



Preoperative Administration of Parecoxib for Postoperative Pain Management in Cervical Laminoplasty: A Retrospective Study

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Abstract

Poor postoperative pain control impairs patient recovery and lengthens the duration of hospitalization after various surgeries. Parecoxib has been proved to be effective in various minor surgeries. However, despite the extensive use of parecoxib, there is still a gap for applying parecoxib in the major surgeries like cervical laminoplasty. This study aimed to investigate the efficacy of preoperative administration of parecoxib for postoperative pain control after cervical laminoplasty. In total, 114 patients undergoing cervical laminoplasty were included for retrospective review and divided into parecoxib and control groups. The Visual Analogue Scale (VAS) score, postoperative morphine consumption, operative indexes (operative duration, intraoperative blood loss volume and incision length), hospitalization duration and incidence of complications were analyzed. There was no significant difference in demographic (gender, age and BMI etc.) and operative indexes between the two groups. The VAS score in parecoxib group of 4, 8, 12 and 24 h postoperatively were significantly lower relative to the control group ($P < 0.001$). The morphine consumption in the parecoxib group was also less than the control group in each time point postoperatively ($P < 0.001$). Parecoxib group exhibited significantly shorter total hospitalization duration (11.2 ± 13.9 days) than the control group (12.6 ± 3.1 days, $P = 0.028$). Significant differences were also observed in the postoperative hospitalization duration between the parecoxib and control groups ($P = 0.004$). There was no significant difference in complications between the two groups. In conclusion, preoperative administration of parecoxib could effectively reduce postoperative pain, and postoperative analgesic consumption, and promote recovery after cervical laminoplasty.

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Introduction

Since cervical laminoplasty was proposed in 1973, it has been widely applied and achieved satisfactory outcomes in treating multilevel cervical lesions, including Cervical Spondylotic Myelopathy (CSM), Congenital Cervical Stenosis (CCS), and Ossification of the Posterior Longitudinal Ligament (OPLL) [1-3]. The procedures of cervical laminoplasty require extensive dissection of muscle from spinal vertebrae leading to severe postoperative pain, which prolonged hospitalization and impair the rehabilitation of the patients. Until now, the management of the severe postoperative pain often requires large amounts of opioids [4]. However, it is also associated with a series side-effect such as respiratory distress, sedation, nausea, vomiting, debility, slower postoperative rehabilitation and drug addiction [5]. Therefore, there is a need for simple, economic, and effective analgesic protocol for managing the postoperative pain.

In past decades, it has been shown that the preventive analgesia (i.e., medication or any analgesic intervention before surgery) could largely reduce the postoperative pain in spine surgery [6-8]. Currently, parecoxib has been widely used as preventive analgesia for managing postoperative pain [9-12]. It is metabolized by the liver to produce valdecoxib which inhibited the Cyclooxygenase 2 Enzymes (COX-2) and effectively reduce the pain [13]. Moreover, parecoxib has been proved to be effective in various minor surgeries including thyroid carcinoma surgery [14], colorectal surgery [15], hip arthroplasty surgery [9], etc. and has been shown to have few side effects (e.g., not affecting platelet aggregation) [16]. However, despite the extensive use of parecoxib, there is still a gap for applying parecoxib in the major surgeries like cervical laminoplasty. Therefore, to fill such research

gap, our study is aimed to retrospectively evaluate the efficacy of preventive use of parecoxib for managing severe postoperative pain following cervical laminoplasty.

Materials and Methods

Subjects

The data of our current study was retrospectively collected at the Department of Spinal Surgery, Tianjin Medical University General Hospital from December 2010 till December 2019. The inclusion criteria were as follows: (1) Age 18 to 75 years; (2) primary diagnosis was CSM, CCS, or OPLL (involved of 3 or more segments); (3) patients underwent expansive open-door cervical laminoplasty. The exclusion criteria include: (1) History of cervical surgery; (2) the presence of myelopathy caused by trauma, tumors or infections; (3) patients with incomplete follow-up data were excluded; (4) patients with other systematic diseases.

All patients were reviewed from a pool of patients who underwent cervical laminoplasty performed by the same surgical team with the same support staff, operating rooms, surgery equipment and post-anesthesia care. Therefore, a total of 114 patients were included in our current study.

Preoperative preventive analgesia

The patients received perioperative antibiotic therapy (i.e., weight-based dose of cefazolin) based on the standard process at 1 h before the incision. For the patients allergic to cephalosporin, clindamycin was used. From December 2010 to December 2015, patients were not administrated parecoxib preoperatively. From December 2015 to December 2019, the patients were administrated parecoxib 40 mg intraoperatively 30 min before the incision. Therefore, 75 patients who received parecoxib preoperatively comprised the parecoxib group, and 69 patients who did not receive parecoxib comprised the control group.

This study protocol was approved by the Investigation and Ethics Committee of the Tianjin Medical University General Hospital. Informed written consents were obtained from every patient before each procedure. Based on previous studies, we assumed normal distribution and a VAS Standard Deviation (SD) of 0.8. With a two-sided $\alpha=0.05$, a sample size of 42 patients in each group gave a power of 0.8 to detect a mean difference of 0.5 in VAS. Therefore, our sample size is enough.

Surgical procedure

All patients underwent a standard preoperative preparation and a standard posterior expansive open-door cervical laminoplasty. The preoperative preparation includes a general anesthesia and an endotracheal intubation. After preparation, patients were lateral decubitus placed with their neck was slightly flexed and fixed. A middle incision was conducted to expose the cervical laminae from the caudal edge of C3 to the cranial edge of C7 and extended laterally for complete exposure for the dorsal cortex of the bilateral facet joints. Subsequently, a hinge was made on the lateral side, from which patients suffered less neurological symptoms due to the compression of the nerve root by removing the dorsal cortex and cancellous bone. Then, an open-door side was created contralaterally to the hinge side by removing the lamina along the medial margin of the facet joints. After elevating the opened-lamina approximately 1 cm, a titanium plate was placed for fixation of the lamina on each segment. Two screws were implanted to fix the plate tightly to the lamina and lateral mass. Patients were required to stay in bed after

surgery. Electrocardiography, blood pressure, pulse oximetry, and arterial blood gas were monitored.

Postoperative pain management

After surgery, all patients received a Patient-Controlled Analgesia (PCA) with 1mg/ml morphine for 24 h postoperatively. For PCA settings: 1 mg/mL morphine was administered when they underwent intolerable pain with a lockout interval of 10 min and a 4-h limit of 16 mg.

All patients were encouraged to start out-of-bed activity with a cervical brace within one week after surgery. Mechanical procedures (e.g., compression stockings) for preventing thromboprophylaxis were given to patients in both legs. Clinical and radiological assessments were performed in the orthopedic outpatient clinic 3 months after discharge from the hospital.

Data collection and clinical assessment

The postoperative Visual Analog Scale (VAS) (0 mm = no pain; 100 mm = worst imaginable pain) and morphine consumption were recorded at 4, 8, 12 and 24 h after surgery for evaluating pain severity. Data on patients' demographics, clinical outcomes, and the incidence of postoperative hospitalization complications were collected. Demographic items included age, sex, body mass index, smoking history, and alcohol consumption history. The intraoperative blood loss, incision length, and operative time were quantified to evaluate the surgical trauma. The recovery times including the length of total and postoperative hospital duration were recorded. The incidence of complications, including postoperative nausea and vomiting and wound infection were also analyzed in this study.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS version 20.0, Chicago, IL). In this study, continuous data, including VAS, morphine consumption, operative indexes and recovery time are presented as the mean \pm standard deviation and were analyzed using the two-sample t-test. The chi-squared test was performed to analyze categorical data, such as the incidence of complications. All tests were set as two-sided and the significant threshold was set at $P<0.05$.

Results

Demographic and baseline clinical data

In this study, 144 patients underwent posterior expansive open-door cervical laminoplasty were included. 75 patients were given parecoxib (i.e., parecoxib group) preoperatively and 69 were not (i.e., control group). Patient characteristics are summarized in Table 1 and there were no significant differences between the two groups.

Operative indexes

No significant differences were observed between parecoxib group and control group in terms of operative indexes (Table 2). The operative duration was slightly longer in the parecoxib group (107.4 ± 26.5 min) than in the control group (105.9 ± 23.0 min), but there is no significant difference between the two groups ($P=0.711$). For the intraoperative blood loss volume and incision length (244.8 ± 82.8 ml vs. 248.8 ± 88.6 ml, $P=0.778$; 13.5 ± 1.5 cm vs. 13.2 ± 1.5 cm, $P=0.190$; parecoxib group vs. control group, respectively), no significant difference was observed between the two groups.

Recovery time

In terms of the recovery time, relative to the control group,

Table 1: Characteristics of the patients in both groups.

Characteristics	Parecoxib group	Control group	P value
Number of patients	75	69	
Age (year)	52.3 ± 13.3	53.2 ± 13.6	0.685
Sex, male/female	32/43	27/42	0.734
BMI (kg/m ²)	24.8 ± 2.1	24.5 ± 2.3	0.332
Smoking history	28 (37.3%)	27 (39.1%)	0.865
Alcohol history	39 (52.0%)	33 (47.8%)	0.739
Diagnosis			
CSM	36 (48.0%)	32 (46.4%)	
OPLL	19 (25.3%)	20 (29.0%)	
CSS	20 (26.7%)	17 (24.6%)	

CCS: Cervical Canal Stenosis; CSM: Cervical Spondylotic Myelopathy; OPLL: Ossification of the Posterior Longitudinal Ligament

Table 2: Operative indexes for both groups.

Operative index	Parecoxib group	Control group	P value
Operative duration (minute)	107.4 ± 26.5	105.9 ± 23.0	0.711
Intraoperative blood loss (ml)	244.8 ± 82.8	248.8 ± 88.6	0.778
Incision length (cm)	13.5 ± 1.5	13.2 ± 1.5	0.19

Table 3: Operative indexes for both groups.

Recovery time (days)	Parecoxib group	Control group	P value
Total hospitalization duration	11.2 ± 3.9	12.6 ± 3.1	0.028
Postoperative hospitalization duration	9.0 ± 3.8	10.6 ± 3.0	0.004

parecoxib group exhibited significantly shorter total hospitalization duration (11.2 ± 13.9 days for the parecoxib group and 12.6 ± 3.1 days for the control group, P=0.028). Significant differences were also observed in the postoperative hospitalization duration between the parecoxib and control groups (9.0 ± 3.8 days parecoxib group and 10.6 ± 3.0 days for control group, P=0.004, Table 3).

Evaluation of pain severity and morphine consumption

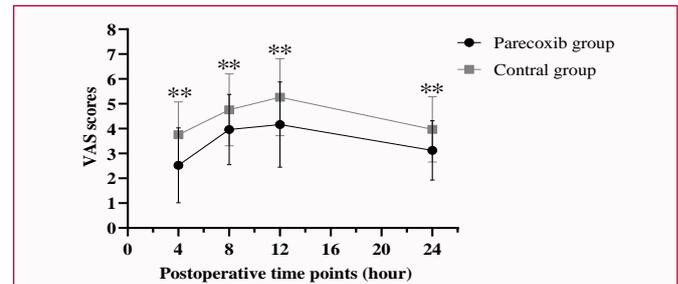
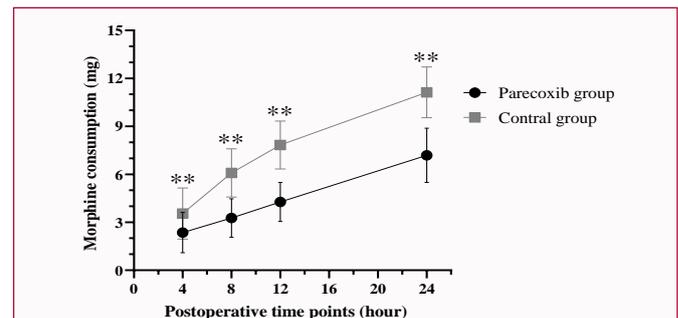
The VAS score (i.e., mean ± standard deviation) of 4, 8, 12 and 24 h postoperatively were 2.52 ± 1.51, 3.96 ± 1.418, 4.160 ± 1.717, 3.120 ± 1.196 in parecoxib group; and were 3.754 ± 1.322, 4.754 ± 1.449, 5.261 ± 1.550 in the control group. For each timepoint, the parecoxib group exhibited significantly lower VAS score relative to the control group (all P ≤ 0.001, Figure 1). Furthermore, the morphine consumption in the parecoxib group was also less than the control group in the first 4 h postoperatively (2.36 ± 1.26 mg vs. 3.55 ± 1.60 mg, P<0.001). Similar results were also observed in the first 8, 12 and 24 h after surgery (all P<0.001) (Figure 2).

Complications

No clinical deterioration, permanent morbidity or mortality were observed in current study. In terms of the incidence of nausea and vomiting, no significant difference was observed between the two groups (17.3% for the parecoxib group and 14.5% for the control group, P=0.658). No other side effects from postoperative analgesia were observed in this study.

Discussion

Three main results were observed in our current study, (1) relative to the control group, parecoxib group exhibited significantly lower VAS score and less morphine consumption; (2) parecoxib exhibited less recovery time and postoperative hospitalization than the control group; (3) the preventive use of parecoxib would not affect

**Figure 1:** VAS scores in two groups at different time points. (**: The difference is statistically significant)**Figure 2:** Morphine consumption in two groups at different time points. (**: The difference is statistically significant)

the intraoperative blood loss or operative duration of the open-door laminoplasty.

Cervical laminoplasty, which is known as an alternative to the cervical laminectomy, has been widely applied due to the preservation of the posterior tension band allows for a more physiologic loading, thereby preventing the development of postoperative spinal deformity [17]. In addition, maintaining dorsal coverage over the dura with laminoplasty prevents the formation of the post-laminectomy membrane and allows for safer revision procedure if necessary. However, the laminoplasty requires an extensive dissection of muscle from the lamina leading to severe postoperative pain which further increase the use of postoperative analgesics. Until now, opioid is still the first-choice medication for managing postoperative pain due to its powerful analgesic effect [4]. However, it is also associated with a series side-effect such as respiratory distress, sedation, nausea, vomiting, debility, slower postoperative rehabilitation and drug addiction [5]. Therefore, there is a need for simple, economic, and effective analgesic protocol for managing the postoperative pain. Among several pain management procedures, it has been showed that the postoperative pain could be largely reduced by the preventive analgesia due to its utility for protecting peripheral and central nervous systems from sensitization [18].

Currently, parecoxib has been widely applied as a preventive analgesia for managing postoperative pain in many minor surgeries (e.g., laparoscopic cholecystectomy, bunionectomy) [19,20] or surgeries with less time consumption (e.g., hip arthroplasty) [9]. Paul J et al. [10] showed that preoperative administration of parecoxib could largely reduce the postoperative pain while not induce additional side effects in oral surgery. They concluded that the preoperative use of parecoxib is effective, safe and well tolerated. Similar results were also observed in the patients who underwent bunionectomy that patients with preoperative administration of parecoxib exhibited significantly lower postoperative pain [20]. Furthermore, Martinez et al. [13]

also illustrated that patients who received preoperative parecoxib exhibited significantly lower VAS score and morphine consumption compared with the placebo group after hip arthroplasty surgery. Their results were repeated by Bao et al. [9]. In addition, Pandazi et al. [15] also found that pre incisional administration of parecoxib could largely reduce postoperative pain, morphine consumption, and inflammation (e.g., IL-6 and IL-8 production) compared with post incisional group following colorectal cancer surgery. In the current study, we also similar results that the preoperative use of parecoxib could also reduce the pain severity and the morphine consumption. Our results provided preliminary evidence for the effectiveness of parecoxib for managing postoperative pain following major surgeries such as cervical laminoplasty.

Furthermore, the mechanism for the analgesic effect of parecoxib has been widely illustrated. After administration, the parecoxib was metabolized by the liver to produce valdecoxib which inhibited the Cyclooxygenase 2 Enzymes (COX-2) and effectively reduce the pain and the inflammation [21,22]. By controlling the pain and the inflammation, parecoxib could further prevent the patients from the peripheral or central sensitization caused by long-term and severe pain. Having said this, effective pain management has been recognized as one of the fundamental aspects for enhancing the recovery for patients underwent surgery [23]. Therefore, effective pain management during perioperative period could further provide additional value for the rehabilitation of patients. In our current study, we also found that the parecoxib group exhibited a significant shorten total hospitalization duration and postoperative hospital duration following cervical laminoplasty. The postoperative hospital duration has been shown to be a reliable indicator for evaluating the recovery of patients following surgery by Rao et al. [24]. Therefore, these results further indirectly support the idea that preoperative use of parecoxib could reduce the postoperative pain thus contributes to the fast rehabilitation following surgery.

In current study, there was no significant difference in intraoperative blood loss between the two groups, which proved that parecoxib is safe for spinal surgery. This result is consistent with previous research results [25,26].

Limitations

There are some limitations in current study. First, this study was retrospective, not randomized and not blinded, and was performed at a single center. Second, the sample size of our current study is relatively small, therefore could not give a substantial conclusion. Prospective, randomized controlled and multi-center studies with larger sample size are further needed to evaluate the efficacy of parecoxib for managing postoperative pain after cervical laminoplasty.

Conclusion

In conclusion, Preoperative administration of single dose of 40 mg parecoxib intravenously could effectively reduce postoperative pain severity and postoperative analgesic consumption after cervical laminoplasty. Moreover, it could promote recovery after surgery.

Data Availability

The data of this study were available upon reasonable request to the corresponding author.

Authors' Contribution

XG and RZ designed this study, XG, RZ and JMZ collected the

data, XG and RZ performed the data analysis, XG and RZ wrote the manuscript, YX revised the manuscript.

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