Adhesiolysis and targeted steroid/local anesthetic injection during epiduroscopy alleviates pain and reduces sensory nerve dysfunction in patients with chronic sciatica.

Author(s)
Sakai, Tetsuya; Aoki, Hiroshi; Hojo, Minoru; Takada, Masafumi; Murata, Hiroaki; Sumikawa, Koji

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Adhesiolysis and targeted steroid/local anesthetics injection during epiduroscopy improves pain and sensory nerve dysfunction in patients with chronic sciatica

Short title: Epiduroscopy and sensory nerve function

Key words: Epiduroscopy – sensory nerve function – chronic sciatica – adhesiolysis – current perception threshold
Abstract

Purpose. The aim of this study was to evaluate the effect of adhesiolysis followed by the injection of steroid and local anesthetic during epiduroscopy on sensory nerve function, pain and functional disability in patients with chronic sciatica.

Methods. Epidural adhesiolysis using epiduroscopy followed by the injection of steroid and local anesthetic were scheduled in 19 patients with chronic sciatica refractory to lumbar epidural block. Sensory nerve function in legs by a series of 2000 (Aβ fibers), 250 (Aδ fibers) and 5 Hz (C fibers) stimuli using current perception threshold (CPT), pain and Roland Morris Disability Questionnaire (RMDQ) scores were assessed before and 1 and 3 months after epiduroscopy.

Results. At all frequencies, the CPT values in the affected legs of patients before the epiduroscopy were significantly higher than those in unaffected legs. Epidural adhesiolysis was successfully performed in 16 out of 19 patients. In these patients, the CPT values at 2000 and 250 Hz, pain and RMDQ scores 1 and 3 months after the epiduroscopy were significantly lower than those before the epiduroscopy, while the CPT value at 5 Hz did change.

Conclusion. Epidural adhesiolysis followed by the injection of steroid and local anesthetic during epiduroscopy improved pain, functional disability and dysfunction of
Aβ and Aδ fibers in patients with chronic sciatica.
Introduction

Recently, epiduroscopy has been shown to offer significant diagnostic and therapeutic interventions for patients with chronic low back pain and sciatica [1]. Although previous studies have shown that adhesiolysis in epidural space and targeted steroid injection during epiduroscopy is useful for pain relief in these patients [2-4], there are currently very few studies that show the effect of these procedures on sensory nerve function.

It is known that current perception threshold (CPT) testing can evaluate sensory nerve fibers in both a quantitative and selective manner: CPTs at 2000, 250 and 5 Hz stimuli directly represent the functions of Aβ, Aδ and C fibers, respectively [5,6]. Recent clinical studies have demonstrated that the CPT testing is useful for quantitative evaluation of sensory function associated with diabetic neuropathy [7,8], toe-to-digit transplantation [9], lumbar radiculopathy [10], and postherpetic neuralgia [11].

The present study was carried out to evaluate the effect of adhesiolysis followed by the injection of steroid and local anesthetic during epiduroscopy on sensory nerve function using the CPT testing, pain and functional disability in patients with chronic sciatica refractory to lumbar epidural block.
Materials and Methods

Patients

After institutional approval was obtained along with written informed consent, 19 patients with chronic sciatica were recruited for this study. Although all of the patients had received lumbar epidural local anesthetic (4 ml of 1% mepivacaine) and dexamethasone sodium phosphate (4 mg) at the L4-5 or L5-S1 level before the study, the duration of pain relief was less than 1 day. Sciatica was defined as the pain in the distribution of a lumbar nerve root, accompanied by neurosensory and motor deficits [12]. All of our patients had unilateral single radiating leg pain (L5 or S1) and low back pain with or without a history of previous back surgery. Patients who had obstructive arteriosclerosis, arachnoiditis or coagulopathy were excluded from the study.

One week before epiduroscopy, they had received an epidural injection consisting of 16 ml of a 1:1 diluted contrast medium (iotoran, Isovist; Schering, Japan) mixed with local anesthetics (1% mepivacaine) via the sacral hiatus under fluoroscopy in order to evaluate the degree of epidural adhesion.

The epiduroscopy technique

Patients were positioned prone on a translucent x-ray operating table with a pillow...
placed under the abdomen. Patients were then sedated with propofol (2mg·kg⁻¹·hr⁻¹). Under aseptic conditions, and following local anesthesia with 1% mepivacaine 5ml, a Touhy needle was inserted into the sacral canal. The tip of the needle in the sacral canal was confirmed by the injection of x-ray contrast medium (iotrolan 5ml, Isovist; Schering, Japan). A guide-wire was introduced through the Touhy needle, and the needle was replaced by a dilator. Then, a video-guided catheter (2000; Mylotec, Ruswell, GA, USA) with a 0.9-mm endoscope (3000E; Mylotec) was slowly advanced to the target area under direct vision and fluoroscopy. Adhesions in the epidural space were torn using the tip of epiduroscope and intermittent flushes of saline. After adhesiolysis, dexamethasone sodium phosphate (4 mg) and 1% mepivacaine 4 ml were injected. Then, epidurography was performed close to the intervertebral foramen of the affected nerve root.

**Assessment before and after epiduroscopy**

Leg pain and low back pain were evaluated using numerical rating scale (NRS) from 0 to 10, in which 0 = no pain and 10 = excruciating pain, separately. Functional disability caused by low back and leg pain was presented using the Japanese version of Roland Morris Disability Questionnaire (RMDQ) which was modified by adding the phrase, “my back or leg problem” to the end of all 24 questions [13,14].
Neurometer CPT/C (Neurotron, Baltimore, USA) was used to measure the current perception threshold at 2000, 250 and 5 Hz. The CPT testing was performed at the midpoint of the leg below the knee corresponding to the distribution of the affected nerve root, and at an identical location on the unaffected leg. The exact placement of the testing electrode was based upon the dermatome map developed by Bonica [15]. The methods of the CPT testing were similar to those described previously [11,16].

Sensory deficits were evaluated using hairy brush stroke in the same area as CPT testing. Subjects reported the intensity of touch sensation in the affected leg as the relative intensity compared to the unaffected leg. Sensory deficits in affected leg was graded as severe (50% and more decrease compared with the unaffected leg), mild (<50% and > 20%), slight (< 20%) and none.

Patients were allowed to continue to receive the conservative therapies including oral medications and physiotherapy, but were not allowed to start new oral medications or neural block. The intensity of pain, RMDQ score, CPT value and sensory deficits were assessed before and 1 and 3 months after the epiduroscopy.

**Data analysis**

For repeated measures over time, the Friedman test was used. When significance was found, the Wilcoxon signed rank test was used for post-hoc testing. The
Spearman rank correlation was used for correlation analysis between the severity of sensory deficit and the CPT value at 2000 Hz in affected leg. Results were expressed as median, and $P < 0.05$ was considered statistically significant.
Results

Epidurography before the epiduroscopy revealed that the epidural space surrounding the affected nerve root could not be filled with contrast medium, whereas that surrounding the unaffected nerve root was successfully filled in all of the patients.

In 16 out of 19 patients, adhesions close to the intervertebral foramen of the affected nerve root within the epidural space were found and epidural adhesiolysis followed by the injection of steroid and local anesthetic were successfully performed. The affected nerve root, suspected by neurological examination and preoperative epidurography was identified by reproducing pain when the tip of the epiduroscope gently touched the nerve root. The epidurography after the adhesiolysis showed that the epidural space surrounding the affected nerve root was filled with contrast medium. In another 3 patients, extensive adhesions were found around L5 and S1 and epiduroscopic adhesiolysis was gave up because of hard adhesions. Therefore, remaining 16 patients completed the study. Characteristics of these 16 patients were shown in Table 1. The total volume of infused saline during the epiduroscopy was 30-70 ml. The whole procedure was finished within 1 h in all of the patients.

At 2000, 250 and 5 Hz, the CPT values in the affected legs of patients before the epiduroscopy were significantly higher than those in the unaffected legs (302 vs. 188.5,
56.5 vs. 50.5 and 43.5 vs. 26, respectively). The CPT values at 2000 and 250 Hz in the affected legs, measured 1 and 3 months after the epiduroscopy were significantly lower than those before the epiduroscopy (2000 Hz: 192.5, 200.5 and 302; 250 Hz: 35, 44 and 56.5, respectively) (Fig 1A-B). The CPT value at 5 Hz in the affected leg, measured 1 and 3 months after epiduroscopy was lower than that before the epiduroscopy (22.5, 30.5 and 43.5, respectively), but statistically significant differences were not observed (Fig 1C.). In 3 patients, the CPT values at 5 Hz in the affected legs before the epiduroscopy were more than 100. The CPT value in the unaffected leg did not change during the study period at any frequency.

The severity of sensory deficits after epiduroscopy was significantly lower than that before epiduroscopy. Sensory deficits of the affected leg improved after the epiduroscopy in 15 patients (Table 2). Significant correlation between severity of sensory deficit and the CPT value at 2000 Hz in the affected leg was observed before, 1 month and 3 month after the epiduroscopy (Fig 2A-C).

NRS scores for leg pain and low back pain and the RMDQ scores, assessed 1 and 3 months after the epiduroscopy, were significantly lower than those before the epiduroscopy (Table 2). None of our patients experienced operative or postoperative complications.
Discussion

The present study demonstrated that the adhesiolysis followed by the injection of steroid and local anesthetic during the epiduroscopy could provide pain relief, improvement of nerve function and functional disability in patients with chronic sciatica refractory to lumbar epidural block.

The Neurometer CPT/C produces constant-current sine wave stimulation at 2000, 250, and 5 Hz. The sine waves at 2000, 250 and 5 Hz correspond to depolarization periods of 0.25, 2, and 100 msec, respectively. The electrical stimulus selectively excites distinct subpopulations of nerve fibers as a function of the sinusoid frequency [17,18]. Correlations between the CPT value at 2000 Hz and large fiber function, and between the CPT values at 250 and 5 Hz and small fiber function has been demonstrated with thermal perception threshold testing and quantitative vibration testing, respectively [7,8,19]. Thus, large myelinated A (Aβ), small myelinated A (Aδ) and unmyelinated C (C) nerve fibers are evaluated with a series of 2000, 250, and 5 Hz stimuli, respectively.

In our study, the CPT values at all frequencies in the affected legs of patients before the epiduroscopy were significantly higher than those in unaffected legs. Several studies investigated quantitative sensory testing in patients with sciatica, and
demonstrated that the thresholds of Aβ, Aδ and C fibers were increased in the affected dermatome compared with the unaffected dermatome [10,20,21]. These findings are consistent with our results.

In our study, the CPT testing demonstrated that the values at 2000 and 250 Hz in the affected legs after epiduroscopy decreased significantly as compared with those before the epiduroscopy. We have found that all of our patients had adhesion close to the intervertebral foramen of the affected nerve root. Epidural adhesions are known to develop as a result of the extrusion of nucleus pulposus, chronic chemical radiculitis and nerve root inflammation [22,23]. Adhesion around nerve root may lead to reduce their microcirculation, resulting in ischemic pain and abnormalities in nerve conduction [23]. We speculate that demyelination damage by the ischemia associated with epidural adhesion of nerve roots may be responsible for the elevated CPT values at 2000 and 250 Hz in the affected leg before the epiduroscopy.

On the other hand, the CPT value at 5 Hz in the affected leg after the epiduroscopy was not significantly lower than that before the epiduroscopy. Nygaard et al. [24] examined quantitative sensory testing in the patients with lumbar radiculopathy before and after surgical decompression. They demonstrated that the preoperative warmth detection threshold (mediated by C fibers) was significantly higher in the patients with a
poor result than in the patients with a good result. In our study, the CPT value at 5 Hz, pain and RMDQ scores in 3 patients who had high CPT value at 5 Hz before the epiduroscopy did not change. This may indicate that damage to C fibers before epiduroscopy is a negative prognostic factor.

Recently, Dashfield et al. [25] demonstrated that epiduroscopy did not show improved outcome compared with traditional epidural steroid injection in the patients with sciatica in a randomized controlled study. However, most of their patients did not have adhesion in epidural space. In contrast, all of our patients had adhesion close to the intervertebral foramen of the affected nerve root. For this reason, we included patients with previous back surgery and/or long-lasting symptom.

Pain and RMDQ scores decreased 1 and 3 months after the procedure in our study. Re-myelination after adhesiolysis might also contribute to the improvement of pain [26] and functional disability. As another factor, injected steroid possibly worked at the affected nerve root that was implied by the epidurography after epiduroscopy showing the epidural space surrounding the affected nerve root filled with contrast medium. Steroids reduce edema of injured nerve root and improve intraneural blood flow [27].

Lumbar epidural block with steroid and local anesthetic before epiduroscopy
provided only limited effects in all of our patients. Epidurography also revealed that
the epidural space surrounding the affected nerve root could not be filled with contrast
medium before the epiduroscopy, whereas these were successfully filled in all of the
patients after the epiduroscopy. These results imply that epidural steroid given before
the epiduroscopy could not have reached the affected nerve roots because of the
adhesion. Therefore, it seems possible that adhesiolysis by the epiduroscopy would
improve the effect of epidural steroids injection.

We recruited 19 patients with chronic sciatica for our study, and then epidurography
before epiduroscopy demonstrated that all of them had the deficits of the epidural space
surrounding the affected nerve root. In 3 patients out of these 19 patients, we could
not achieve adhesiolysis because of hard and extensive adhesions. Therefore, our
patient selection method by physical symptom and epidurography might overlook the
cases in which adhesiolysis is difficulty.

In conclusion, when the patients with chronic sciatica had adhesion close to the
intervertebral foramen of the affected nerve root within the epidural space, adhesiolysis
followed by the injection of steroid and local anesthetic during epiduroscopy improved
pain, functional disability and sensory nerve dysfunction of A\(\beta\) and A\(\delta\) fibers in the
affected legs.
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**Figure Legends**

**Figure 1A-C.**

The current perception threshold (CPT) values in the unaffected and affected legs at 2000, 250 and 5 Hz before and 1 and 3 months after epiduroscopy. CPT values in the affected leg at all frequencies were significantly higher than that in the unaffected leg before epiduroscopy (*p < 0.05). CPT values in the affected leg at 2000 and 250 Hz 1 and 3 months after epiduroscopy were significantly lower than that before epiduroscopy (§p < 0.05). CPT value in both legs at 5 Hz did not change during the study period. Data are presented as median, 25th and 75th percentile and range.

**Figure 2A-C.**

Relationship between severity of sensory deficit and current perception threshold (CPT) values in the affected leg at 2000 Hz before and 1 and 3 months after epiduroscopy. Significant correlation between severity of sensory deficit and CPT value in the affected leg at 2000 Hz was observed before and 1 month and 3 month after epiduroscopy.
Fig. 1A–C.
Fig. 2A–C.
Table 1. Patient Characteristics (n = 16)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>71.5 (41-84)</td>
</tr>
<tr>
<td>Male/Female (n)</td>
<td>7/9</td>
</tr>
<tr>
<td>Duration of symptom (month)</td>
<td>71 (5-156)</td>
</tr>
<tr>
<td>Intensity of leg pain (NRS)</td>
<td>7 (3-9)</td>
</tr>
<tr>
<td>Intensity of low back pain (NRS)</td>
<td>6 (2-9)</td>
</tr>
<tr>
<td>Sensory deficit</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
</tr>
<tr>
<td>Mild</td>
<td>4</td>
</tr>
<tr>
<td>Slight</td>
<td>8</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Previous back surgery (n)</td>
<td>4</td>
</tr>
<tr>
<td>Level of pathology</td>
<td></td>
</tr>
<tr>
<td>L5 (n)</td>
<td>10</td>
</tr>
<tr>
<td>S1 (n)</td>
<td>6</td>
</tr>
<tr>
<td>Pain treatments</td>
<td></td>
</tr>
<tr>
<td>non-steroidal anti-inflammatory drug (n)</td>
<td>15</td>
</tr>
<tr>
<td>antidepressant drug (n)</td>
<td>1</td>
</tr>
<tr>
<td>antiarrhythmic drug (n)</td>
<td>1</td>
</tr>
<tr>
<td>MRI findings on the side associated with clinical symptoms</td>
<td></td>
</tr>
<tr>
<td>degenerative disc (n)</td>
<td>12</td>
</tr>
<tr>
<td>no abnormalities (n)</td>
<td>4</td>
</tr>
</tbody>
</table>

Values are median (range) or absolute count. NRS, numerical rating scale; MRI, magnetic resonance imaging
Table 2  Pain, Roland Morris Disability Questionnaire score and severity of sensory deficit before and after epiduroscopy.

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>1 month</th>
<th>3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leg (NRS)</td>
<td>7 (3-9)</td>
<td>3.5 (0-8)*</td>
<td>3 (0-7)*</td>
</tr>
<tr>
<td>Low back (NRS)</td>
<td>6 (2-9)</td>
<td>3 (0-7)*</td>
<td>5 (0-8)*</td>
</tr>
<tr>
<td>RMDQ score</td>
<td>15 (6-18)</td>
<td>11 (1-16)*</td>
<td>10 (0-20)*</td>
</tr>
<tr>
<td>Sensory deficit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Slight</td>
<td>8</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

NRS, numerical rating scale; RMDQ, Roland Morris Disability Questionnaire. Values are median (range) or absolute count. *p < 0.05 compared with before epiduroscopy.