Dilution of Spinal Lidocaine Does Not Alter the Incidence of Transient Neurologic Symptoms

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Background: Although it has been suggested that the dilution of 5% hyperbaric lidocaine before injection for spinal anesthesia may decrease the incidence of transient neurologic symptoms, previous studies have not noted a decreased incidence between 5% and 2% lidocaine. The aim of the current study was to determine whether the incidence of transient neurologic symptoms could be altered by further diluting spinal lidocaine from 2.0% to 0.5%.

Methods: One hundred nine patients with American Society of Anesthesiologists physical status 1 or 2 undergoing outpatient knee arthroscopy were randomized in a double-blind fashion to receive 50 mg hyperbaric spinal lidocaine as a 2.0%, 1.0%, or 0.5% concentration. On the third postoperative day, patients were contacted by a blinded investigator and questioned regarding the incidence of postoperative complications, including transient neurologic symptoms, defined as pain or dysesthesia in one or both buttocks or legs occurring within 24 h of surgery.

Results: The incidence of transient neurologic symptoms did not differ among patients receiving 2.0% (incidence of 15.8%), 1.0% (incidence of 22.2%), and 0.5% (incidence of 17.1%) lidocaine (P = 0.756).

Conclusions: For ambulatory patients undergoing arthroscopy, the incidence of transient neurologic symptoms is not reduced by decreasing spinal lidocaine concentrations from 2.0% to 1.0% or 0.5%. The incidences of transient neurologic symptoms with the 0.5%, 1.0%, and 2.0% solutions are similar to previously reported incidences for 5.0% lidocaine, suggesting that dilution of lidocaine from 5.0% to 0.5% does not change the incidence of these symptoms. (Key words: Complications of regional anesthesia; lidocaine toxicity; spinal anesthesia.)

QUESTIONS have been raised regarding the potential neurotoxicity of single-dose 5.0% lidocaine-induced spinal anesthesia. In response to these concerns, in 1995, Astra USA (Westborough, MA) published revisions to the precautions and dosage and administration sections of the package insert for 5% Xylocaine-MPF Injection with Glucose 7.5%.‡ Astra suggested that mixing of xylocaine with an equal volume of cerebrospinal fluid or preservative-free 0.9% saline solution may decrease the risk of nerve injury because of pooling of concentrated local anesthetic agent, thus reducing the incidence of "transient postoperative radicular pain." The usefulness of this practice is unproven, however, and in two studies the incidence of transient neurologic symptoms (TNS) after spinal anesthesia was not decreased by diluting lidocaine from a 5.0% to a 2.0% concentration.1,2 We designed this randomized, double-blind study to assess the effects of dilution of lidocaine from 2.0% to 1.0% and 0.5% on the incidence of TNS.

Materials and Methods

After obtaining approval of the Institutional Review Board and informed consent, 109 patients with American Society of Anesthesiologists physical status 1 or 2 undergoing outpatient knee arthroscopy were randomized in a double-blind fashion to receive 50 mg hyperbaric spinoan administered lidocaine as a 2.0%, 1.0%, or 0.5% concentration. The number of patients enrolled in this study was determined by power analysis (80%; P = 0.05, suspected incidences of 22% and 1% for 2.0% and 0.5% concentrations, respectively), which was performed after a previous study on patients undergoing outpatient arthroscopy at this institution and which identified a 22% incidence of TNS after 2.0% lidocaine.
spinal anesthesia.\textsuperscript{1} Exclusion criteria included a history of radicular pain or back pain of any type or the presence of neurologic disease. Patients were randomized to receive 50 mg lidocaine, 2.0\%, (Abbott Laboratories, North Chicago, IL; specific gravity, 1.034 at 25°C; osmolarity, 384), 1.0\% lidocaine, (Abbott Laboratories; diluted to specific gravity 1.016 at 25°C; osmolarity, 557), or 0.5\% lidocaine (Abbott Laboratories; diluted to specific gravity 1.011 at 25°C; osmolarity, 528). Osmolarity was determined by advanced microosmometer and specific gravity by refractometry.

Patients received a peripheral intravenous infusion with lactated Ringer's solution and were sedated for block placement with intravenously administered midazolam (Roche, Manati, Puerto Rico) in a mean dose of 0.02 $\mu$g/kg (range, 0.01 to 0.07 $\mu$g/kg) and fentanyl (Janssen, Titusville, NJ) in a mean dose of 1.5 $\mu$g/kg (range, 0.5 to 3.0 $\mu$g/kg). Spinal anesthesia was performed at the L2-L3 or L3-L4 interspace with the patient in the lateral decubitus position using a 22- or 25-gauge Whitacre needle with the orifice directed laterally. Needle size was determined by the patient's relative risk of postdural puncture headache, with patients younger than 60 yr old receiving a 25-gauge needle and those older than 60 yr old receiving a 22-gauge needle. Patients received supplemental oxygen and were monitored with electrocardiography, automated blood pressure, and pulse oximetry. Hypotension (systolic blood pressure < 90 mmHg or a $>20\%$ decrease from baseline) was treated with 5-mg increments of ephedrine, 100-$\mu$g increments of phentylephrine, or crystalloid infusion. Bradycardia (heart rate < 45 beats/min or a $>20\%$ decrease from baseline) was treated with 0.2-0.4 mg atropine. Nausea was treated with 5 mg ephedrine or 0.2 mg atropine. Further intraoperative sedation was provided as needed with midazolam (mean dose, 0.01 $\mu$g/kg) or as a continuous infusion of 0.2% methohexital or propofol. Total dose of fentanyl was limited to 250 $\mu$g. Patients and the investigator doing the follow-up interviews (C.A.S.) were blinded to patient group assignment, but the anesthesiologist performing the spinal anesthesia procedure was not.

Data regarding patient demographics, degree of block placement difficulty, paresthesias, patient position during block placement, needle size and type, duration of surgery, adequacy of the block for surgery, and the use of ketorolac (Syntex, Palo Alto, CA) were prospectively collected. Arthroscopy was performed by four surgical attending physicians, with no attempt to stratify patients. Patients were positioned with their nonoperative leg straight at the hip and flexed 90° at the knee. The operative leg position varied throughout the surgery to obtain the best views of the knee joint.

On the third postoperative day, patients completed a telephone interview with the blinded investigator who questioned them about postoperative recovery in general and specifically about the presence of headache, backache, pain into the buttocks or legs, difficulty with ambulation, degree of activity, and pain control (appendix 1). For this study, neurologic symptoms were defined as pain in one or both buttocks or legs beginning within 24 h of surgery. Patients were questioned regarding the onset, duration, and treatment used for any symptoms. Pain was assessed using a verbal pain rating scale (0 = no pain, to 10 = worst pain imaginable). Back pain without pain in the buttocks or legs was not considered to be TNS but was recorded separately. Patients reporting TNS were monitored for 2 weeks.

\textbf{Statistical Analysis}

Differences in the incidence of TNS, back pain without radiation, patient demographics, and anesthetic factors (needle type, needle size, difficulty of block placement, or paresthesia) were analyzed separately using Pearson chi-square analysis of contingency tables and linear-by-linear association. Pain scores were analyzed using the Kruskal-Wallis nonparametric test. The onset time of TNS was analyzed with analysis of variance and the Kruskal-Wallis test. Significance was defined as a probability value $< 0.05$. Results are expressed as actual number of occurrences, percentages, or mean $\pm$ SD for parametric variables.

\textbf{Results}

Demographics were comparable among groups (tables 1, 2, and 3). There were no postdural puncture head-
Table 2. Anesthetic Factors

<table>
<thead>
<tr>
<th></th>
<th>Difficult Block</th>
<th>Paresthesias</th>
<th>Needle Size</th>
<th>Surgery Duration</th>
<th>Ketorolac</th>
</tr>
</thead>
<tbody>
<tr>
<td>2% lidocaine with TNS (N = 6)</td>
<td>0</td>
<td>0</td>
<td>1/22#, 5/25#</td>
<td>37 (26-60)</td>
<td>1</td>
</tr>
<tr>
<td>without TNS (N = 32)</td>
<td>3</td>
<td>1</td>
<td>4/22#, 28/25#</td>
<td>37 (17-65)</td>
<td>14</td>
</tr>
<tr>
<td>1% lidocaine with TNS (N = 8)</td>
<td>1</td>
<td>0</td>
<td>2/22#, 6/25#</td>
<td>31 (18-60)</td>
<td>3</td>
</tr>
<tr>
<td>without TNS (N = 28)</td>
<td>4</td>
<td>0</td>
<td>2/22#, 26/25#</td>
<td>49 (20-150)</td>
<td>2</td>
</tr>
<tr>
<td>0.5% lidocaine with TNS (N = 6)</td>
<td>0</td>
<td>1</td>
<td>6/25#</td>
<td>41 (22-63)</td>
<td>1</td>
</tr>
<tr>
<td>without TNS (N = 29)</td>
<td>3</td>
<td>1</td>
<td>2/22#, 27/25#</td>
<td>44 (21-120)</td>
<td>8</td>
</tr>
</tbody>
</table>

* Mean time in min (range).

Aches. All blocks were adequate for the initiation of surgery. Median block heights were T4 for patients receiving the 0.5% concentration and T5 for patients receiving the 2.0% and 1.0% concentrations. Two patients in the 0.5% group and two patients in the 2.0% group required intravenous or nitrous oxide supplementation for the completion of surgery. Mean surgical duration was 40 min.

Incidence of Transient Neurologic Symptoms

The incidence of TNS did not differ among patients receiving lidocaine at concentrations of 2.0%, 1.0%, and 0.5% (table 4). The test results for differences in rate were not significant (P = 0.756), nor were the test results for trend (P = 0.765). There was no association between the incidence of TNS and patient weight or age. Although there was a trend toward increasing incidence of TNS among female patients, this did not reach statistical significance (P = 0.14). In addition, there was no association between neurologic symptoms and needle type, difficulty of block placement, or paresthesia (table 2).

Characteristics of Transient Neurologic Symptoms

Of the 20 patients who reported TNS, 18 reported bilateral symptoms and 2 reported unilateral pain (table 5). Both patients who experienced unilateral pain were symptomatic in the operative extremity. Ten patients stated that their pain radiated to the hips, buttocks, and posterior thighs, whereas the other 10 patients reported that the pain extended past their buttocks and into their lower legs. All patients in this study who reported TNS also reported low back pain. Patients reported an onset of symptoms between 4 and 24 h after surgery (mean, 14 h) and a duration of 2 h–4 days (mean, 43 h). There was a trend toward earlier onset of TNS with the 2.0% solution (12.5 vs. 13.3 h for the 1.0% and 16.3 h for the 0.5% solution); however, this trend was not statistically significant (P = 0.723). The median verbal pain rating score for patients reporting transient neurologic pain (scale of 1-10) was 6.0 (range, 2 to 10). Verbal pain rating scores were not different among the three patient groups (P = 0.34). No patients exhibited continued symptoms at 2-week follow-up.

Discussion

This is the first randomized, double-blind, prospective study to report the incidence of TNS for spinal lidocaine concentrations of less than 2.0%. Numerous case reports and clinical studies reported TNS after 5% lidocaine spinal anesthesia. In response to these reports, Astra recommended dilution of lidocaine with an equal volume of cerebrospinal fluid or preservative-free saline to decrease the risk of TNS. Our results indi-

Table 3. Patients Reporting Transient Neurologic Symptoms (TNS)

<table>
<thead>
<tr>
<th></th>
<th>Yes (N = 20)</th>
<th>No (N = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean) (yr) SD</td>
<td>48.0</td>
<td>50.01</td>
</tr>
<tr>
<td>Weight (mean) (kg) SD</td>
<td>12.79</td>
<td>12.49</td>
</tr>
<tr>
<td>Sex (F) (M) (N)</td>
<td>13 (P = 0.14)</td>
<td>52</td>
</tr>
<tr>
<td>(M) (N)</td>
<td>7</td>
<td>57</td>
</tr>
</tbody>
</table>

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Table 4. Incidence of Transient Neurologic Symptoms (TNS)

<table>
<thead>
<tr>
<th></th>
<th>2% (N = 36)</th>
<th>1% (N = 36)</th>
<th>0.5% (N = 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of TNS*</td>
<td>6 (15.8)</td>
<td>8 (22.2)</td>
<td>6 (17.1)</td>
</tr>
<tr>
<td>Incidence of backpain without TNS*</td>
<td>6 (15.8)</td>
<td>6 (16.7)</td>
<td>6 (17.1)</td>
</tr>
</tbody>
</table>

Values are number (%).

* Categories are mutually exclusive.
Table 5. Characteristics of Transient Neurologic Symptoms (TNS)

<table>
<thead>
<tr>
<th>Age (yr)/Sex</th>
<th>Agent (% lidocaine)</th>
<th>Onset (h)</th>
<th>Duration</th>
<th>VPRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>73/F</td>
<td>2</td>
<td>18</td>
<td>2 days</td>
<td>7.5</td>
</tr>
<tr>
<td>53/F</td>
<td>2</td>
<td>4</td>
<td>3 days</td>
<td>10</td>
</tr>
<tr>
<td>40/F</td>
<td>2</td>
<td>24</td>
<td>2 days</td>
<td>2.5</td>
</tr>
<tr>
<td>32/F</td>
<td>2</td>
<td>6</td>
<td>2 days</td>
<td>8</td>
</tr>
<tr>
<td>35/F</td>
<td>2</td>
<td>5</td>
<td>2 h</td>
<td>8</td>
</tr>
<tr>
<td>46/M</td>
<td>2</td>
<td>18</td>
<td>1 day</td>
<td>5</td>
</tr>
<tr>
<td>71/M</td>
<td>1</td>
<td>24</td>
<td>2 days</td>
<td>5</td>
</tr>
<tr>
<td>44/F</td>
<td>1</td>
<td>12</td>
<td>3 days</td>
<td>8</td>
</tr>
<tr>
<td>46/M</td>
<td>1</td>
<td>6</td>
<td>2 days</td>
<td>5</td>
</tr>
<tr>
<td>49/F</td>
<td>1</td>
<td>18</td>
<td>1 day</td>
<td>3</td>
</tr>
<tr>
<td>54/F</td>
<td>1</td>
<td>18</td>
<td>1 day</td>
<td>2</td>
</tr>
<tr>
<td>36/F</td>
<td>1</td>
<td>5</td>
<td>1.5 days</td>
<td>6</td>
</tr>
<tr>
<td>46/M</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>75/F</td>
<td>1</td>
<td>2</td>
<td>2 days</td>
<td>6.5</td>
</tr>
<tr>
<td>45/M</td>
<td>0.5</td>
<td>24</td>
<td>2 days</td>
<td>3</td>
</tr>
<tr>
<td>43/F</td>
<td>0.5</td>
<td>18</td>
<td>2 days</td>
<td>6</td>
</tr>
<tr>
<td>35/M</td>
<td>0.5</td>
<td>24</td>
<td>2 days</td>
<td>2.5</td>
</tr>
<tr>
<td>54/F</td>
<td>0.5</td>
<td>18</td>
<td>2 days</td>
<td>5</td>
</tr>
<tr>
<td>32/F</td>
<td>0.5</td>
<td>10</td>
<td>2 days</td>
<td>7</td>
</tr>
<tr>
<td>51/M</td>
<td>0.5</td>
<td>4</td>
<td>3 days</td>
<td>8</td>
</tr>
</tbody>
</table>

VPRS = verbal pain rating score; NA = not available.

* Unilateral.

Data from this study confirm previously published material. The 18% incidence of TNS in patients undergoing arthroscopy with lidocaine-induced spinal anesthesia in this study is similar to the 19% incidence reported in similar patients receiving 5.0% and 2.0% lidocaine1 and similar to the 22% incidence in patients undergoing arthroscopy reported by Liquori et al.19 Overall, the incidence of TNS reported in previous randomized, prospective studies for other patient populations varies from 4% to 37%.1,2,17-20 The variability in incidence may be related to different surgical procedures with different patient positioning. When these studies are separated by surgical procedure, there is a great deal of consistency in the incidence of TNS within the same surgical group. For example, patients undergoing knee arthroscopy consistently have a 18-22% incidence of TNS with lidocaine-induced spinal anesthesia,1,18 patients undergoing lithotomy have an incidence of 30-37%,1,17,20 and supine patients have an incidence of 4-8%.4 The lowest reported incidence is found in mixed patient groups (3 to 4%)19,21 and in a nonrandomized study of patients in the prone jackknife position receiving low doses (30-45 mg) of 3.0% lidocaine.22 Previous studies concluded that the incidence of TNS is not reduced by diluting lidocaine from 5.0% to 2.0%, and the current study indicates that further dilution to 0.5% also does not decrease the incidence of these symptoms. Therefore, from a clinical standpoint, dilution of lidocaine does not decrease the incidence of TNS.

The cause of TNS remains undefined and has been speculated to be local anesthetic toxicity,25,24 needle trauma, neural ischemia secondary to sciatic stretching,3 patient positioning, pooling of local anesthetic agents secondary to maldistribution caused by pencil-point needles,25 glucose addition, muscle spasm, myofascial trigger points,26 early mobilization, or irritation of dorsal ganglia.27 Several authors have suggested that pencil-point needles may be responsible for TNS by causing caudal layering of local anesthetic agents, similar to that seen with spinal catheters. This theory, however, is not supported by work performed in glass spine models.28,29

Although patients in this study were not specifically examined for the presence of myofascial trigger points, another theory of the cause of TNS is that it may be secondary to muscle spasm or a myofascial syndrome. Naveira et al.26 described two patients with a similar syndrome of back pain and lower extremity pain 2 weeks after spinal anesthesia who were successfully treated with trigger-point injections. A recent, large prospective, nonrandomized study identified ambulatory surgery status, the lithotomy position, and obesity as the only predictive factors in the development of TNS in patients receiving lidocaine spinal anesthesia.21 The increased incidence of TNS in the ambulatory surgical population that undergoes early mobilization may lend credence to a muscular or myofascial cause.

Several limitations to our study design must be recognized. Four different surgical attending physicians participated in this study; therefore, differing surgical techniques cannot be ruled out as a contributing factor in the development of TNS. In addition, there was no bupivacaine spinal control group. Bupivacaine spinal anesthesia has been shown in numerous studies3,16,20,17,13,30 and at our own institution in the same study population1 not to be associated with the development of TNS. Nonetheless, addition of a bupivacaine control group would have served to more completely rule out spinal needle placement and surgical positioning as causal factors in the development of TNS. Finally, although the study solutions were of identical milligram dose and were all hyperbaric, they did not have identical specific gravity, osmolarity, or volume. Therefore, no conclusions can be
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drawn regarding the importance of injectate volume, osmolarity, or specific gravity from this study.
This is the first randomized, prospective, double-blind study to determine the incidence of TNS in ambulatory patients undergoing knee arthroscopy with low-concentration lidocaine spinal anesthesia. We determined that, for ambulatory patients undergoing arthroscopy, the incidence of TNS is not reduced by decreasing the anesthetic concentration from 2.0% to 0.5%, and that incidence of TNS with the 0.5% solution is not significantly different from a previous report in a similar population receiving 5.0% lidocaine. Thus, dilution of spinal lido
caine does not appear to have clinical usefulness for decreasing the incidence of TNS.

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dic Surgery and the Research Staff at Virginia Mason Medical Center for their cooperation during this study; Dan J. Kopacz, M.D., for editorial assistance; and Scott Lancaster for statistical analysis.

References

3. Salmela L, Cozantis DA: Leg and back pain after spinal anesthe
sia involving hyperbaric 5% lidocaine. Anesthesia 1996; 51:391–3
7. Sjostrom S, Blass J: Severe pain in both legs after spinal anesthe
sia with hyperbaric 5% lidocaine solution. Anesthesia 1994; 49:700–2
11. Alfredt A, Hogg M, Robinson S: Transient radicular irritation as a complication of spinal anesthesia with hyperbaric 5% lidocaine. Anaesth Intens Care 1996; 24:508–10
18. Liguori GA, Zayas VM, Chisholm MF: Transient neurologic symp
ptoms after spinal anesthesia with mevipacaine and lidocaine. Anesthesiology 1998; 88:619–23
ptoms after hyperbaric subarachnoid anesthesia with 5% lidocaine and 5% prilocaine. Anesthesiology 1998; 88:624–8
ptoms after spinal anesthesia. Anesthesiology 1998; 88:629–33
23. defong R: Last round for a "Heavyweight"? Anesth Analg 1994; 78:3–4
27. Dahlgren N: Transient radicular irritation after spinal anesthe
30. Holman SJ, Frey K, Sheikh T, Ryan K, Kao TC, Stevens RA: Transient radicular irritation after hyperbaric spinal lidocaine (ab
Appendix

Transient Neurologic Symptoms Follow-up

Follow-up (48 h)
Backache: Yes/No
Leg Pain: Yes/No
If yes, then
Location
Description
Severity (scale, 0–10)
When pain began
Duration of pain
What has patient done to treat the pain?
Degree of activity
Crutches: Yes/No