than the average peak block level in the 6-mg group.

It is interesting to note that patients who had pain during surgery were younger than those with complete analgesia. This result is consistent with reports that aging

increases the sensitivity of nerves to conduction blockade induced by local anesthetics.[15,16] Similarly, in a prospective study of failed spinal anesthesia, there was a trend for a higher failure rate in younger patients (although this was not statistically significant).[17] However, the mean age of our "younger" group was 65 yr, whereas the mean age of the "older" group was 70 yr. Although this difference in age is statistically significant, we question the clinical significance of this observation.

In conclusion, we anticipate that epinephrine will also improve the effectiveness of a low dose of tetracaine for other operations. A larger dose of tetracaine may be equally effective, yet produce higher dermatomal levels of spinal anesthesia and is more likely to cause adverse side effects.

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