Cocktail Treatment with a Gelatin Sponge Impregnated with Ropivacaine, Dexamethasone, and Vitamin B12 Promotes Early Postoperative Recovery after Percutaneous Endoscopic Lumbar Discectomy: A Retrospective, Case-Controlled Study

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Background: Percutaneous endoscopic lumbar discectomy (PELD) can only relieve mechanical compression but cannot directly reduce the inflammatory reaction of the adjacent nerve root, which contributes to persistent pain and physical disabilities postoperatively. Numerous studies have explored the application of epidural steroids after an open lumbar discectomy in relieving pain by reducing local inflammatory reactions and further peridural scar formation.

Objectives: To explore whether “cocktail treatment” in which a gelatin sponge was impregnated with ropivacaine, dexamethasone, and vitamin B12 promoted early postoperative recovery after PELD.

Study Design: Retrospective, case-controlled study.

Setting: All data were from Hong-Hui Hospital in Xi’an.

Methods: Between January 2016 and January 2017, 100 patients of single-level lumbar disc herniation were treated with PELD in our hospitals. The cocktail treatment was applied in the first 50 patients (group cocktail) and an equal size gelatin sponge without drugs was used in the other 50 patients as control (group noncocktail). The clinical outcome evaluation included the Visual Analog Scale (VAS) score for back and leg pain and Oswestry Disability Index (ODI) score.

Results: There was a significant difference in the mean periods of return to work (4.25 ± 1.88 weeks in the cocktail group and 5.18 ± 2.19 weeks in the noncocktail group) (P < 0.01). Compared with the preoperative data, a significant improvement in VAS scores of back pain and sciatica and ODI were observed in each follow-up interval (P < 0.05, respectively). In the noncocktail group, there were visible fluctuations in the 3 indicators within the first week after surgery. This phenomenon was not observed in the cocktail group, a difference that was statistically significant (P < 0.05, respectively). In further follow-up, no significant differences were observed between the 2 groups (P > 0.05, respectively).

Limitations: The nonrandomized, single-center, retrospective design is a major limitation of this study.

Conclusions: The “cocktail treatment” with a gelatin sponge impregnated with ropivacaine, dexamethasone, and vitamin B12 promotes early and satisfactory back and leg pain relief and fast functional recovery after PELD.

Key words: Endoscopic lumbar discectomy, lumbar disc herniation, steroids, nerve root block, gelatin sponge

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Lumbar disc herniation (LDH) is a common spinal disorder with lower limb numbness and/or pain, which mainly results from an intervertebral disc bulge or nucleus pulposus prolapse from the rupture of the anulus fibrosus, leading to mechanical compression and local inflammation to the adjacent nerve root. Since the first discectomy was published by Mixter and Bar (1,2), the surgical technique has evolved with the development of new instruments. Contrary to traditional open surgery, lumbar discectomy is mainly performed under a microscope or percutaneous endoscope as this helps prevent iatrogenic injury. Percutaneous endoscopic lumbar discectomy (PELD) via the Kambin triangle (3), as a representative minimally invasive operative procedure, provided satisfactory neural decompression with an efficacy of 90%, which is equivalent to traditional open surgery (4-6). The existing discectomy techniques can only relieve mechanical compression but cannot directly reduce the inflammatory reaction of the adjacent nerve root and impede perineural fibrosis. This contributes to persistent pain and physical disabilities postoperatively.

As steroids play an important role in reducing inflammation and blocking afferent C fiber nociception and vascular responses causing inflammation, numerous studies have explored the application of epidural steroids after an open lumbar discectomy in relieving pain by reducing local inflammatory reactions and further peridural scar formation (7-15). However, the local concentration of steroid is low in such drug administration, which impairs the therapeutic duration. Du et al (16) used a gelatin sponge impregnated with 3 drugs (ropivacaine, dexamethasone, and vitamin B12) in lumbar fusion surgery to improve the concentration of drug around local nerve root. In this study, we have introduced the “cocktail treatment” in which a gelatin sponge impregnated with 3 drugs (ropivacaine, dexamethasone, and vitamin B12) was used in PELD, and explored that whether it promotes early postoperative recovery after PELD.

**METHODS**

Between January 2016 and January 2017, 100 patients of single-level LDH were treated with PELD in our hospitals. The cocktail treatment was applied in the first 50 patients (group cocktail), an equal size gelatin sponge without drugs was used in the other 50 patients as control (group noncocktail). Patient demographics, surgical levels, and approaches are summarized in Table 1. Approval to conduct the study was granted by the ethics committees of hospitals. This study was approved by our hospital institutional review boards, and informed consent was obtained from each patient. Patients with the following scenarios were included: lumbar and/or sciatic pain that lasted for over 6 weeks and conservative treatment failed; single-level LDH observed on the magnetic resonance imaging (MRI) or computed tomography scans; and the neurologic symptom was in accordance with the radiologic examination. Patients in the following cases were excluded: definite cauda equina syndrome; previous history of epidural steroid injection; allergy to ropivacaine, dexamethasone, and vitamin B12; multiple-level LDH; obvious spinal instability (the anterior or posterior displacement >3 mm or the angle change of the endplate >15 degrees on the dynamic radiography); LDH accompanied by diabetes mellitus or hematomasis; suspected lumbar infection or metastatic tumor; uncontrolled acute or chronic medical illness; pregnant or lactating women.

<table>
<thead>
<tr>
<th>Surgical Technique and Cocktail Treatment</th>
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| All techniques were performed under local anesthesia in the prone position. Intravenous usage of dexmedetomidine (0.5 µg/kg bolus, followed by 0.1-0.5 µg/kg per hour) was performed to provide an ideal sedative effect and improve surgical tolerance. According to a previous study (17), the puncture, establishment of working cannula, foraminoplasty (if necessary), and discectomy were achieved sequentially by PELD via the transforaminal or interlaminar approach based on the location of herniated disc. Sufficient neural decompression was confirmed when the epidural and nerve root pulsation was identified. A piece of gelatin sponge (2

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Table 1. Patient demographics, surgical levels, and approaches.

<table>
<thead>
<tr>
<th></th>
<th>Group Cocktail</th>
<th>Group Noncocktail</th>
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<tbody>
<tr>
<td>Demographics</td>
<td></td>
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<tr>
<td>Female gender (%)</td>
<td>22 (44)</td>
<td>23 (46)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean age (yrs) (range)</td>
<td>34.8 (17-59)</td>
<td>35.3 (18-61)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Treatment level</td>
<td></td>
<td></td>
<td>&gt; 0.05</td>
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<tr>
<td>L3-4 (%)</td>
<td>5 (10)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td>L4-5 (%)</td>
<td>34 (68)</td>
<td>32 (64)</td>
<td></td>
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<tr>
<td>L5-S1 (%)</td>
<td>11 (22)</td>
<td>12 (24)</td>
<td>&gt; 0.05</td>
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<tr>
<td>Surgical approach</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interlaminar</td>
<td>13</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Transforaminal</td>
<td>37</td>
<td>35</td>
<td></td>
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</table>
Cocktail Treatment Promotes Early Postoperative Recovery After PELD

cm\(^*\)1.5 cm\(^*\)0.5 cm) was placed at ventral of dura and nerve root toward the disc (Fig. 1). For the patients from the group cocktail, the gelatin sponge was impregnated with a mixture of 3 drugs about 4 mL (Fig. 1), whose proportion was 0.4% ropivacaine injection 3 mL:37.5 mg plus dexamethasone injection 3 mL:15 mg and vitamin B12 injection 2 mL:0.5 mg. The skin incision was sutured and covered by a waterproof dressing.

Application of a spinal-supporting corset was encouraged for 4 weeks postoperatively to ensure that the ruptured annular fibrosis could heal and that the postoperative muscle spasm could be relieved. The clinical outcome evaluation included the Visual Analog Scale (VAS) score for back and leg pain and Oswestry Disability Index (ODI) score. To truly reflect the intensity of back and leg pain, the pain score was recorded without the usage of analgesics. The physical examinations and clinical scoring were performed by another spinal surgeon who did not participate in the surgical procedures. The related parameters were recorded via telephone interviews or at the outpatient clinic, at each day of the first week, 1 month, 3 months, 6 months, and 12 months postoperatively, respectively. The related complications, including intraoperative transfer to open injury, postoperative dysesthesia, and motor weakness were also recorded. Modified Macnab criteria were applied to evaluate the clinical results at 1 year postoperatively. Postoperative MRI or computed tomography examinations were recommended for the patients without satisfactory symptom relief at the follow-up.

Statistical Analysis

All statistical analyses were performed using Statistical Product and Service Solution Version 18.0 (SPSS Inc., Chicago, IL). Mean values are presented as the mean ± standard deviation. The Student t test was used for statistical analysis of continuous variables. The enumeration data were analyzed using the chi-square test. Significance level was set at \( P = 0.05 \).

Results

Five patients were lost to follow-up, with 2 patients in the cocktail group. There were no significant differences in patient demographics, surgical levels, and approaches between the 2 groups (\( P < 0.05 \)). No case required conversion to an open procedure. There was no significant difference in the mean operative duration between the 2 groups (56.0 ± 12.5 vs. 55.5 ± 13.0 minutes in interlaminar approach, 80.5 ± 11.5 vs. 81.0 ± 10.5 minutes in the transforaminal approach, \( P < 0.05 \), respectively). Operative failure due to incomplete removal of the disc fragment was observed in 2 patients who complained of unsatisfactory pain relief. In one case in each group, subsequent open decompression was performed with favorable symptom relief after revision surgery. Three patients experienced transient dysesthesia: one case belonged to cocktail group after interlaminar discectomy, 2 were observed at the non-cocktail group, in which each approach was performed for one case. No dura tears, motor weakness, or infections were observed for the 2 groups. There were no
significant differences in the mean hospital stay duration (2.09 ± 0.98 days in the cocktail group and 2.16 ± 0.86 days in the noncocktail group, \( P > 0.05 \)). However, there was a significant difference in the mean periods of return to work (4.25 ± 1.88 weeks in the cocktail group and 5.18 ± 2.19 weeks in the noncocktail group; \( P < 0.01 \)).

Pre- and postoperative VAS scores of low back pain and sciatica, as well as ODI, are summarized in Figs. 2-6. Compared with the preoperative data, a significant improvement in VAS scores of back pain and sciatica and ODI were observed in each follow-up interval (\( P < 0.05 \), respectively). In the noncocktail group, there were visible fluctuations in the 3 indicators within the first week after surgery. This phenomenon was not observed in the cocktail group, a difference that was statistically significant (\( P < 0.05 \), respectively). In further follow-up, no significant differences were observed between the 2 groups (\( P > 0.05 \), respectively). Among the 95 patients with 12 months’ follow-up, according to the modified Macnab criteria, the outcomes rated as excellent were 59 (62.1%), good 31 (32.6%), fair 4 (4.2%), and poor 1 (1.1%).

**Discussion**

Compared with the preoperative status, a favorable clinical outcome was observed in both groups. Although there were no significant differences in the VAS scores of back pain and sciatica and ODI between the 2 groups at the follow-up after 1 month, a significantly higher score was observed in the noncocktail group within the first week postoperatively. Additionally, the patients from the
cocktail group could return to work earlier. These findings demonstrate that the “cocktail treatment” is beneficial for relieving back and leg pain and promoting fast recovery at the early stage. Further, there was no obvious increase in surgical complications.

Besides the direct mechanical compression to the nerve root, the prolapsed nucleus can induce local inflammatory reaction and release of tumor necrosis factor alpha, further activating neutrophils and monocytes, which can indirectly lead to neurologic dysfunction (18,19). The mechanical stretch stimulation due to intraoperative retraction and nerve root ischemia-reperfusion injury (16) also caused persistent pain and physical disabilities postoperatively. After neural decompression, for improving the clinical outcome, it is important to quickly eliminate the inflammation of nerve root and surrounding tissue. That explains why postoperative dehydration, nonsteroidal antiinflammatory drugs, and glucocorticoids were recommended after the lumbar discectomy. Steroids can relieve inflammatory reaction by suppressing chemotactic aggregation of inflammatory cells, adhesion of leucocytes, and release of histamine and kinin (20). Increasing the local drug concentration is the key to effective steroid therapy. In consideration of the half-life period of steroids, dexamethasone, a long-acting steroid with a half-life period of approximately 36–54 hours, was selected. Zhang et al (21) proved that patients who underwent PELD with epidural steroid administration for large LDH showed favorable curative effect compared

**Fig. 4. Changes of pre- and postoperative ODI scores within 1 year after surgery.**

**Fig. 5. Changes of pre- and postoperative VAS scores of low back pain within 1 week after surgery.**
with those who underwent PELD with intravenous steroid administration. In another randomized study, Shin et al (22) observed that epidural steroids after PELD reduced back pain and leg pain while improving functional outcomes in the short-term postsurgical period. To further increase the local drug concentration, Du et al (16) placed a gelatin sponge impregnated with 3 drugs (ropivacaine, dexamethasone, and vitamin B12) to cover the nerve root. Ropivacaine is an amide local anesthetic with long-term effects. Low concentration (0.2%) of ropivacaine can produce significant sensory block without an obvious blocking effect on motor nerve (23). The anesthetic performance related to the drug concentration improved the surgical safety. Vitamin B12 can not only be beneficial for acceleration of nerve regeneration but can also reduce the abnormal discharge of the damaged nerve, indirectly relieving pain (24). The combination of the 3 drugs can induce a synergistic effect; for example, dexamethasone molecules have a large molecular volume and complex spatial structure, which affect the release and absorption of ropivacaine and prolong the pharmacologic action of ropivacaine (25). When they are impregnated into the gelatin sponge, with the slow release of drugs and the elevation of local concentration, the therapeutic effect is enhanced and the duration prolonged. In contrast to the study of Du et al (16), we introduced the “cocktail treatment” in PELD, a nonfusion surgery with less trauma. Because drainage is not required postoperatively, the drugs can persist in the area of administration. In addition, the gelatin sponge was placed at the epidural space between the ventral disc and the dorsal dura and nerve root under endoscopic guidance. Therefore it was not washed away by the hemorrhage or the fluid in the incision. Additionally, the placed gelatin sponge impregnated with 3 drugs can exert antiinflammatory, analgesic, and neurotrophic effects in the surrounding sinuvertebral nerves. The sinuvertebral nerves were described first by Luschka in 1850 (26), which have been proved to be associated with low back pain and lower extremity neuralgia (27,28). Anatomically, this nerve innervates the dorsal longitudinal ligament, intervertebral disc, and ventral part of the dura mater. Because of the accurate administration, the cocktail group showed better back and leg pain relief within the first week postoperatively. With the progression of the postsurgical edema and inflammatory reactions in the nerve root and surrounding tissues, the symptoms of the noncocktail group recurred slightly.

Compared with other studies (21,22), in which a similar minimally invasive PELD was performed, the medication method was different. The therapeutic efficacy of “cocktail treatment” should be better than that of single steroid usage; the drugs are delivered through the gelatin sponges, which can exert a more targeted effect on the nerves, raising the local drug concentration and prolonging the action time. This effect was beneficial for the patients in achieving faster function recovery and earlier return to work.

**Fig. 6. Changes of pre- and postoperative VAS scores of sciatica within 1 week after surgery.**
One of the problems with this technique is whether indwelling gelatin sponges in the spinal canal can lead to acute exacerbation of symptoms. Because the highest surgical level was L3-4, below this level, only the thin cauda equina nerve is present in the dura sac and the volume of spinal canal is increased. The foramen and lateral recess were expanded during the transforaminal approach. Theoretically, there is enough space to hold a small piece of gelatin sponge. If the endoscopic examination indicates that the tension of nerve root is high, the gelatin sponge can be pushed to the ventral side of the dural sac to relieve the compression to the nerve root.

The nonrandomized, single-center, retrospective design is a major limitation of this study. The time to return to work is not only related with back and leg pain, but also influenced by the compliance of the patients’ functional exercise, expectation of the effect, and occupation. In addition, the size of gelatin sponge and the ratio of the mixed drugs were based on clinical experience; these aspects should be further explored to ensure the best clinical outcomes.

**Conclusions**

The “cocktail treatment” with a gelatin sponge impregnated with ropivacaine, dexamethasone, and vitamin B12 promotes early and satisfactory back and leg pain relief and fast functional recovery after PELD.

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Author contributions: Lei Chu and Tuan-Jiang Liu conceived the study design. Peng Liu, Yun-Kai Chan, Hong Fan, and Xuan-Ming Li supervised the data collection. Jun-Song Yang drafted the manuscript. Kai-Xuan Liu contributed to the revision. Ding-Jun Hao is responsible for this article.

**REFERENCES**

2013; 16:547-556.


