Comparison of 5% with Dextrose, 1.5% with Dextrose, and 1.5% Dextrose-Free Lidocaine Solutions for Spinal Anesthesia in Human Volunteers

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The use of lidocaine in concentrations less than 5% for spinal anesthesia may be advantageous but has not been carefully studied. Lidocaine 50 mg (1.5% with dextrose and 1.5% dextrose-free) was administered to eight volunteers in a randomized, double blind, cross-over fashion. All of these subjects had previously received 5% lidocaine with dextrose using the same experimental protocol. Sensory analgesia was assessed with pin-prick, transcutaneous electrical stimulation (TES) equivalent to surgical incision, and duration of tolerance of pneumatic thigh tourniquet. Motor block was assessed with isometric force dynamometry. Peak dermatomal level was the highest and duration until regression of pinprick the longest with the 5% solution (P < 0.05). Duration of tolerance to TES was increased (33 ± 10 min) with the 5% solution (P < 0.04). Duration of tolerance to tourniquet pain was increased (11 ± 3 min) with the 5% solution (P < 0.02). Duration of motor block was increased (45 ± 9 min) with the 5% and the 1.5% without dextrose solutions (P < 0.04). Time to void was increased (33 ± 5 min) with the 5% solution (P < 0.03). In conclusion, the use of different solutions of lidocaine for spinal anesthesia results in significant differences in sensory and motor block and time until recovery of micturition.

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Spinal anesthesia with lidocaine as a 5% hyperbaric solution is popular for brief surgical procedures due to rapid regression of sensory and motor block (1). However, recent interest has arisen in the use of less concentrated solutions of lidocaine due to potentially quicker patient recovery (2) and concerns over potential neurotoxicity of 5% lidocaine (3-5). Unfortunately, differences in sensory and motor block from various solutions of lidocaine have not been examined in a carefully controlled fashion (2,6), and thus it remains unclear whether there are clinically relevant differences. In addition, previous studies have documented wide intersubject variability of sensory and motor block from lidocaine spinal anesthesia (6,7). This wide variability increases the difficulty of determining differences between various solutions of lidocaine for spinal anesthesia. However, we have previously used paired human data (cross-over design) and quantitative assessments of sensory and motor block to sensitively examine the effects of addition of intrathecal fentanyl and epinephrine on lidocaine spinal anesthesia (8,9). Thus, this study was designed to compare the characteristics of sensory and motor block after spinal anesthesia from 5% lidocaine with dextrose, 1.5% lidocaine with dextrose, and 1.5% lidocaine dextrose-free in a carefully controlled manner.

Methods

After institutional review board approval and informed consent were acquired, eight healthy volunteers (three male and five female) were enrolled in this study. Each subject underwent spinal anesthesia with 50 mg lidocaine 1.5% with and without dextrose 7.5% (Astra Pharmaceutical Products, Inc., Westborough, MA) in a randomized, balanced, double-blind, cross-over fashion. The two spinal anesthetics were separated by at least 24 h in each subject. All of these subjects had previously undergone spinal anesthesia with 5% lidocaine with dextrose 7.5% (50 mg) using the same study protocol. Data obtained from these subjects with 5% lidocaine have been published previously (8,9) and are included for comparison with the current study.
Subjects had received nothing by mouth for 8 h and voided immediately prior to each study. Lactated Ringer’s solution was administered as a bolus of 6 mL/kg over 15 min prior to subarachnoid block, followed by 8 mL·kg⁻¹·h⁻¹ for the first hour, then maintenance infusion at a rate of 2 mL·kg⁻¹·h⁻¹. Lumbar puncture was performed (in the left lateral decubitus position) at the L2-3 interspace with a 25 gauge Whitacre spinal needle through a 20-gauge introducer with the orifice of the spinal needle turned cephalad. Cerebrospinal fluid, 0.2 mL, was aspirated and study solution was injected at a rate of 0.25 mL/s; an additional 0.2 mL of cerebrospinal fluid was aspirated and reinjected after injection of study solution.

After injection, subjects were immediately placed supine and remained level for the duration of the study. All subjects were monitored in the usual manner.

Hypotension (systolic blood pressure <90 mm Hg or a >20% decrease from baseline) was treated with 5-mg increments of ephedrine, bradycardia (heart rate < 50 bpm or a >20% decrease from baseline) was treated with 0.4 mg of atropine, respiratory depression (pulse oximetry oxygen saturation <90% while breathing room air) was treated with oxygen via a face mask, and nausea was treated with 5 mg of ephedrine followed by 10 mg of metoclopramide. Subjects were questioned 24 and 48 h after each study period for symptoms of transient radicular irritation (4).

Toleration to transcutaneous electrical stimulation (TES) equivalent to surgical incision was assessed as previously described (8,9). TES leads were placed in the midline at T10 and T12 dermatomes and bilaterally at L2-3 (medial aspect above knee) and L5-S1 (lateral aspect above ankle). Five seconds of 50-Hz tetanus at 60 mA with a commercially available nerve stimulator (Model NS252; Fisher & Paykel, Auckland, New Zealand) was considered equivalent to surgical incision (10). Toleration to electrical stimulation was assessed 4 min after injection of spinal solution and measured every 10 min thereafter by initially testing with 10 mA and then increasing in 10 mA increments to a maximum of 60 mA for 5 s. Each TES location was tested in a systematic order moving from distal to proximal sites. In addition, dermatomal levels to pinprick (18-gauge needle) were measured every 5 min after injection of spinal solution until 40 min postinjection, and then every 10 min until recovery of pinprick sensation at S2.

Tourniquet pain was assessed as previously described (9,11). Thirty minutes after injection of spinal solution, the left leg was exsanguinated by gravity, and a 7-cm orthopedic pneumatic tourniquet inflated around the left midtibial to 300 mm Hg. At the first study session, each subject was shown a visual analog scale (VAS) marked from 0 to 100 mm with 0 representing no discomfort and 100 representing the worst discomfort imaginable. The subjects were instructed that the tourniquet would be deflated due to discomfort at any time. Immediately prior to deflation, subjects were asked to rate their discomfort on the VAS scale and to fix the degree of discomfort in their mind.

At the next study session, subjects were shown their previous level of discomfort on the VAS scale and instructed to request tourniquet deflation at the same level of discomfort as the previous session. Tourniquets were left inflated until subjects requested deflation or for a maximum of 2 h after inflation.

A commercially available isometric force dynamometer (Micro FET; Hoggan Health Industries, Draper, UT) was used to assess 5-s isometric maximum force contraction of the right quadriceps and gastrocnemius as previously reported (8,9). Measurements were performed at baseline and then every 10 min after injection until return to at least 90% of baseline. Measurements were performed in triplicate and averaged for each measurement period. Isometric force dynamometry has been previously shown to be a reliable, quantitative method for evaluation of motor block during spinal and epidural anesthesia (8,12).

Ability to micturate was assessed as previously reported (8,9). All subjects received a standardized intravenous fluid infusion as outlined above. Subjects attempted to void when the level of pinprick reached dermatomal level S2. A bladder ultrasound (Bladder-Scan No. BV12500; Diagnostic Ultrasound Corporation, Kirkland, WA) was used to quantify the volume of urine within the bladder prior to attempting to void. If subjects were unable to immediately void, then repeat attempts were made every 15 min, and time from injection of spinal solution was recorded.

Differences between the three lidocaine solutions in onset and regression of sensory block (pinprick) and motor block were assessed with repeated-measures analysis of variance followed by post hoc testing with Fisher’s protected least significant difference. Differences between the three lidocaine solutions in peak dermatomal block heights, times of duration of sensory (pinprick and 1Es) and motor block, and time until recovery of ability to void were assessed with multiple paired t-tests with Bonferroni correction. The incidence of side effects was analyzed with Fisher’s exact test. Significance was P < 0.05. Results are reported as mean ± se unless otherwise noted.

Results

Subject ages ranged from 28–41 yr, heights from 140–162 cm, and weights from 51–85 kg.

Peak dermatomal levels to pinprick were higher with the 5% and 1.5% with dextrose solutions (Table 1). In contrast, regression of pinprick was prolonged
Table 1. Sensory Block to Pinprick After Spinal Anesthesia

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Lidocaine 5% with dextrose</th>
<th>Lidocaine 1.5% with dextrose</th>
<th>Dextrose-free</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak dermatome (median ± interquartile range)</td>
<td>T3 ± 2*</td>
<td>T4 ± 3*</td>
<td>T6 ± 4</td>
</tr>
<tr>
<td>Time to 2-segment regression (min)</td>
<td>65 ± 5*</td>
<td>39 ± 5</td>
<td>56 ± 8</td>
</tr>
<tr>
<td>Time to regression to dermatome L1 (min)</td>
<td>109 ± 6*</td>
<td>73 ± 10</td>
<td>104 ± 5*</td>
</tr>
<tr>
<td>Time to regression to dermatome S2 (min)</td>
<td>150 ± 8*</td>
<td>99 ± 11</td>
<td>130 ± 18*</td>
</tr>
</tbody>
</table>

Values are mean ± se unless otherwise noted.
* Different from lidocaine 1.5% dextrose free (P < 0.005).
\* Different from lidocaine 1.5% with dextrose (P < 0.02).

Table 1 demonstrates that significant differences in sensory and motor block occur after the use of equal doses of various solutions of lidocaine for spinal anesthesia. These differences may result from differences in baricity or in concentration, and thus volume, of the local anesthetic solution.

Discussion

Our results demonstrate that significant differences in sensory and motor block occur after the use of equal doses of various solutions of lidocaine for spinal anesthesia. These differences may result from differences in baricity or in concentration, and thus volume, of the local anesthetic solution.

Peak dermatomal level to pinprick was more cephalad with both hyperbaric solutions (5% and 1.5% with dextrose) as compared to the essentially isobaric 1.5% without dextrose solution (13). This finding of increased cephalad spread is consistent with previous studies examining solution baricity (14,15) and is thought to occur due to gravitational distribution of a hyperbaric solution to the lowest point of the thoracic curvature in the supine subject (14,16,17). Differences in regression to pinprick between the 1.5% hyperbaric and isobaric solutions may also have been due to baricity of solution. The faster regression observed with the 1.5% hyperbaric solution may be explained by greater spread and dilution of the hyperbaric solution within the spinal sac, thus resulting in a more transient sensory block. We also noted a difference in regression of pinprick between the 5% and 1.5% hyperbaric solutions (both with 7.5% dextrose) that has
Table 2. Duration of Tolerance to Electrical Stimulation Equivalent to Surgical Incision and of Pneumatic Thigh Tourniquet

<table>
<thead>
<tr>
<th>Dermatomal site</th>
<th>Lidocaine 5% with dextrose (min)</th>
<th>Lidocaine 1.5% With Dextrose (min)</th>
<th>Lidocaine 1.5% dextrose free (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T10</td>
<td>41 ± 9a,b</td>
<td>23 ± 8</td>
<td>14 ± 9</td>
</tr>
<tr>
<td>T12</td>
<td>61 ± 15a,b</td>
<td>29 ± 10</td>
<td>20 ± 13</td>
</tr>
<tr>
<td>L2-3 (above knee)</td>
<td>103 ± 8a,b</td>
<td>56 ± 8</td>
<td>73 ± 14</td>
</tr>
<tr>
<td>L5-S1 (above ankle)</td>
<td>106 ± 10a,b</td>
<td>50 ± 10</td>
<td>93 ± 9b</td>
</tr>
<tr>
<td>Tourniquet</td>
<td>55 ± 10a,b</td>
<td>40 ± 8</td>
<td>38 ± 4</td>
</tr>
</tbody>
</table>

Values are mean ± se unless otherwise noted.

a Different from lidocaine 1.5% dextrose free (P < 0.02).
b Different from lidocaine 1.5% with dextrose (P < 0.02).

Figure 2. Time course of motor strength in the quadriceps and gastrocnemius muscles after spinal anesthesia as assessed by isometric force dynamometry. Values are expressed as percent of baseline (prior to spinal anesthesia) measurement. Mean and se are displayed. Quadriceps: lidocaine 1.5% with dextrose is different from other groups (P < 0.05). Gastrocnemius: all three groups are different from each other (P < 0.05). Differences were detected with repeated-measures analysis of variance followed with post hoc testing with Fisher's protected least significant difference.

not been reported previously (2,16). There is a theoretical basis for concentration-dependent effects on the block of neural conduction, as laboratory studies demonstrate greater conduction block in isolated nerves after exposure to 5% vs 1.5% lidocaine (3,5). In contrast, most clinical studies examining sensory block after spinal anesthesia with solutions of different concentrations have not observed significant differences in sensory block to pinprick (16). However, the majority of these clinical studies examined bupivacaine spinal anesthesia and had low statistical power to detect differences due to enrollment of relatively few subjects. No previous study has examined the effects of drug concentration on sensory block after lidocaine spinal anesthesia with paired human data. As the intersubject variability of sensory block after lidocaine spinal anesthesia is large (7), our use of a cross-over study design would allow greater sensitivity to detect such differences.

Although measurement of dermatomal levels to pinprick is a commonly accepted measure of sensory block, the relevance of pinprick levels to surgical anesthesia remains uncertain (8). TES has been shown to provide a stimulus equivalent to surgical incision during general anesthesia (10) and should be a more realistic measure of surgical anesthesia than pinprick. Solution baricity affected intensity of sensory block, as the isobaric 1.5% solution produced a greater duration of tolerance to TES at the ankle as compared to the hyperbaric 1.5% solution. We theorize that the isobaric solution kept a greater amount of lidocaine in proximity to the L5-S1 nerve roots, whereas the hyperbaric solution underwent greater cephalad spread and dilution. The higher peak dermatomal level to pinprick after hyperbaric versus isobaric 1.5% supports this speculation. Solution concentration also affected intensity of sensory block, as the 5% solution produced consistently greater duration of toleration to TES equivalent to surgical incision at every site tested (umbilicus, hip, knee, and ankle). This finding may again be due to greater ability of a more concentrated lidocaine solution to block neural conduction. Overall, our data suggest that the 5% solution may provide the greatest duration of surgical anesthesia at the umbilicus, hip, knee, and ankle, while the 1.5% isobaric solutions may be superior to the 1.5% hyperbaric solution in duration of surgical anesthesia at the ankle.

Another clinically useful modality of sensory testing is the application of a pneumatic thigh cuff. Tourniquet pain is a poorly understood phenomena that may result in intolerable patient discomfort during an otherwise satisfactory spinal anesthetic (18). Although previous studies suggest that use of an isobaric solution may result in greater toleration of tourniquet pain after bupivacaine spinal anesthesia (19), our results found little difference between the isobaric and hyperbaric 1.5% solutions of lidocaine. An explanation for our findings may be that bupivacaine has intrinsically different effects on tourniquet pain than lidocaine (20), and may therefore be more affected by baricity. In...
contrast, toleration of tourniquet pain was prolonged with the use of the more concentrated 5% solution. Thus, it appears that concentration is a more important determinant of tolerance to tourniquet pain after lidocaine spinal anesthesia than baricity.

The effects of baricity and drug concentration on motor block after lidocaine spinal anesthesia are controversial (2,6). Our data offer some insight into relative effects of baricity and drug concentration on different muscle groups. The 5% with dextrose and the 1.5% dextrose-free solutions produced equivalent motor block at the quadriceps muscles (innervated by spinal roots L2-4) that was greater than the 1.5% hyperbaric solution. We theorize that the 1.5% hyperbaric solution lacked sufficient drug concentration for equivalent motor block after the extensive cephalad spread characteristic of hyperbaric solutions. Further effects of baricity and drug concentration may be seen at the more caudal gastrocnemius muscle (innervated by spinal roots S1-2), where the 1.5% isobaric solution became less effective than the 5% hyperbaric solution. As the 5% solution consistently produced the most intense motor block, it appears that drug concentration may be the overriding factor for motor block after lidocaine spinal anesthesia.

An important yet infrequently investigated recovery variable is recovery of the ability to void. Spinal anesthesia inhibits both micturition reflexes and detrusor function (21), and urinary disorders commonly persist for longer than 24 h after spinal anesthesia (22). Effects of different solutions of spinal lidocaine on recovery of ability to void are controversial (2,6) and may reflect a lack of control of patient hydration and a lack of frequent, scheduled testing of this recovery. We standardized intravenous fluid administration, determined the presence of significant amounts of urine in subject bladders, and tested ability to void every 15 min after regression of pinprick to S2. Although use of the 5% solution resulted in prolonged time until able to void, all subjects were able to void immediately after regression of pinprick to S2. Thus, the delay in voiding may only reflect prolonged sensory block with the 5% solution rather than a delay in intrinsic ability to void.

Side effects after spinal anesthesia were comparable between solutions and well tolerated. Recently, the use of 5% lidocaine has generated controversy regarding possible transient neurologic toxicity (23). Two subjects reported symptoms of transient radicular irritation after the use of 5% and one each after the 1.5% with dextrose and the 1.5% dextrose-free solutions. All four subjects reported resolution of the symptoms within 1-2 days. Although laboratory studies suggest that 1.5% lidocaine may be less toxic to isolated nerves than a 5% solution (3,5), it appears that a 1.5% solution is not entirely free of the potential for transient radicular irritation. This finding is consistent with preliminary results suggesting that the incidence of transient radicular irritation after spinal anesthesia does not differ between 5% with dextrose or 2% plain lidocaine and may be as high as 19% (24). However, our study was not designed to ascertain incidences or differences in side effects, as such surveillance studies frequently require the enrollment of hundreds of patients (25) due to the relatively low incidences of side effects.

Thus, conclusions as to relationships between lidocaine solutions and side effects should not be drawn from our study. A final limitation in the interpretation of our results is the inclusion of some nonrandomized data in our study. All participants were aware that subjects had previously received 5% lidocaine with dextrose, and it is possible that this knowledge may have resulted in some systematic bias.

In summary, the use of different solutions of lidocaine for spinal anesthesia results in significant differences in sensory and motor block and time until recovery of micturition. The use of a 5% solution produces prolonged duration of anesthesia, but also prolongs the time until recovery of micturition. The 1.5% isobaric solution provides greater sensory block at the ankle and greater motor block than the 1.5%
hyperbaric solution. Differences in solution concentration and/or baricity may explain these findings. Finally, a 1.5% solution of lidocaine does not eliminate the risk of transient radicular irritation.

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