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Original Contribution

Nonsteroidal anti-inflammatory drugs for postoperative pain control after lumbar spine surgery: A meta-analysis of randomized controlled trials

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ABSTRACT

Study objective: Nonsteroidal anti-inflammatory drugs (NSAIDs) play a role in pain relief, especially in postoperative pain caused by inflammation. They have demonstrated significant opioid dose-sparing effects, which help in reducing postoperative effects and opioid side effects. The objective of this meta-analysis was to explore the role of NSAIDs in reducing postoperative pain at different time intervals and provide reference for medication after lumbar spine surgery by a meta-analysis of randomized controlled trials (RCT).
Design: A meta-analysis study of randomized controlled trials.
Setting: Postoperative recovery area.
Patients: Adult patients who have undergone lumbar spine surgery.
Intervention: Patients received NSAIDs for pain control after lumbar spine surgery.
Measurements: Standardized mean difference (SMD) and 95%CI were used to evaluate the visual analog scale of postoperative pain.
Main results: Four hundred and eight participants from eight studies were included in this study. The difference between the NSAIDs group and placebo is significant in 0–6, 12, and 24 h groups (overall: SMD = −0.72, 95%CI −0.98 to −0.45; 0–6 h: SMD = 0.50, 95%CI −0.81 to −0.19; 12 h: SMD = −1.07, 95%CI −1.45 to −0.70; 24 h: SMD = −1.16, 95%CI −1.87 to −0.45). Heterogeneity and publication bias were observed in the 0–6 and 24 h groups.
Conclusion: NSAIDs are effective in postoperative analgesia after lumbar spine surgery. The study type, NSAID dose, different surgery types, and analgesic type might influence the efficacy of NSAIDs.

1. Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) play an important role in pain relief, especially in postoperative pain caused by inflammation. The mechanism underlying NSAID action involves the inhibition of cyclooxygenase (COX) activity to reduce prostaglandin synthesis [1]. Inflammatory pain depends on prostaglandin E2 synthesized by COX in neural cells. COX exists as three distinct isoforms: constitutive COX-1, inducible COX-2, and COX-3. COX-1 is responsible for the essential physiologic functions [2]. Inducible COX-2 is expressed in cells playing a role in inflammation, such as the macrophages, mononuclear cells, and endothelial cells [3]. COX-3 has been found to have no COX activity [4].

Opioid analgesics are very useful in the management of moderate-to-severe pain. However, several side effects of opioid use have been reported, including respiratory depression and potential drug addiction [5–7]. Studies and systematic reviews about lumbar spine surgery have demonstrated that NSAIDs have a significant opioid dose-sparing effect, which helps in reducing postoperative effects as well as opioid side effects [8,9]. New studies and analysis methods have been put forward in recent years. Therefore, conclusions of the related studies should be reorganized and re-analyzed. In this study, we conducted a

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meta-analysis to explore the role of NSAIDs in reducing postoperative pain after lumbar spine surgery. We also summarize the side effects of NSAIDs in lumbar spine patients and provide reference to clinical medicine.

2. Methods

2.1. Search strategy and selection criteria

This study was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Electronic databases (PubMed, EBSCO, Elsevier, Springer, Wiley, Cochrane) were searched systematically up to August 31, 2016, using the search terms: "lumbar," "spine," "surgery," and "NSAIDs." This search was carried out without language restriction. Studies were included if they met the following criteria: a. randomized controlled trials; b. trials performed in humans; patients underwent lumbar spine surgery; c. pain score reported with Visual Analog Scale (VAS: 0–10 cm, 0 = no pain and 10 = maximum pain); and d. adult patients. The exclusion criteria were as follows: a. duplication of research literature; b. systematic reviews and meta-analysis; and c. results and full study details were unavailable after contacting the authors.

2.2. Data extraction

Two workers were in charge of data extraction. The data included the first author's name, year of publication, type of study, number of patients, age(mean), gender, type of operation, VAS score[time, mean, and standard deviation(SD)], type of NSAIDs, and placebo. The VAS score of 0–100 mm in one study was transformed into 0–10 cm VAS [10]. The 0–6, 12, and 24 h groups were divided according to the contents of the included studies.

2.3. Statistical analysis

We evaluated the postoperative VAS by using standardized mean difference (SMD) and 95%CI. The heterogeneity of the study was estimated by I^2 statistic. I^2 statistic shows that the difference between studies was a random error or chance. Random-effect model was utilized for all results where heterogeneity existed across studies [11,12]. We performed Begg's test to assess the possible publication bias among studies. If heterogeneity was found, subgroup analyses were conducted. Subgroup analysis was conducted according to the type of operation and placebo in this study to assess their influence. All statistical analyses were performed using Stata11.0. A P value <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of the included studies

Forty-seven studies were obtained through literature screening; however, 39 studies were not eligible and excluded. Finally, eight RCTs met the criteria (Fig. 1). Eight studies involving 408 participants were included in the meta-analysis, and the details are presented in Table 1.

The outcome measure of pain is depicted as VAS in the included studies. In these studies, COX-2 selective NSAIDs were piroxicam, ketorolac, celecoxib, parecoxib, and paracetamol, and the nonselective NSAIDs were dexketoprofen and metamizol. Two studies included patients who underwent spinal fusion surgery and six studies included those who underwent lumbar disc surgery. Two studies focused on dose efficacy [13,14]. One study used a VAS of 0–100 mm scale [10]. In six studies, the patients were allowed intravenous morphine as needed. Two studies used piritramide during the first 24-h postoperative period as needed [10,15].

Five studies received Institutional Review Board approval [9,13,15–17]. In five studies, written informed consent was obtained from patients who participated in the study [10,13–15,18]. In one study, approval was obtained from ethics committee as well as the participating patients [9].

3.2. Summary of pain scores

From the results of meta-analysis, the overall SMD is −0.72 and 95%CI −0.98 to −0.45, and heterogeneity was observed among studies (I^2 = 71.0%, $P<0.0001$, Fig. 2). Pain scores were summarized at three time ranges or points: 0–6, 12, and 24 h (Fig. 2).VAS was significantly lower in the NSAID group (0–6 h: SMD = −0.50, 95%CI −0.81 to −0.19; 12 h: SMD = −1.07, 95%CI −1.45 to −0.70; 24 h: SMD = −1.16, 95%CI −1.87 to −0.45). In the time range of 0–6 h, eight studies were included. Heterogeneity existed between the eight studies according to the results of meta-analysis (I^2 = 70.2%, $P<0.0001$). Five RCTs were included in the meta-analysis in the time range of 12 h, and no

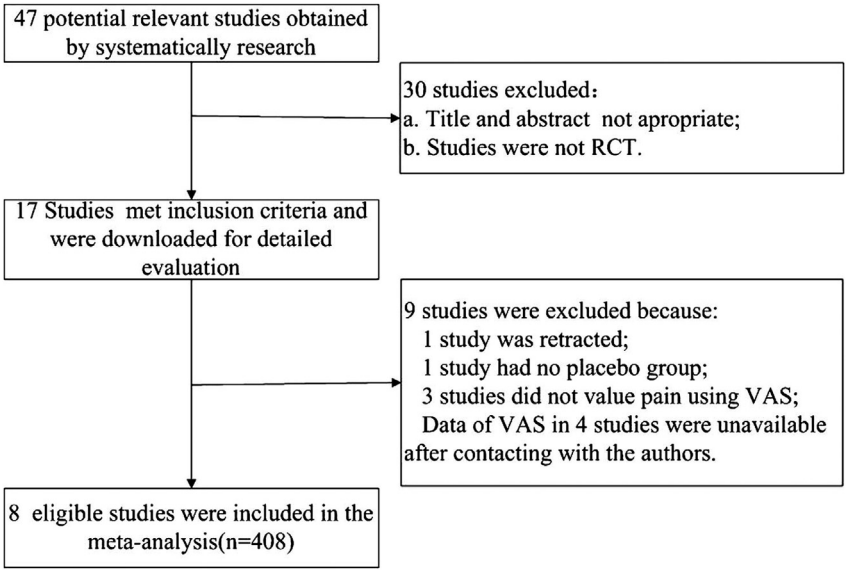

Fig. 1. Flow chart of literature screening process.

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