Effect of Warm Lidocaine on the Sensory Onset of Epidural Anesthesia: A Randomized Trial

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Background: Administration of local anesthetics at body temperature has been reported to shorten the onset time of regional block; however, studies examining the effects of warmed lidocaine on the onset of epidural anesthesia are limited. Here, we ascertain whether warming lidocaine solution to body temperature shortens the time to onset of epidural anesthesia.

Methods: Eighty patients were randomly allocated into two groups of equal size. Both received 16 ml of lidocaine solution injected via the epidural route at the L4-5 interspace, with one group receiving the solution at room temperature (RT, 18°C) and the other receiving the solution warmed to body temperature (BT, 36°C). Sensory blocks at the T10, T12, and L3 dermatomes, perianal region, and upper level dermatomes were assessed by pinprick and their onset times recorded. Patients with incomplete anal sensory block were excluded.

Results: Seventy-seven patients were included for analysis. The pH value of the local anesthetic solution was significantly increased at BT compared to RT (6.57 ± 0.11 vs. 6.47 ± 0.11, p < 0.05). Significantly shorter onset times of sensory block were observed at the T12 (10.03 ± 3.55 vs. 11.71 ± 3.76 min) and L3 (7.49 ± 3.19 vs. 9.92 ± 3.46 min) dermatomes for the BT compared to the RT group (p < 0.005). The onset time of sensory block at the anal region was also shorter in the BT than the RT group (11.54 ± 4.35 vs. 12.50 ± 4.06 min, p < 0.05). No differences between groups with respect to gender, age, height, weight, visual analogue pain score, upper sensory level, or adverse events were observed.

Conclusions: Administration of lidocaine at BT compared to RT shortens the onset time of sensory block in epidural anesthesia with no associated adverse effects.


Key words: warm, lidocaine, epidural anesthesia, sensory block, onset time

Epineural anesthesia is usually employed for obstetric, urologic, partial orthopedic and anal surgeries because it is thought to provide greater patient satisfaction and safety than local and general anesthesia. However, the relatively longer time to onset of sensory block with epidural anesthesia is sometimes unacceptable to the surgical team. The addition of fentanyl or morphine to local anesthetic
preparations\textsuperscript{(1,2)} and adequate mixing\textsuperscript{(3)} and alkalinization\textsuperscript{(4,5)} of local anesthetic solutions have the potential to shorten the time to onset of sensory block. Although warming of local anesthetic preparations has been reported by some investigators to reduce the time to onset of sensory block during caesarean sections\textsuperscript{(6)} and caudal\textsuperscript{(7)} and axillary brachial plexus\textsuperscript{(8)} surgeries, other investigators found no significant temperature effects.\textsuperscript{(9,10)}

Lidocaine [2-diethylamino-N-(2,6-dimethylphenyl) acetamide] is an amide-type local anesthetic with clinical application world-wide.\textsuperscript{(11-14)} Nonetheless, studies examining the effects of warmed lidocaine preparations on the onset of epidural anesthesia are limited and their findings are controversial. This study was therefore conducted to determine whether administration of a lidocaine preparation at body temperature reduces the time to onset of epidural sensory block.

**METHODS**

This is a prospective, randomized, double-blind study, and the analysis follows the intention-to-treat principle. After approval of this study by the Ethics Committee of the Chang Gung Memorial Hospital, informed consent was obtained from each patient. Subjects with a history of neurological, cardiopulmonary, or psychiatric disturbances or sensitivity to local anesthetics were excluded. Eighty patients with ASA physical status class I-II, who were 18-64 years of age, and who were scheduled for elective anal surgery (hemorrhoidectomy and fistulectomy) were included. A computer-generated random-number table was used to divide these patients randomly into two equal-sized groups: the room temperature (RT, 18°C) group and the body temperature (BT, 36°C) group. All patients were monitored during anesthesia with electrocardiograms, non-invasive blood pressure measurements, and pulse oximetry. The technique of “one-shot” epidural anesthesia was employed in this study. With the patient in the left lateral decubitus position, the epidural space at the L4-5 level was identified with an 18-gauge Tuohy needle by the “loss of resistance” technique. With the bevel of the Tuohy needle in the caudal direction, a single injection of local anesthetic was performed without inserting an epidural catheter. Three ml of an RT test solution containing 2% lidocaine (AstraZeneca AB, Sodertalje, Sweden) and epinephrine (1:200,000) was injected first. If no signs of intravascular or subarachnoid injections were observed within 3 min, four aliquots (4 ml each, total volume of 16 ml) of epinephrine-free lidocaine were then injected through the epidural needle over a 10 second period. The local anesthetic solution, the epidural set, and the epidural glass syringe were placed in a warming cabinet (FIRSTEK model OV-80, Taipei, Taiwan) controlled thermostatically at 38°C so that the temperature of the local anesthetic solution reached approximately 36°C before administration to subjects in the BT group. The temperature of the test solution was measured immediately prior to performing the epidural injection. Additionally, a 3 ml sample was removed immediately prior to the injection for pH determinations using a pH meter (Thermo Orion, 350, Massachusetts, U.S.A.). After the epidural injection, patients were maintained in the left lateral decubitus position for surgery. A blind observer assessed the time to sensory block after the injection using the pinprick method applied along the left middle mammary line from the thoracic level to the perianal region. Assessments were performed at 2.5 min intervals for a total of 45 min. The time of onset of sensory blockade was defined as the time to loss of pinprick sensation from a blunt 21-gauge needle at the T10, T12, and L3 dermatomes, and the perianal region. The highest level of sensory block was recorded 45 min after epidural administration of lidocaine. Heart rate and oxygen saturation (SpO\textsubscript{2}) were continually monitored and recorded, and arterial blood pressure was measured every 3 min after the epidural injection. Hypotension (systolic blood pressure < 100 mm Hg or a decrease in systolic blood pressure of more than 30% from baseline) was treated with 4 mg of intravenous ephedrine as needed. A visual analogue scale (VAS, 0-10) was used to assess pain at the start of surgery, with 0 indicating no pain and 10 indicating the worst possible pain. Epidural anesthesia was administered to all subjects in this study by the same anesthesiologist whereas assessments of all subjects were performed by a different anesthesiologist who was unaware of the group assignments.

Side effects such as paresthesia during the injection, nausea, vomiting, shivering during the operation, and postoperative headache or backache were
recorded. Patients who required narcotics due to an incomplete anal block or whose time to onset of blockade at the anal region exceeded 40 min were excluded.\(^{(15,16)}\)

All continuous data are expressed as mean ± SD or range, and Student’s \(t\)-test was used to compare data between the two groups. The upper levels of sensory block and the pH values of the local anesthetic solutions were also analyzed by Student’s \(t\)-test. Differences in the incidences of side effects between the groups were analyzed by the chi-square or Fisher’s exact test. A \(p < 0.05\) was considered significant. Statistical analyses were performed using the SPSS package (version 10.1 for Windows) and Graph Pad software (version 4.0).

The choice of sample size for this study was based on estimates of the differences in anesthetic solution temperatures and times to onset of sensory block. The mean onset time for analgesia at the L3 level was 9.92 ± 3.46 min for the RT group and 7.49 ± 3.19 min for the BT group. By the estimation formula \(n = 15.7/ (ES)^2 + 1\), where \(ES = \text{effect size} = (\text{difference between the two group means}) / \text{(standard deviation of the RT groups)}\), a sample size of 36 subjects in each group would be sufficient to obtain a two-tailed type I error of 0.05 and a power of 80%.\(^{(17)}\)

### RESULTS

Three of the 80 patients enrolled in this study were excluded, one (BT group) because of dural tap and the other two (RT group) because of incomplete sensory block at the anal region requiring additional local anesthesia. The two study groups were similar with respect to gender, age, weight, height, and operation type. Values for the VAS and upper level of sensory block did not differ significantly between the two lidocaine solutions (Table 1). The pH value was significantly higher \((p < 0.05)\) in the BT group (6.57 ± 0.11) than the RT group (6.47 ± 0.11) (Fig. 1). The onset times of the two local anesthetic solutions are presented in Table 2. The onset time for sensory block was significantly shorter at the T12 and L3 dermatomes \((p < 0.005)\) and anal region \((p < 0.05)\) in the BT group than the RT group. Adverse events in the two groups are listed in Table 3. The incidence of shivering in the BT group (7 of 39 subjects) was lower than in the RT group (10 of 38 subjects), although this difference was not statistically significant. No significant differences in adverse effects were observed between groups. No systemic toxicity or serious adverse events were noted in any patient in this study.

### DISCUSSION

Procedures that speed the onset of epidural

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**Table 1. Patient Data**

<table>
<thead>
<tr>
<th></th>
<th>2% Lidocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RT (n = 38)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>17/21</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>41.1 ± 8.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.5 ± 10.0</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.0 ± 7.2</td>
</tr>
<tr>
<td>Type of operation</td>
<td></td>
</tr>
<tr>
<td>Hemorrhoidectomy</td>
<td>27</td>
</tr>
<tr>
<td>Fistulectomy</td>
<td>11</td>
</tr>
<tr>
<td>VAS (range)</td>
<td>0.33 ± 0.48 (0-1)</td>
</tr>
<tr>
<td>Upper level (range)</td>
<td>7.61 ± 1.65 (3-11)</td>
</tr>
</tbody>
</table>

Abbreviations: VAS: visual analogue scale score. Data are expressed as mean ± SD (range) or the number of patients; Upper level: highest level of sensory block. The chi-square test and Student’s \(t\)-test were used. There were no significant differences between the two groups.

**Fig. 1** pH values of 2% lidocaine solutions at room temperature (RT) and body temperature (BT). Student’s \(t\)-test was used. *: \(p < 0.05\), there were significant differences between groups.
anesthesia are highly favored by surgical teams. Although alkalinization of local anesthetics can be used to shorten the onset time for sensory block, the potential for drug precipitation limits the amount of sodium bicarbonate that can be added to local anesthetic solutions.\(^{4,18}\) The interaction of local anesthetics with bicarbonate can induce precipitate formation when the temperature is increased.\(^{19}\) Preparations containing local anesthetics in combination with narcotics may speed the onset time for sensory block\(^ {6-8}\) but are associated with postoperative urine retention and respiratory depression.\(^ {21,22}\) In contrast, warming local anesthetic solutions is a simple and efficient procedure to shorten the time to onset of sensory block.

In the present study warmed lidocaine was found to accelerate the onset of sensory block compared to non-warmed anesthetic in epidural anesthesia. However, the mechanism for this is not clear. Possible mechanisms include an increased rate of passive diffusion across non-neural structures and an increase in the non-ionized (more penetrable) form of the local anesthetic.\(^ {6-8}\) The pKa of lidocaine, a basic drug, is approximately 7.8 at 25°C.\(^ {23}\) At physiological pH, therefore, a significant fraction of the drug will be present in the non-ionized, free base form. Raising the pH of a lidocaine preparation to the pKa of this local anesthetic further increases the fraction of non-ionized drug. For example, the shortened onset time of epidural anesthesia because of alkalinization of local anesthetic preparations has been attributed to an increase in the non-ionized form of the drug.\(^ {23}\) In the present study, the mean pH value of the lidocaine solutions increased modestly but significantly when these solutions were raised to BT compared to solutions maintained at RT. The fraction of non-ionized, more penetrable drug may therefore have been greater in the solutions at BT than RT. It should be noted, however, that the pKa values of local anesthetics decrease with increasing temperature.\(^ {24,25}\) As defined by the van’t Hoff equation, a decrease in pKa should increase the fraction of non-ionized drug. The difference in onset time for epidural block observed in response to warming of lidocaine preparations may therefore be attributable to an alteration in the pKa for lidocaine. Tetzlaff et al reported that the baricity of local anesthetics is decreased during increased temperature\(^ {26}\) but the effect of baricity on sensory block onset is controversial for spinal anesthesia and evidence is also limited for epidural anesthesia.\(^ {27}\)

When compared to preparations at RT, local anesthetic preparations warmed to temperatures approaching BT are reported to reduce the time to onset of caudal block when using lidocaine with adrenaline by 39%\(^ {10}\) and of obstetric epidural block with bupivacaine by 20%.\(^ {10}\) In one study\(^ {40}\) the time to onset of brachial plexus block was found to be reduced by almost 50% with a lidocaine preparation at BT compared to one at RT. However, in other studies of obstetric epidural block using bupivacaine or lidocaine with adrenaline\(^ {40}\) and brachial plexus

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### Table 2. Onset Time (minutes) of Sensory Block at T10, T12, L3 and Anal Region

<table>
<thead>
<tr>
<th>Dermatomes</th>
<th>2% Lidocaine</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RT (n = 38)</td>
<td>BT (n = 39)</td>
</tr>
<tr>
<td>T12</td>
<td>11.71 ± 3.76</td>
<td>10.03 ± 3.55</td>
</tr>
<tr>
<td>L3</td>
<td>9.92 ± 3.46</td>
<td>7.49 ± 3.19</td>
</tr>
<tr>
<td>Anal region</td>
<td>12.50 ± 4.06</td>
<td>11.54 ± 4.35</td>
</tr>
<tr>
<td>T10</td>
<td>14.25 ± 3.85</td>
<td>13.59 ± 3.80</td>
</tr>
</tbody>
</table>

**Abbreviations:** RT: room temperature; BT: body temperature. Data are expressed as mean ± SD or number of patients (n). Student’s t-test was used. A p < 0.05 indicates significant difference between groups.

### Table 3. Adverse Effects

<table>
<thead>
<tr>
<th>2% Lidocaine</th>
<th>RT (n = 38)</th>
<th>BT (n = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paresthesia</td>
<td>4 (10.5)</td>
<td>3 (7.7)</td>
</tr>
<tr>
<td>Shivering</td>
<td>10 (26.3)</td>
<td>7 (17.9)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>7 (18.4)</td>
<td>7 (17.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (7.9)</td>
<td>4 (10.3)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (5.3)</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (2.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Backache</td>
<td>2 (5.3)</td>
<td>1 (2.6)</td>
</tr>
</tbody>
</table>

**Abbreviations:** RT: room temperature; BT: body temperature. Data are presented as numbers (percentages). The chi-square test or Fisher’s exact test was used. There were no significant differences between groups.
Warm lidocaine speeds epidural block

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Warm lidocaine speeds epidural block using lidocaine with adrenaline, no significant effects on time to onset were observed with warming of local anesthetic preparations.

In the present study, significantly faster sensory blockade (approximately 8-24% reduction in onset time) at the anal region and at the T12 and L3 dermatomes was observed for the BT compared to the RT group. A shorter onset time for T10 block was also found for the BT than the RT group, although the difference was not statistically significant. Furthermore, the level of maximal cranial spread of sensory block was not significantly different between the two groups. These findings consistently show that temperature effects on the time to onset of sensory block are most significant for dermatomes that lie close to the injection site.

Epinephrine possesses the capacity to decrease local blood flow, slow the systemic absorption of local anesthetic agents, and increase the diffusion of anesthetic molecules to the nerve membrane. In the present study, however, epinephrine was included only in the initial test solution. It is therefore concluded that warmed lidocaine will enhance the time to onset of epidural sensory block regardless of the presence of epinephrine.

Two patients in the present study displayed incomplete sensory block at the anal region. Many factors, such as age, epidural pressure, anatomy of the epidural space, injection site, injection technique, and solution volume are known to influence the spread of local anesthetics. It is therefore proposed that increasing the volume of the anesthetic solution and/or injecting the anesthetic at a lower site may improve delivery of the anesthetic to the desired location. Spinal/saddle block has a faster onset time, is more predictable, and requires smaller doses of local anesthetic than epidural block. However, spinal/saddle block is associated with an increased risk of postdural puncture headache.

No serious adverse events were noted in this study. In previous studies, injection of local anesthetics at BT was found to be less painful and more comfortable for patients than injection of local anesthetics at RT, however, no differences in the degree of pain during injection were observed between groups in the present study. In this regard, the distribution of subcutaneous small nerves may differ from that of small nerves in the epidural space. The incidence of shivering in the BT group was lower than that in the RT group: although not statistically significant, this finding is consistent with that of a previous study. One patient in the present study had a dural tap. It is conceivable that the rigid Tuohy needle was held in situ for an inappropriately long period in this patient. The possibility that prolonged placement of this needle is associated with dural tap will be considered in future studies.

Our results showed that warmed lidocaine can shorten the onset time of sensory block about 2 to 3 minutes in epidural anaesthesia. The use of warmed lidocaine preparations not only increases the time needed to perform anesthesia and the use of material resources, but the warming procedure, which requires temperature-controlled access, could also change the shelf life of the anesthetic preparation and increase the risk of contamination and infection.

In conclusion, administration of lidocaine solutions at BT compared to RT decreases the time to onset of sensory block during epidural anesthesia and is not associated with an increase in adverse events.

Acknowledgements

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REFERENCES

Warm lidocaine speeds epidural block

加溫 Lidocaine 對硬脊膜外麻醉感覺起始作用影響之隨機研究

柳復兆1,2 劉錦榮1,2 戴元基 李漢倫 余黃平

背景：過去曾報導加溫之局部麻醉藥可縮短局麻阻斷作用起始時間，然而此說法仍有爭論。目前有關加溫 Lidocaine 使用於硬脊膜外麻醉上之研究資料很少。故本研究即在檢視是否加溫之 Lidocaine 可縮短硬脊膜外麻醉感覺阻斷作用起始時間。

方法：八十位接受常規肛門手術病患隨機分為兩組：室溫 (18°C) Lidocaine 組及體溫 (36°C) Lidocaine 組，每組各四十人。總量十六毫升 Lidocaine 局部麻醉藥經由腰椎第四、五節間硬脊膜外注入。並利用針尖測量第十、第十二胸椎、第三腰椎及肛門區域等皮節之感覺阻斷情形及麻醉阻斷之高度。研究中病患之血流動力學的變化、視覺類比重 (VAS)、不良副作用及注射之局部麻醉藥的酸鹼度值均被記錄。發生有不完全肛門區域感覺阻斷之病患則排除在本研究外。

結果：七十七位病患被納入本研究。局部麻醉藥之酸鹼度值在體溫 Lidocaine 組明顯增加比室溫 Lidocaine 組有較明顯增加 (6.57 ± 0.11 vs. 6.47 ± 0.11, p < 0.05)。感覺阻斷作用起始時間，體溫 Lidocaine 組比室溫 Lidocaine 組明顯縮短 (p < 0.005)，在第十二胸椎時間比為 (10.03 ± 3.55 分鐘 vs. 11.71 ± 3.76 分鐘)，在第三腰椎時間比為 (7.49 ± 3.19 分鐘 vs. 9.92 ± 3.46 分鐘)；另外在肛門區域在體溫 Lidocaine 組比室溫 Lidocaine 組有較快感覺阻斷起始時間 (11.54 ± 4.35 分鐘 vs. 12.50 ± 4.06 分鐘, p < 0.05)。而兩組病患在性別、年齡、身高、體重、視覺類比重表、麻醉深度及不良副作用作用均無差別。

結論：本研究結果顯示加温之 Lipocaine 確實較室溫 Lidocaine 可縮短硬脊膜外麻醉感覺阻斷作用起始時間，且不會增加不良副作用。

(長庚醫誌 2009;32:634-9)

關鍵詞：加溫，Lidocaine，硬膜外麻醉，感覺阻斷，起始作用時間