Pain Ther (2023) 12:1065–1078
https://doi.org/10.1007/s40122-023-00500-6

ORIGINAL RESEARCH

The Efficacy and Safety of Parecoxib Multimodal Preemptive Analgesia in Artificial Joint Replacement: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Zhuoqi Ge · Mingnian Li · Yu Chen · Yufeng Sun · Rui Zhang · Jiaxing Zhang · Xue Bai · Yanyan Zhang · Qi Chen

Received: February 20, 2023 / Accepted: March 15, 2023 / Published online: June 7, 2023

ABSTRACT

Background: Postoperative pain after artificial joint replacement is intense and remains an unsolved problem. Some studies have shown that parecoxib can provide better analgesia in postoperative multimodal analgesia, however, doubts arise about whether its multimodal preemptive analgesia can reduce postoperative pain.

Objectives: The purpose of this systematic review and meta-analysis was to evaluate the impact of preoperative injection of parecoxib on postoperative pain in patients undergoing artificial joint replacement.

Study Design: Systematic review and meta-analysis.

Setting: Embase, PubMed, Cochrane Library, CNKI, VIP, Wangfang databases were searched to identify relevant randomized controlled trials. The last search was in May 2022.

Methods: Randomized controlled trials of efficacy and adverse reactions of intra-operative and postoperative injection of parecoxib in artificial joint replacement were collected. The primary outcome was postoperative visual analog scale scores and the secondary outcomes included cumulative postoperative opioid consumption and incidence of adverse reactions. Using the Cochrane systematic review method to screen the studies, evaluate the quality of the included studies, and extract feature information, RevMan 5.4 software performs a meta-analysis of the corresponding research indicators.

Results: In total, nine studies were involved in the meta-analysis with 667 patients. The trial and control group were given the same dose of parecoxib or placebo at the same time point before and after surgery. The results showed that compared with the control group, the trial group is associated with substantially reduced visual analog scale scores in 24, 48 h at rest ($P < 0.05$), visual analog scale scores in 24, 48, 72 h at movement ($P < 0.05$), dose of opioid need in trial group is notably lower than that in control group ($P < 0.05$), but shows no obvious effect on visual analog scale scores in 72 h at rest, and adverse events ($P > 0.05$).

Qi Chen is the main corresponding author.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40122-023-00500-6.

Z. Ge · R. Zhang · J. Zhang · X. Bai · Q. Chen (✉)
Department of Pharmacy, Guizhou Provincial People's Hospital, Guiyang 550002, China
e-mail: chenqi@gz5055.com

Z. Ge · M. Li · Y. Chen · Y. Zhang (✉) · Q. Chen
College of Pharmacy, Guizhou Medical University, Guiyang 550025, China
e-mail: chinazyy201@163.com

Y. Sun · Q. Chen
College of Pharmacy, Guizhou University of Traditional Chinese Medicine, Guiyang 550025, China

Limitations: The major limitation of this meta-analysis relates to some low-quality studies.
Conclusions: Our results support parecoxib multimodal preemptive analgesia in reducing postoperative acute pain in hip and knee replacement patients, and reduces cumulative opioid consumption without increasing the risk of adverse drug events. Its multimodal preemptive analgesia is safe and effective in hip and knee replacement.
PROSPERO Registration: CRD42022379672.

Keywords: Analgesia; Artificial hip replacement; Artificial knee replacement; Meta-analysis; Multimodal preemptive analgesia; Parecoxib

Key Summary Points
This meta-analysis evaluated the clinical efficacy of preemptive use of parecoxib in alleviating pain after artificial joint replacement.
We included nine randomized controlled trials comparing preemptive use of parecoxib with placebo treatment.
Preemptive analgesia with parecoxib can relieve pain after artificial joint replacement, while sparing opioid analgesic consumption without increasing the incidence of adverse events.
We recommend preemptive analgesia with parecoxib in patients with artificial joint replacement.

INTRODUCTION

Artificial joint replacement (AJR) is the most effective method for the treatment of severe advanced joint disease, improving the mobility of the affected limb and improving the quality of life of patients, especially artificial hip replacement (AHR) and artificial knee replacement (AKR) [1–3]. However, AHR/AKR surgery is traumatic and the severe pain generated after surgery can last for more than 48 hours without relief, making it the type of surgery with the highest degree of postoperative pain [4]. The use of an effective analgesia method can reduce the patient's postoperative pain so early rehabilitation training and reduce perioperative complications [5].

With the development of enhanced recovery after surgery (ERAS), the concept of multimodal preemptive analgesia was developed [6]. Among them, multimodal analgesia is the combination of drugs of different mechanisms of action to exert synergistic and additive analgesic effects. Preemptive analgesia refers block the pain sensation center before harmful stimulation occurs to inhibit the center sensitization and to raise the threshold of pain sensation. The combination of the above two methods can prevent various postoperative bleeding, effectively relieve pain, reduce the number of anesthetic drugs, and also reduce the incidence of opioid postoperative adverse reactions [7]. Currently, multimodal analgesia advocates the use of selective cyclooxygenase-2 (COX-2) inhibitors as the basic drug to retain the strong analgesic effect of central analgesics while reducing the adverse reactions caused by the use of central analgesics [8]. In addition, selective COX-2 has weak inhibition on COX-1, which can reduce the occurrence of adverse reactions caused by the use of non-steroidal anti-inflammatory drugs (NSAIDs).

The specific methods and drugs for preemptive analgesia have not been standardized [9], and whether the preemptive use of COX-2 selective inhibitors under multimodal analgesia is effective has become a widely debated issue in clinical practice [10].

Parecoxib is a novel injectable COX-2 selective inhibitor that works by reducing central sensitivity and peripheral nociceptor inflammation [11], and is widely used clinically for short-term multimodal analgesia after artificial joint replacement, but the results of its preemptive analgesia in multimodal analgesia are controversial. That is, whether parecoxib can be used as a preemptive analgesic is controversial in terms of reducing pain, opioid consumption

compared with the traditional opioid analgesic drug delivery scheme, and on-demand administration mode [12], so we conducted a meta-analysis of the related randomized controlled trials (RCTs) to make a comprehensive assessment of the safety and effectiveness of multimodal preemptive analgesia with parecoxib intraoperative and postoperative injection for joint replacement.

METHODS

This systematic review and meta-analysis were conducted following the PRISMA statement and the Cochrane Handbook, and has been registered on PROSPERO (CRD42022379672). It was approved by the Ethics Committee of Guizhou Provincial People's Hospital. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Dates Sources and Search Strategy

The computer system searched the PubMed, Embase, Cochrane Library, CNKI, VIP, Wanfang databases, and the search time was from the establishment of the library until May 2022. Using a combination of subject words and free words, Parecoxib, (Arthroplasty, Replacement, Hip), (Arthroplasty, Replacement, knee) was used as the subject word search, and Analgesia was used as the subject word for secondary search, and the search method was adjusted according to the specific database. See Table S1 in the electronic supplementary material for details.

Study Selection and Eligibility Criteria

Studies were selected on the basis of the following inclusion criteria: (1) RCTs intra-operative and postoperative injection of parecoxib and placebo to relieve pain; (2) having enrolled patients undergoing AHR or AKR, regardless of age and sex; (3) reporting data on postoperative pain visual analogue scale (VAS) scores, cumulative analgesic consumption, and incidence of adverse events. The exclusion criteria were as follows: (1) trials with no placebo or treatment group; (2) abstracts, letters, editorials, conference articles, or duplicated studies; and (3) original text cannot be obtained.

Two reviewers independently carried out the initial search, deleted duplicate records, screened the titles and abstracts, and determined the final included publications. Any disagreement was resolved by discussion among researchers.

Data Extraction and Risk of Bias Assessment

Two reviewers extracted the data independently using a standardized extraction form. When any disputes between the two reviewers occurred, a third reviewer helped to reach a consensus. The researchers who lacked the necessary data in the included literature first contacted the article and used Getdata software to extract the data if the data were not available. The following data were extracted from the studies using the criteria listed in the Cochrane manual: (1) Basic research information: first author, publication year; (2) Study population characteristics: sample size, sex, age; (3) Analgesic plan: administration time, dose, course of treatment; (4) Outcomes: VAS scores, cumulative opioid consumption, the incidence of adverse reactions.

The methodological quality of each included RCT study was conducted by two investigators independently using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions, we reviewed each included study and scored it as "low", "high", and "unclear" risk based on the following seven domains mentioned in the handbook: (1) Random sequence generation; (2) Allocation sequence concealment; (3) Blinding of patients and personnel; (4) Blinding of outcome assessment; (5) Incomplete outcome data; (6) Selective outcome reporting; (7) Other biases. If there was a discrepancy between the evaluations, a third reviewer was asked to discuss the results.

Outcome Definition

The primary outcomes of this current meta-analysis were VAS scores at rest and movement for the first 3 days after surgery. Secondary outcomes included cumulative opioid consumption and incidence of adverse effects.

Statistical Analysis

All statistical analysis was conducted using the Review Manager (RevMan version 5.4, The Cochrane Collaboration, Oxford, UK). VAS scores and cumulative opioid consumption as continuous data, with mean difference (MD) and its 95% confidence interval (CI) as the pooled effect amount. The incidence of adverse reactions was a dichotomous date, with relative risk (RR) and its 95% CI as the combined effect size.

I^2 was applied to assess statistical heterogeneity. If heterogeneity is not statistically significant ($P \geq 0.1$, $I^2 \leq 50\%$), we use a fixed effects model. otherwise, a random effects model was adopted instead and its heterogeneity sources are analyzed. The low-quality studies (Jadad Scale of 1–3 scores) are excluded to explore their effect on pooled effects. $P < 0.05$ were considered statistically significant.

RESULTS

Search Results

In this study, we identified 909 possible studies to incorporate initial search strategies. In these studies, 540 replicated studies were excluded; 207 studies were excluded after being identified as irrelevant based on title and abstract. After thorough review of the full text of 162 studies that may qualify, nine RCTs were selected for final analysis. A flowchart depicting the study selection strategy is shown in Fig. 1.

Study Characteristics

The main characteristics of the included studies are shown in Table 1. A total of 667 patients from nine RCTs were included. Five RCTs [13, 16–18, 21] in English and four RCTs [14, 15, 19, 20] in Chinese were included, which were published between 2007 and 2019. Parecoxib was given preoperatively and postoperatively in all study groups, placebo was given to the control groups at the same time point, and opioids were given when the pain was severe.

Risk of Bias

Six RCTs [13, 16–19, 21] described the generation of random sequences, three RCTs [16, 18, 19] performed allocation concealment, and five RCTs [13, 17–19, 21] reported the blinding of participants and personnel. All the included studies provided complete baseline information. Each risk of bias item was presented as the percentage across all included studies, which indicated the proportion of different levels of risk of bias for each item. The detailed qualities of the RCTs are shown in Fig. 2.

Results of Meta-Analysis

Postoperative VAS Scores at Rest

Nine studies [13–21] reported the VAS scores for 24 h postoperatively at rest. A fixed effects model was adopted because no significant heterogeneity was found ($P = 0.07$, $I^2 = 43\%$). The pooled results indicated that there was significant difference between groups at 24 h (MD = − 0.34, 95% CI − 0.43 to − 0.25, $P < 0.00001$). Eight studies [13–15, 17–21] reported the VAS scores for 48 h postoperatively at rest. A random effects model was adopted because significant heterogeneity was found ($P = 0.03$, $I^2 = 53\%$). There was significant difference in VAS scores at 48 h between groups (MD = − 0.15, 95% CI − 0.30 to − 0.01, $P = 0.04$). Four studies [13, 17–19] reported VAS scores for 72 h postoperatively at rest, a fixed effects model was adopted because no significant heterogeneity was found at 72 h ($P = 0.09$, $I^2 = 50\%$). There was no significant difference in pain scores at 72 h between groups (MD = − 0.00, 95% CI − 0.10 to 0.09, $P = 0.95$) (Fig. 3).

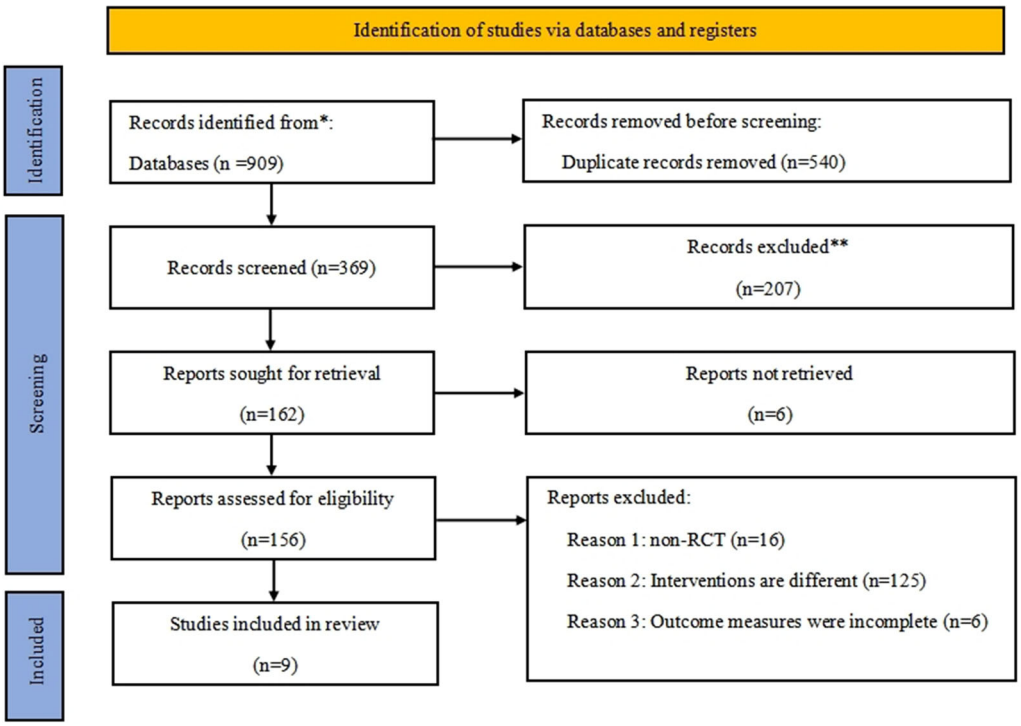

Fig. 1 Search flowchart of studies included in the meta-analysis. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers); **if automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools

Postoperative VAS Scores at Movement

Six studies [13, 15–19] reported the VAS scores for 24 h postoperatively at movement, a random effects model was adopted because significant heterogeneity was found ($P < 0.05$, $I^2 = 81\%$), and the pooled results indicated that there was significant difference between groups at 24 h (MD = − 1.06, 95% CI − 1.55 to − 0.58, $P < 0.0001$). Five studies [13, 15, 17–19] reported the VAS scores for 48 h postoperatively at movement, a random effects model was adopted because significant heterogeneity was found ($P = 0.01$, $I^2 = 67\%$), and there was significant difference in VAS scores at 48 h between groups (MD = − 0.90, 95% CI − 1.31 to − 0.50, $P < 0.0001$). Four studies [13, 17–19] reported VAS scores for 72 h postoperatively at movement, a random effects model was adopted because significant heterogeneity was found at 72 h ($P = 0.02$, $I^2 = 67\%$), and there was significant difference in pain scores at 72 h between groups (MD = − 0.58, 95% CI − 1.09 to − 0.06, $P = 0.03$) (Fig. 4).

Cumulative opioid consumption

Four studies [13, 16, 18, 19] reported the outcome of cumulative opioid consumption, all using morphine. There was no significant heterogeneity among studies ($P = 0.31$, $I^2 = 17\%$) and a fixed effect modal was adopted. The pooled results showed that preoperative administration of parecoxib significantly reduced postoperative cumulative opioid consumption (MD = − 16.98, 95% CI − 19.53 to − 14.43, $P < 0.00001$) (Fig. 5).

Incidence of Adverse Reactions

Five studies [13, 16–19] provided the outcome of adverse effects, including nausea, vomiting, headache, and pruritus. As the adverse reaction rate of one of the studies included the patients who had withdrawn from the study [19], the

Table 1 Characteristics of the included studies

First author	Year	Surgery type	Sample size (A/B)	Mean age (A/B)	Sex (M/F)	Intervention (A/B)	Outcome indicators	Jada scores
Bian [13]	2018	AKR	98 (46/42)	66.64 ± 7.27/66.12 ± 8.34	24/64	A: 40 mg of parecoxib sodium was injected intravenously 30 min before surgery and 12 h after surgery B: Inject the same dose of normal saline at the same time	①②③	4
Han [14]	2014	AKR	40 (20/20)	–	18/22	A: Parecoxib sodium 40 mg was given intravenously 30 min before surgery and every 12 h within 2 days after surgery B: Inject the same dose of normal saline at the same time	①	1
Huang [15]	2012	AKR	30 (15/15)	–	–	A: Parecoxib sodium 40 mg was given intravenously 15 min before and 12 h after surgery B: Inject the same dose of normal saline at the same time	①	2
Martinez [16]	2007	AHR	43 (22/21)	65 ± 9/63 ± 11	24/19	A: Parecoxib 40 mg was injected intravenously at the time of anesthesia induction and 12 h after surgery B: Inject the same dose of normal saline at the same time	①②③	5
Peng [17]	2018	AHR	94 (48/46)	57.22 ± 12.51/55.19 ± 10.97	38/56	A: Parecoxib sodium 20 mg intravenously is given 30 min before surgery and every 12 h for 2 days after surgery B: Inject the same dose of normal saline at the same time	①③	4
Xiao [18]	2019	AHR	141 (69/72)	53.79 ± 12.46/54.35 ± 11.93	–	A: Parecoxib sodium 40 mg intravenously every 12 h 30 min before and 2 days after surgery B: Inject the same dose of normal saline at the same time	①②③	5

Table 1 continued

First author	Year	Surgery type	Sample size (A/B)	Mean age (A/B)	Sex (M/F)	Intervention (A/B)	Outcome indicators	Jada scores
Xiao [19]	2014	AHR	29 (15/14)	52 ± 12/55 ± 14	17/12	A: Parecoxib sodium 40 mg was injected intravenously 30 min before excision, 9 p.m. after surgery, and every 12 h for 2 days after surgery B: Inject the same dose of normal saline at the same time	①②③	6
Xiao [19]	2014	AKR	38 (19/19)	67 ± 8/66 ± 8	13/25	A: Parecoxib sodium 40 mg was injected intravenously 30 min before excision, 9 p.m. after surgery, and every 12 h for 2 days after surgery B: Inject the same dose of normal saline at the same time	①②③	6
Zhao [20]	2010	AHR AKR	42 (20/22)	71.1 ± 4.4/70.5 ± 4.9	19/23	A: Parecoxib 40 mg was given intravenously 15 min before anesthesia induction and 12 h postoperatively B: Inject the same dose of normal saline at the same time	①	1
Zhu [21]	2016	AKR	122 (60/62)	75.1 ± 8.2/74.3 ± 7.6	–	A: Intravenous parecoxib sodium 40 mg was given intravenously before and 12 h after surgery B: Inject the same dose of normal saline at the same time	①	4

A parecoxib group, *B* placebo group, *M* male, *F* female, ① VAS scores, ② Cumulative opioids consumption, ③ Incidence of adverse reactions; Jadad scores were based on an improved Jadad Scale (a score of 1–3 is considered a low-quality study, and a score of 4–7 is considered a high-quality study)

study was excluded and the final statistical analysis was conducted for the four studies [13, 16–18]. There was no significant heterogeneity among studies ($P = 0.21$, $I^2 = 34\%$). Our study demonstrated that preoperative administration of parecoxib did not increase the risk of adverse reactions (RR = 0.77, 95% CI 0.58 to 1.03, $P = 0.07$) (Fig. 6).

Sensitivity Analysis

The sensitivity analysis results are shown in Table 2. To study whether the effect model has a significant impact on the overall combined effect value, two effect models were used for sensitivity analysis of each outcome indicator, and the results showed good consistency, indicating that the studies included in this study

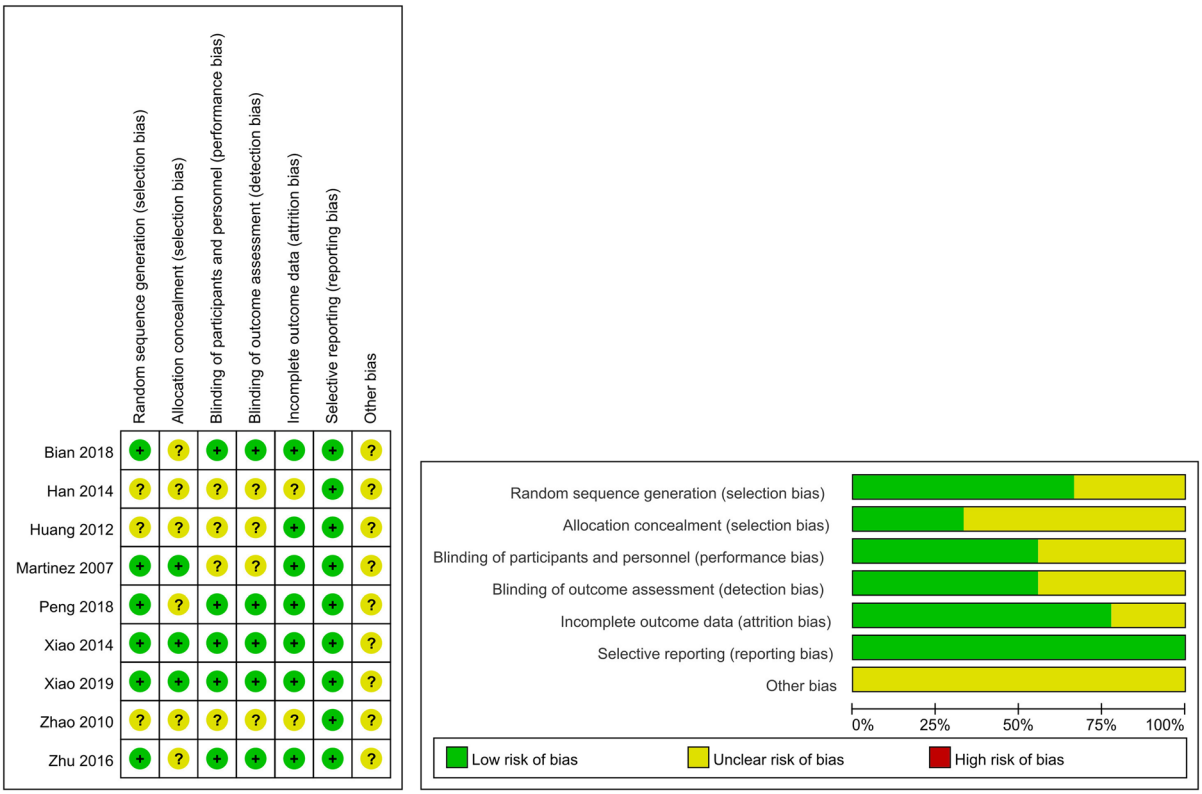

Fig. 2 Risk of bias and methodologic quality of the randomized controlled trials. *Green* and + , low risk of bias; *Red* and −, high risk of bias; *Yellow* and ?, unclear risk

was relatively stable. In addition, after the exclusive exclusion of low-quality Jadad scores (< 3) studies [14, 15, 20], the results showed that the response value changed in postoperative 48 h at rest, and the effective values of other outcome indicators did not change, suggesting that low-quality studies may affect the research results.

DISCUSSION

In this systematic review of the effects of preemptive parecoxib, we found that people with a joint replacement who received an intraoperative and preoperative preemptive injection of parecoxib compared to the placebo group experienced less pain at rest and during exercise after surgery, reduced opioid consumption, and no increase in adverse events.

AHR/AKR is the best treatment method in recent years for joint diseases such as trauma, osteoarthritis, necrosis of the femoral head, and tumors [22], which places artificial prosthetic joints in the body's diseased joints and reconstructs the anatomy of the joints to help patients restore normal physiological functions and life capabilities [23]. However, AHR and AKR belong to the highest postoperative pain level of surgery because the operation itself will release a large number of inflammatory substances, resulting in the body's central and peripheral nervous system pain sensitivity. Postoperative acute pain is a common problem in the perioperative period of joint replacement surgery. About 60% of patients have severe postoperative pain, 30% of patients have moderate pain [24–26]. Pain management is the core of ERSA, which is related to postoperative rehabilitation effects and complications. Severe pain can cause patients to resist postoperative rehabilitation training and thus affect the efficacy of surgery, and unreasonable postoperative pain control may cause complications such as

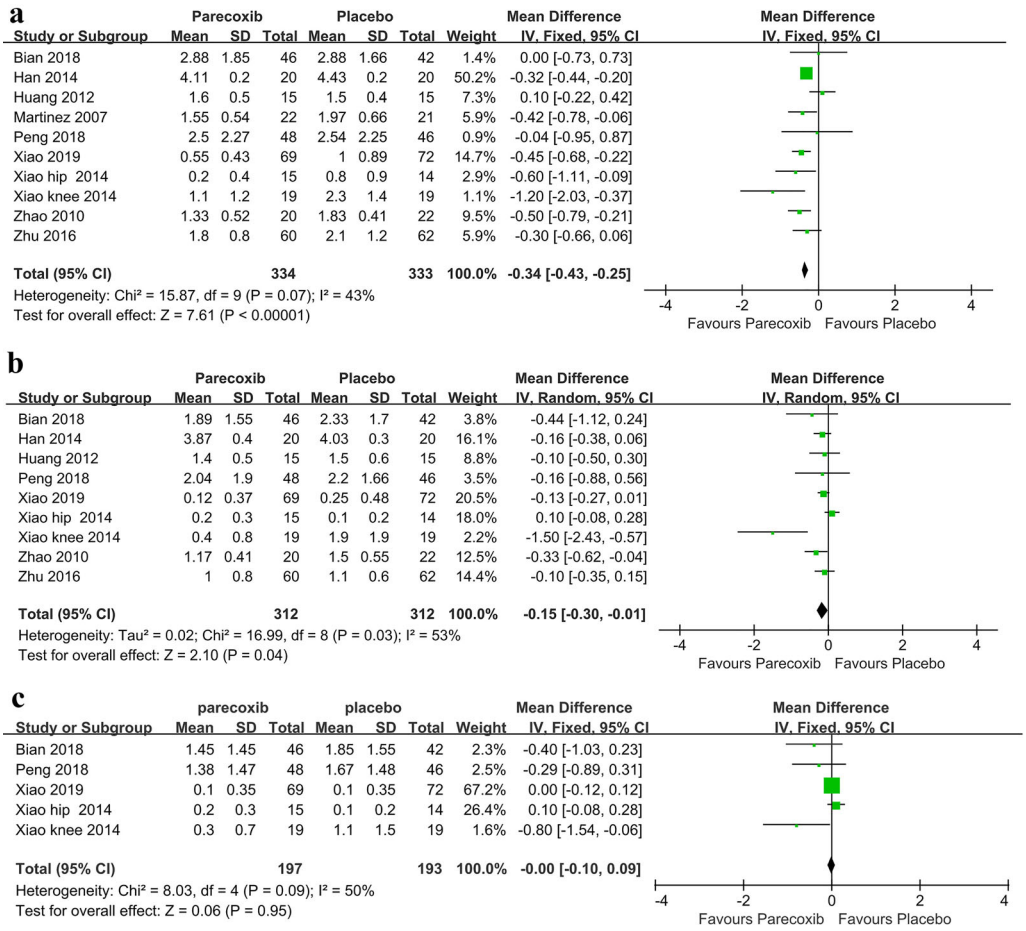

Fig. 3 Forest plot of meta-analysis of postoperative VAS in resting state after surgery between two group. **A** Postoperative 24 h; **B** postoperative 48 h; **C** postoperative 72 h

atelectasis, pulmonary edema, hypoxemia, and cardiovascular system disease [27, 28].

Although the commonly used opioid analgesics in the past can effectively relieve postoperative pain, their side effects such as nausea and vomiting after large doses cause patients to delay recovery [29]. The previous on-demand analgesic mode of administering analgesics only when the pain is severe causes patients to suffer physically and mentally, which greatly limits the physical recovery of patients in the postoperative rehabilitation stage. The multimodal analgesia and preemptive analgesia produced under the ERSA concept provide a new way of pain management, and multimodal analgesia based on NSAIDs plays an increasingly important role in reducing opioid dosage and its adverse effects in postoperative analgesia [30]. Although preemptive analgesia is a new concept, a large number of animal studies have shown that preemptive analgesia has a good role in preventing and inhibiting peripheral and central sensitization phenomena [31]. WALL [32] and WOOLF et al. [33] further research on the theory of preemptive analgesia confirms that it can effectively improve postoperative pain. At present, the multimodal preemptive analgesia model has become very popular in the clinic, and the combination of the on-time administration principle of preemptive analgesia and the three-step administration principle of multimodal analgesia has regularized and individualized the analgesia regimen, but there is still controversy over its effectiveness in the treatment of postoperative acute pain [34].

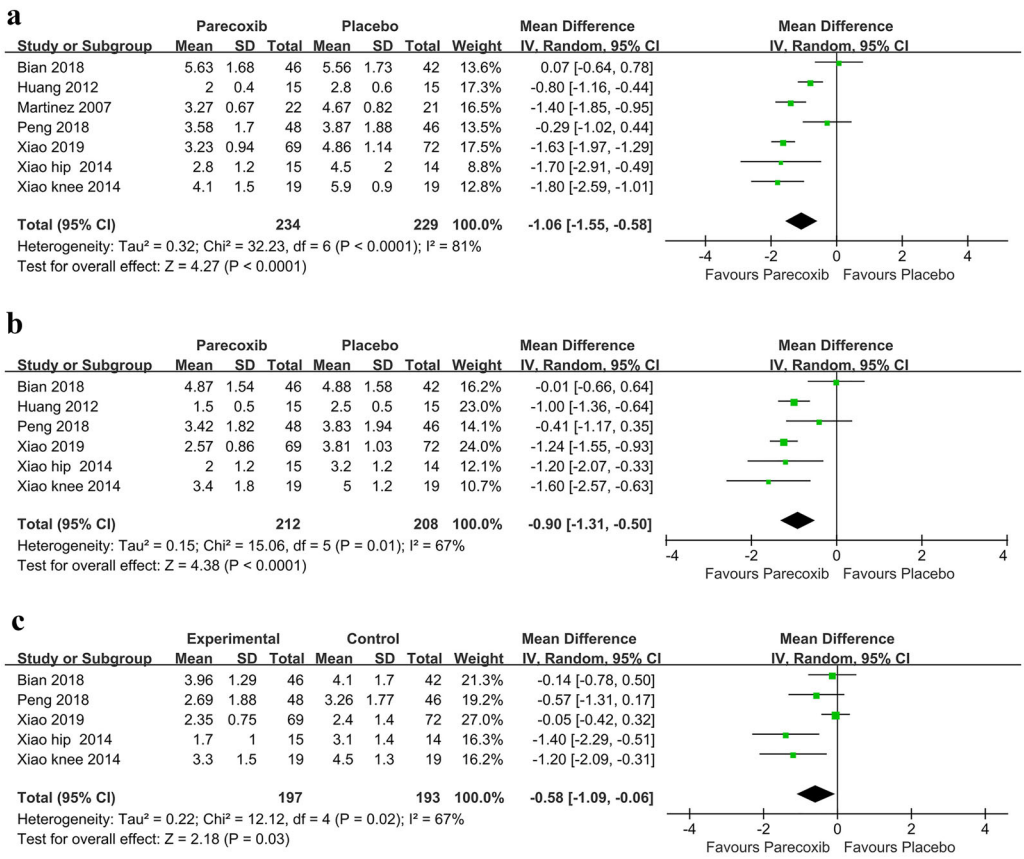

Fig. 4 Forest plot of meta-analysis of postoperative VAS score in moving state between the two groups. **A** Postoperative 24 h; **B** postoperative 48 h; **C** postoperative 72 h

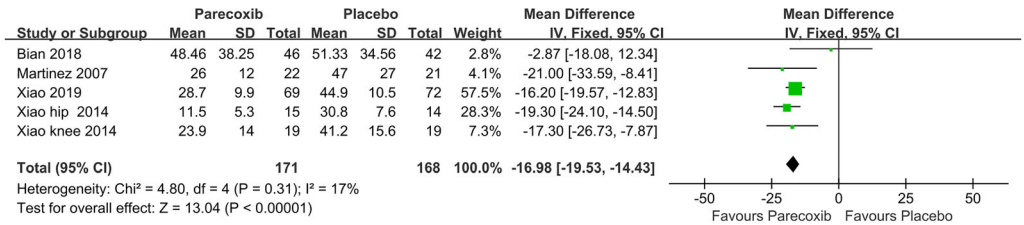

Fig. 5 Forest plot of meta-analysis of the postoperative cumulative opioid consumption between the two groups

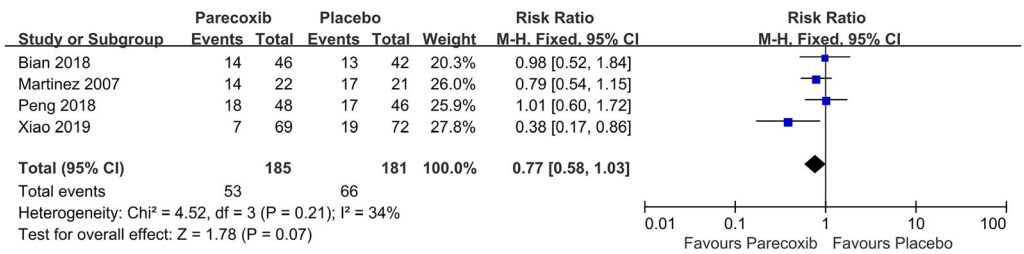

Fig. 6 Forest plot of meta-analysis of the incidence of postoperative adverse reactions between the two groups

Table 2 Sensitivity analysis results of VAS scores in 48-h resting state

	Heterogeneity		Analysis model	MD (95% CI)	*P*
	P	I^2 (%)			
Before culling studies	0.03	53	Random-effects model	− 0.15 (− 0.30 to − 0.01)	0.04
After the studies are excluded	0.01	65	Random-effects model	− 0.15 (− 0.37 to 0.07)	0.17

Parecoxib was the first intramuscular and intravenous COX-2 selective inhibitor to be used primarily for short-term postoperative acute pain, and injecting parecoxib is more advantageous when patients are unable to take the drug orally. Unlike other non-selective COX inhibitors on the normal function of the gastric mucosa and platelets, perioperative use of parecoxib has the advantage of not causing prolonged bleeding time and adverse events with gastrointestinal complications [35], and is safer to use and more extensive [36]. A large number of studies have shown that parecoxib for orthopedics, general surgery, obstetrics, and gynecology, and other clinical departments of postoperative analgesia has a good analgesic effect. Its analgesic effect after joint replacement surgery has been confirmed, and the use of parecoxib may be related to organ protection, anxiolysis, improvement of immune response, and tumor prognosis and postoperative chills and delirium. A meta-analysis by Huang et al. [37] showed that parecoxib can prevent the occurrence of early postoperative cognitive dysfunction in elderly patients in China, which provides a basis for the use of parecoxib in the elderly population of China with a high incidence of joint replacement.

Most of the studies on parecoxib preemptive analgesia were conducted in orthopedics and the results of analgesic efficacy were different. Based on the difference in efficacy, this meta-analysis studies the efficacy of preemptive analgesia with parecoxib in AHR and AKR, with the aim of comparing the efficacy and safety of preemptive use of parecoxib and placebo for AHR and AKR postoperative pain. Postoperative pain scores and opioid consumption are important aspects of analgesic effect evaluation. Our findings are consistent with the results of several RCTs [38, 39] showing that the preemptive administration of parecoxib is related to the reduction of postoperative pain and opioid consumption. However, Peng et al. [17] showed that the injection of parecoxib 30 min before the incision does not provide effective preemptive analgesia for the management of postoperative pain after AHR. We suspect that the difference in efficacy may be related to the type of pain and the time of treatment, and other relevant factors in clinical practice may affect its preemptive analgesic effect [12]. In terms of safety, we found that intraoperative and postoperative preemptive administration of parecoxib did not increase the risk of adverse reactions. This conclusion was made in the exclusion of people who were contraindicated to parecoxib. So whether the pre-administration of parecoxib was related to the incidence of adverse reactions needs to be proven by more studies.

The duration of treatment for parecoxib used in the studies included in this meta-analysis varied, and subgroup analyses of studies with different duration of treatment showed no significant effect (see Fig. S1 in the electronic supplementary material). A study of parecoxib for acute pain in adults [40] showed effective analgesia in patients treated with a single dose of parecoxib 20 mg or 40 mg in 50–60% of patients treated, with higher doses of parecoxib requiring less rescue drug in the short term. Therefore, we speculate that the dose and duration of parecoxib do not affect the postoperative efficacy of artificial joint replacement, but that higher doses and long courses of parecoxib may be helpful in reducing opioid use. According to the instructions of parecoxib, it is recommended to inject 20 or 40 mg of

parecoxib in a single dose, and the course of treatment should not exceed 3 days.

To the best of knowledge, this is the first meta-analysis of the effect of the preemptive use of parecoxib on joint replacement. In addition, we reported the different conditions of pain scores, not limited to the pain scores under a single state, but also reported the VAS scores under rest and movement.

Potential Biases in the Review Process

There are some limitations in this meta-analysis that may cause some clinical heterogeneity: (1) The treatment course of parecoxib is different; (2) It is impossible to analyze the effects of drugs included in the study, including drug dose, intraoperative anesthesia scheme, etc.; (3) VAS scores are partly influenced by subjective factors; (4) Some of the included studies did not collect original data and used data extraction software to extract data; (5) The results of sensitivity analysis showed that low-quality studies caused the change in merger affect value.

CONCLUSIONS

Our results support the preemptive analgesia with parecoxib during and after artificial joint replacement, the route of administration of parecoxib is intravenous injection or muscle injection. Preemptive administration of parecoxib significantly reduces postoperative pain, opioid consumption, and does not affect the incidence of adverse reactions. Multimodal hyperanalgesia with parecoxib as the mainstay and opioid analgesics as the supplement is in line with the principle of timely administration of analgesics, three-step administration, and short course of treatment in small doses, in line with the principle of accelerated rehabilitation under the ERSA concept, and has a definite effect on short-term pain after joint replacement. Future rigorously conducted and reported RCTs examining preemptive effect of parecoxib on post-arthroplasty pain are needed, ensuring that publication bias is avoided.

ACKNOWLEDGEMENTS

Funding. This study was supported by the Science and Technology Foundation of Guizhou Provincial Health Commission (GZWKJ2021-553), and Guizhou Province's high-level innovative talent "thousands levels" training funds (GZSYQCC[2023]008). The Rapid Service Fee was funded by the Guizhou Provincial People's Hospital.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author contributions. All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Zhuoqi Ge was responsible for conception and design of the study and drafted the manuscript. Mingnian Li and Yufeng Sun assisted with data collection. Jiaxing Zhang and Rui Zhang contributed to preparation and data analysis. Yu Chen and Xue Bai contributed to study retrieval. Qi Chen and Yanyan Zhang contributed to revision of the manuscript. All the authors contributed to the interpretation of the data and critically reviewed the manuscript for publication.

Disclosures. Zhuoqi Ge, Mingnian Li, Yu Chen, Yufeng Sun, Jiaxing Zhang, Rui Zhang, Xue Bai, Yanyan Zhang and Qi Chen have nothing to disclose.

Compliance with ethics guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

REFERENCES

1. Räsänen P, Paavolainen P, Sintonen H, et al. Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. Acta Orthop. 2007;78(1):108–15.

2. Tao S, Cao QX. Effect of parecoxib sodium preemptive analgesia on the analgesic effect of total knee arthroplasty and serum TNF-α and IL-6 (in Chinese). Zhejiang Clin Med J. 2017;19(7):2.

3. Xiao WY, Dong YQ, Zhang C. Repair of anterior tibiofibular ligament for instable external rotation in patients with ankle fracture: an analysis of short-term outcome (in Chinese). Shanghai Med J. 2017;40(12):4.

4. Allen JG, Denny NM, Oakman N. Postoperative analgesia following total knee arthroplasty: a study comparing spinal anesthesia and combined sciatic femoral 3-in-1 block. Reg Anesth Pain Med. 1998;23(2):142–6.

5. Scuderi GR. The challenges of perioperative pain management in total joint arthroplasty. Am J Orthop. 2015;44(10):S2–4.

6. Sheng B, Weng XS, Liao R. Expert consensus in enhanced recovery after total hip and knee arthroplasty in China: pain and sleep management (in Chinese). Chin J Bone Jt Surg. 2016;9(2):91–7.

7. Kahl L, Parvizi J, Viscusi ER, Hozack WJ, Sharkey PF, Rothman RH. Lessons learned with extended-release epidural morphine after total hip arthroplasty. Clin Orthop Relat Res. 2010;468(4):1082–7.

8. White PF. The role of non-opioid analgesic techniques in the management of pain after ambulatory surgery. Anesth Analg. 2002;94(3):577–85.

9. Yin YF, Luo M, Qin S, Zhang MY, He K, Xia XM. Efficacy and safety parecoxib sodium for preemptive analgesia in laparoscopic cholecystectomy: a meta-analysis (in Chinese). Chin J Gen Surg. 2021;30(9):16.

10. Fan H. Research progress on application of COXIBs in preemptive analgesia of total hip arthroplast (in Chinese). Chongqing Med J. 2021;50(12):3750–4.

11. Alanoglu Z, Ates Y, Orbey BC, Türkçapar AG. Preoperative use of selective COX-II inhibitors for pain management in laparoscopic Nissen fundoplication. Surg Endosc. 2005;19(9):1182–7.

12. Li BB, Wang LS. Research progress on the use of parecoxib sodium in the perioperative period (in Chinese). Bachu Med J. 2020;3(4):117–24.

13. Bian YY, Wang LC, Qian WW, et al. Role of parecoxib sodium in the multimodal analgesia after total knee arthroplasty: a randomized double-blinded controlled trial. Orthop Surg. 2018;10(4):321–7.

14. Han JB, Hao YQ. Application of parecoxib sodium preemptive analgesia in 20 cases of artificial total knee replacement (in Chinese). Chin J Ethnomed Ethnopharm. 2014;23(23):2.

15. Huang LB, Yang G, Cui SY. Effects of perioperative administration parecoxib sodium on postoperative pain and function recovery after total knee arthroplasty (in Chinese). J Clin Anesthesiol. 2012;28(5):3.

16. Martinez V, Belbachir A, Jaber A, et al. The influence of timing of administration on the analgesic efficacy of parecoxib in orthopedic surgery. Anesth Analg. 2007;104(6):1521–7.

17. Peng HM, Wang LC, Wang W, et al. Preemptive analgesia with parecoxib in total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. Pain Physician. 2018;21(5):483–8.

18. Xiao K, Yu L, Xiao W, et al. Pain management using perioperative administration of parecoxib for total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. Pain Physician. 2019;22(6):575–82.

19. Xiao WY. Efficacy of parecoxib sodium preemptive analgesia combined with PCIA in joint replacement perioperative analgesia (in Chinese). Beijing: Peking Union Medical College Hospital; 2014.

20. Zhao P. The effect of parecoxib sodium on postoperative cognitive function in elderly undergoing joint replacement (in Chinese). Zhengzhou: Zhengzhou University; 2010.

21. Zhu YZ, Yao R, Zhang Z, Xu H, Wang LW. Parecoxib prevents early postoperative cognitive dysfunction in elderly patients undergoing total knee arthroplasty: a double-blind, randomized clinical consort study. Medicine. 2016;95(28): e4082.

22. Xie YB, Gao DY. Parecoxib sodium pretreatment Effect on analgesia and coagulation function after hip arthroplasty (in Chinese). Chin Remedies Clin. 2012;12(5):2.

23. Zhang H, Li ZJ. Analysis of the effects of multimodal analgesic care in patients undergoing hip and knee replacement (in Chinese). Contemp Med Forum. 2015;2015(18):2.

24. Wang Y, Zhu YZ, Liu G. Dexmedetomidine complex tramadol hyperechoic analgesia after osteoarthropathy analgesic effect and effect of anesthetic drug use (in Chinese). Hebei Med. 2016;22(3):4.

25. Malviya A, Martin K, Harper I, et al. Enhanced recovery program for hip and knee replacement reduces death rate. Acta Orthop. 2011;82(5): 577–81.

26. McCartney CJ, Nelligan K. Postoperative pain management after total knee arthroplasty in elderly patients: treatment options. Drugs Aging. 2014;31(2):83–91.

27. Su Y, Zhang XY, Lan L. Multimodal analgesic care interventions are used for clinical observation in patients after hip and knee replacement (in Chinese). Yunnan J Tradit Chin Med Materia Medicia. 2013;34(3):77–8.

28. Castorina S, Luca T, Privitera G, El-Bernawi H. An evidence-based approach for laparoscopic inguinal hernia repair: lessons learned from over 1,000 repairs. Clin Anat. 2012;25(6):687–96.

29. Wheeler M, Oderda GM, Ashburn MA, Lipman AG. Adverse events associated with postoperative opioid analgesia: a systematic review. J Pain. 2002;3(3): 159–80.

30. Gan TJ, Joshi GP, Zhao SZ, Hanna DB, Cheung RY, Chen C. Presurgical intravenous parecoxib sodium and follow-up oral valdecoxib for pain management after laparoscopic cholecystectomy surgery reduces opioid requirements and opioid-related adverse effects. Acta Anaesthesiol Scand. 2004;48(9):1194–207.

31. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia I: physiological pathways and pharmacological modalities. Can J Anaesth. 2001;48(10):1000–100.

32. Wall PD. The prevention of postoperative pain. Pain. 1988;33(3):289–90.

33. Woolf CJ, Chong MS. Preemptive analgesia–treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg. 1993;77(2):362–79.

34. Ong CK, Lirk P, Seymour RA, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. Anesth Analg. 2005;100(3):757–73.

35. Wang RD, Zhu JY, Zhu Y, Ge YS, Xu GL, Jia WD. Perioperative analgesia with parecoxib sodium improves postoperative pain and immune function in patients undergoing hepatectomy for hepatocellular carcinoma. J Eval Clin Pract. 2020;26(3): 992–1000.

36. Essex MN, Cheung R, Li C, Xie L. Safety of parecoxib when used for more than 3 days for the management of postoperative pain. Pain Manag. 2017;7(5):383–9.

37. Huang JM, Lv ZT, Zhang B, Jiang WX, Nie MB. Intravenous parecoxib for early postoperative cognitive dysfunction in elderly patients: evidence from a meta-analysis. Expert Rev Clin Pharmacol. 2020;13(4):451–60.

38. Lin FH. Parecoxib sodium was used for analgesia after artificial total knee replacement in 24 patients (in Chinese). China Pharm. 2012;24(23):197.

39. Ittichaikulthol W, Prachanpanich N, Kositchaiwat C, Intapan T. The post-operative analgesic efficacy of celecoxib compared with placebo and parecoxib after total hip or knee arthroplasty. J Med Assoc Thai. 2010;93(8):937–42.

40. Lloyd R, Derry S, Moore RA, McQuay HJ. Intravenous or intramuscular parecoxib for acute postoperative pain in adults. Cochrane Database Syst Rev. 2009;15(2):CD004771.