Introduction

The term transient neurologic symptoms (TNS) is used to describe the symptoms of aches following radiation or dysesthesia in the buttocks or lower extremities\(^1\). TNS have been reported after spinal anesthesia with all local anesthetics. The incidence of TNS after lidocaine, for example, has been reported to be as high as 40\(^{\circ}\)\(^2\). Several studies have shown that bupivacaine, which is currently the most commonly used local anesthetic for spinal anesthesia, is associated with lower neurotoxicity and a lower incidence of TNS (0\%-3\%) compared with other local anesthetics\(^3\)\(^4\).

Incidence of Transient Neurologic Symptoms after Spinal Anesthesia: A Comparative Study between 0.24% Dibucaine/0.12% T-caine Compound and 0.5% Bupivacaine

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[Abstract] Background: The incidence of transient neurologic symptoms (TNS) after spinal anesthesia with dibucaine, which has potent neurotoxicity, is not well documented. In clinical settings, 0.24% dibucaine to which T-caine is added (Neo-Percamin®S) has been used extensively up to the present. In this study, we evaluated the incidence of TNS following spinal anesthesia with 0.24% dibucaine/0.12% T-caine compound (Neo-Percamin®S) and compared it to the incidence of TNS following spinal anesthesia with 0.5% bupivacaine. Methods: The study included 100 patients who were scheduled for brief surgical procedures under spinal anesthesia at our institution. The patients were randomly assigned to receive either 0.24% dibucaine/0.12% T-caine (n = 50) or 0.5% bupivacaine (n = 50). We investigated the presence, nature, and degree of TNS from the evening of surgery until postoperative day 3. Results: TNS were observed in 4 patients (8%) who received dibucaine/T-caine compound and 5 patients (10%) who received bupivacaine. No significant difference was observed in the incidence of TNS between the 2 groups. Conclusions: Although dibucaine has potent neurotoxicity, the incidence of TNS after spinal anesthesia was not significantly different between patients who received 0.24% dibucaine/0.12% T-caine and those who received 0.5% bupivacaine, which has lower neurotoxicity. Key Words: Transient neurologic symptoms, Spinal anesthesia, Dibucaine, T-caine, Bupivacaine
Dibucaine is not used in Europe and America because of reported potent neurotoxicity\(^5\). However, it has long been used for spinal anesthesia in Japan because of its potency of nerve blockade\(^6\). Dibucaine is associated with late onset of anesthetic effects. To expedite its effects in clinical settings, 0.24% dibucaine to which \(\text{T-}\)caine is added (Neo-Percamin\(^7\)S) has been used more frequently to deliver spinal anesthesia compared with 0.3% dibucaine.

Although several cases of cauda equine syndrome have been reported following spinal anesthesia with dibucaine\(^7\), no case reports or prospective studies concerning the incidence of TNS in similar settings have been documented to date. Therefore, this study aimed to evaluate the incidence of TNS following spinal anesthesia with 0.24% dibucaine/0.12% \(\text{T-}\)caine compound (Neo-Percamin\(^7\)S) and compare it with that following spinal anesthesia with 0.5% bupivacaine.

**Methods**

The study period was from August 1, 2007 through September 30, 2007. All patients provided written or oral informed consent, and the study was approved by the institutional review board of Tokatsu Hospital. The study population comprised 100 patients who were scheduled for brief surgical procedures under spinal anesthesia at Tokatsu Hospital. All patients were classified as American Society of Anesthesiologists physical status I or II. Patients with a history of chronic back pain and those with pre-existing neurological abnormalities were excluded. Patients were randomly assigned using a computer-generated randomization scheme to receive either 0.24% dibucaine/0.12% \(\text{T-}\)caine compound (\(n = 50\)) or 0.5% bupivacaine (\(n = 50\)). Neo-Percamin\(^7\)S (specific gravity at 20°C, 1.035–1.039), a 0.24% hyperbaric dibucaine/0.12% hyperbaric \(\text{T-}\)caine compound solution, was commercially obtained from Mylan Pharmaceutical (Osaka, Japan), and Marca\(^7\) (specific gravity at 20°C, 1.025–1.031), a 0.5% hyperbaric bupivacaine solution, was commercially obtained from AstraZeneca (Osaka, Japan).

Dural puncture was performed at the interspace of the L3–5 level using a 25-gauge Quincke–type spinal needle (Top Corporation, Tokyo, Japan) with patients in the lateral decubitus position. The local anesthetic was injected after correct needle position was identified by free flow of cerebrospinal fluid. Thereafter, patients were immediately placed in a supine position.

The segmental level of the sensory block was assessed by the bilateral pinprick or cold tests, and maximum block height was recorded. Patients in whom problems related to spinal puncture were encountered, such as multiple attempts, bleeding, or paresthesia, were excluded. Intraoperative monitoring included electrocardiography, oscillometry, and continuous pulse oximetry.

All patients were interviewed about the occurrence of TNS from the evening of surgery until postoperative day 3. Interviews were conducted once a day by an anesthesiologist blinded to the details of the anesthetic procedure. Symptoms were defined as pain and/or dysesthesia in the buttocks or lower extremities, starting from the recovery process or after recovery from spinal anesthesia. The recovery process indicates the period during which the segmental level of the sensory block is recovering from maximum block height to the L1 area and the degree of motor block evaluated by a modified Bromage scale is recovering from 4 to 0, where 0 = able to move hip, knee, ankle, and toes; 1 = unable to move hip but able to move knee, ankle and toes; 2 = unable to move hip and knee but able to move ankle and toes;
3 = unable to move hip, knee and ankle but able to move toes; and 4 = unable to move hip, knee, ankle, and toes. The date of TNS occurrence was recorded. Neurological examinations were performed on all symptomatic patients, and they were observed until they were symptom-free. The patients were also asked to rate the degree of discomfort using a visual analog scale (0 = no pain, 10 = worst conceivable pain).

The results are expressed as mean ± standard deviation. Patient demographic data were compared using Student’s t-test or Fisher’s exact test. The incidence of TNS and related categorical data were compared using Fisher’s exact test. A p-value of < 0.05 was considered statistically significant.

### Results

Demographic data and relevant aspects of the anesthetic and surgical procedures are summarized in Table 1. Demographic data, except for sex, did not differ significantly between the study groups. Anesthetic volume and dose are shown in Table 2. Satisfactory anesthesia was achieved and the operative course was uneventful in all patients. Complete recovery from anesthesia by the night of surgery was documented in all patients.

The incidence and characteristics of TNS are presented in Table 3. Symptoms were observed in 4 patients (8%) who received dibucaine/T-caine compound and 5 patients (10%) who received bupivacaine.

### Table 1  Characteristics of the study population

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>66 ± 15</th>
<th>63 ± 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n)</td>
<td>39</td>
<td>28</td>
</tr>
<tr>
<td>Female (n)</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160 ± 10</td>
<td>159 ± 10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60 ± 11</td>
<td>58 ± 10</td>
</tr>
<tr>
<td>Maximum height of block (range)</td>
<td>T6 (T3−12)</td>
<td>T6 (T3−10)</td>
</tr>
<tr>
<td>Lithotomy position (n)</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urologic (n)</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Orthopedic (n)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Abdominal (n)</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Inguinal (n)</td>
<td>12</td>
<td>10</td>
</tr>
</tbody>
</table>

* p < 0.05

Values are expressed as mean ± standard deviation.

### Table 2  Anesthetic volume and dose

| Anesthetic volume (ml) | 2.4 ± 0.3 | 2.5 ± 0.5 |
| Anesthetic dose (mg) | 5.8 ± 0.7/2.9 ± 0.4 | 12.5 ± 2.5 |

Values are expressed as mean ± standard deviation.
The cause of TNS remains unknown. Several investigators have assumed that TNS are symptoms of transient anesthetic-induced neurotoxicity. However, that speculation remains controversial. Local anesthetics exert significant neurotoxicity in laboratory settings, and lidocaine, prilocaine, and tetracaine appear to be more neurotoxic than bupivacaine and chloroprocaine in animal models. T-caine, which was added to dibucaine in this study, has not been used for spinal anesthesia independently. Its effects relative to those of other local anesthetics have not been well reported. However, because T-caine is a

| Table 3  Incidence and characteristics of transient neurologic symptoms |
|------------------|------------------|
|                  | 0.24% Dibucaine/0.12% T-caine | 0.5% Bupivacaine |
| Incidence (%)    | 4 (8%)            | 5 (10%)          |
| Onset time       |                  |                  |
| Postoperative day 0 | 2                | 3                |
| Postoperative day 1 | 0                | 0                |
| Postoperative day 2 | 1                | 1                |
| Postoperative day 3 | 1                | 1                |
| Duration (day)   |                  |                  |
| <1               | 2                | 3                |
| 1–2              | 2                | 2                |
| >2               | 0                | 0                |
| Lithotomy position (%) | 2 (50%) | 2 (40%)          |
| Location         |                  |                  |
| Buttocks         | 0                | 2                |
| Lower extremities| 4                | 3                |
| Symptoms         |                  |                  |
| Pain             | 2                | 1                |
| Dysesthesia      | 2                | 4                |
| Pain intensity*  |                  |                  |
| Mild (1–3)       | 3                | 5                |
| Moderate (4–7)   | 1                | 0                |
| Severe (8–10)    | 0                | 0                |

Values indicate the number of patients.

*Pain intensity was rated according to a visual analog scale (0 = no pain, 10 = worst conceivable pain).

There were no significant differences between the two groups.

No significant difference in the incidence of TNS was observed between the study groups, and no symptoms lasted for more than 3 days. Discomfort from TNS was slight, and patients recovered spontaneously or were treated effectively with potent nonsteroidal anti-inflammatory drugs. No patient had a sensory or motor deficit, abnormal muscle tendon reflexes, or bowel or bladder dysfunction.

Demographics and perioperative characteristics did not differ between patients with and without TNS.

Discussion

The present study found no significant difference in the incidence of TNS between patients given dibucaine/T-caine compound and those given bupivacaine for spinal anesthesia.
derivative of tetracaine, its anesthetic effects have been considered to be nearly the same as those of tetracaine. Ogawa et al.\(^1\) showed that dibucaine, tetracaine and bupivacaine concentrations that caused irreversible blockade of type-C nerve fibers were 0.03%, 0.075%, and 0.5%, respectively, in a rabbit desheathed cervical nerve model, indicating that the neurotoxicity of dibucaine and tetracaine was more than 16 and 6 times, respectively, as potent as that of bupivacaine. However, the incidence of TNS was of no significant relevance to the neurotoxic potency of the anesthetics in our study groups. In addition, another study indicated no significant difference in the incidence of TNS after spinal anesthesia between prilocaine and bupivacaine, despite differences in their neurotoxic potency. Therefore, the etiology of TNS may be different from that of permanent neurological symptoms or injury.

Lidocaine spinal anesthesia (odds ratio [OR], 5.1 vs. bupivacaine), lithotomy position (OR, 2.6), and ambulatory anesthesia (OR, 1.6) are important risk factors for TNS\(^2\). Schneider et al.\(^3\) postulated that the lithotomy position stretches the lumbosacral nerves and decreases blood flow, thus contributing to the development of symptoms. In contrast, the present study indicated no significant difference in the incidence of TNS between the lithotomy position and other positions. Another study showed that tetracaine with phenylephrine resulted in a high incidence of TNS, but this incidence was not influenced by the lithotomy position\(^4\). Freedman et al.\(^5\) reported that the risk of TNS was significantly related to the lithotomy position only when lidocaine was used. We hypothesize that such discrepant findings may have resulted from differences in the anesthetics used. Although the etiology of TNS remains to be determined, it is likely that differences in the incidence of TNS are due partly to an intrinsic property of the anesthetics based on the findings of the studies discussed above and the present study.

Several studies have reported a low incidence of TNS with bupivacaine spinal anesthesia (0%–3%)\(^2, 4\). Surprisingly, the incidence of TNS following bupivacaine spinal anesthesia was much higher (10%) in the present study. This may have been because we defined the onset time of TNS as that from the recovery process or after recovery from spinal anesthesia, and we evaluated patients from the evening of surgery until postoperative day 3. Previous studies defined the onset time of TNS as that after recovery from spinal anesthesia and evaluated patients only once on postoperative day 1 or 2\(^2, 4, 10, 11\). Hampl et al.\(^4, 14\) reported in two prospective studies that TNS did not occur after postoperative day 2 in 50 patients who received lidocaine and 90 patients who received lidocaine, bupivacaine, or prilocaine. In the present study, more than half the patients with TNS developed symptoms beginning from the recovery process during the evening of surgery and recovered the next day. If we evaluated patients according to the definition of previous studies\(^2, 4, 10, 11\), the number of patients with TNS in dibucaine/T-caine compound (n = 4: 8%) and bupivacaine (n = 5: 10%) would come down to one for each drug. Therefore, the incidence of TNS may vary greatly according to the definition of onset time. Indeed, it has been noted that the incidence of TNS with one anesthetic should be directly compared with that of another anesthetic because the reported incidences of TNS vary considerably\(^6\). This is also the reason why we must directly compare dibucaine/T-caine compound with bupivacaine.

In the present study, the discomfort of TNS was relatively minor: on a 10-point visual analog scale, the median values for symptomatic patients were 2.0
for dibucaine/T-caine compound and 2.5 for bupiva-
caine. The symptoms also resolved spontaneously or 
were treated effectively with potent nonsteroidal an-
ti-inflammatory drugs. No patient had a sensory or 
motor deficit. Therefore, TNS only had a minimal im-
impact on the patients’ postoperative course in the pres-
ent study. However, we cannot conclude from these 
findings that serious neurological injury will not de-
velop after spinal anesthesia. Accountability for peri-
operative anesthetic management in patients has 
been considered an important issue in recent years. 
The risk of TNS such as pain or dysesthesia in the 
buttocks or lower extremities and the possibility of 
serious neurological injury, albeit with a low frequen-
cy, must be sufficiently explained to patients prior to 
spinal anesthesia and surgery.

Our study had several limitations. First, the num-
ber of patients studied was small. Accordingly, a larg-
er follow-up study may be required to confirm these 
findings. Second, the anesthetists administering the 
spinal blocks were not blinded to the anesthetics 
used. Therefore, bias cannot be excluded. However, 
the research anesthetists who contacted and evaluat-
ed patients after surgery were blinded to all aspects 
of anesthetic care. Third, because we used the comp-
pound of dibucaine and T-caine, the anesthetic poten-
tcies of dibucaine and bupivacaine which were 
used were not equal. Strictly speaking, the anesthetic 
potencies must be the same in comparison with its 
neurotoxicity. Therefore, 0.3% dibucaine should be 
used for future research when compared with 0.5% 
bupivacaine.

In conclusion, the present results suggest no sig-
ificant difference in the incidence of TNS between 
patients given dibucaine/T-caine spinal anesthesia 
and those given bupivacaine spinal anesthesia. The 
relationship between the neurotoxic potency of anes-
thesics and the incidence of TNS remains speculative. 
Further large-scale studies will be required to con-
firm these findings.

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held in June 12–14, 2008

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ジブカイン／テーカイン合剤とブピバカインを用いた脊髄くも膜下麻酔後の一過性神経症状(TNS)の検討

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ジブカイン／テーカイン合剤とブピバカインについて、脊髄くも膜下麻酔後の一過性神経症状(TNS)の発症頻度を前向きに比較検討した。対象はASA分類Ⅰ,Ⅱのジブカイン／テーカイン使用50症例、ブピバカイン使用50症例として、TNSの定義は脊髄くも膜下麻酔による運動・知覚神経の最大遮断作用から回復過程以後に出現した臀部あるいは下肢の疼痛、しびれ感とした。結果はジブカイン／テーカイン使用の4症例(8%)、ブピバカイン使用の5症例(10%)に症状を認めたが、有意差はなかった。ジブカインは高い神経毒性を有するが、ジブカイン／テーカイン合剤については、毒性が低いとされるブピバカインと比較してもTNSの発症頻度に差を認めなかった。

キーワード: 一過性神経症状(TNS), 脊髄くも膜下麻酔, ジブカイン, テーカイン, ブピバカイン