INPLASY PROTOCOL

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The authors declare no conflict of interest.

Comparative efficacy of traditional non-selective NSAIDs and selective cycloxygenase-2 inhibitor in patients with acute gout: a systematic review and meta-analysis

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Review question / Objective: **To assess the comparative efficacy of traditional non-steroidal anti-inflammatory drugs and selective cycloxygenase-2 inhibitor (COXIB) for patients with acute gout.**
Condition being studied: **Acute gout most frequently begins with the involvement of a single joint in the lower limbs (85–90% of cases) – usually, the first metatarsophalangeal joint. The management of acute gout includes rapid treatment of acute flares and effective long-term therapy. The main therapeutic options for an acute flare are colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), and corticosteroids. The deposition of monosodium urate microcrystals in the articular and periarticular tissues elicits acute or chronic inflammatory responses that are known as gouty arthritis.There is evidence that monosodium urate microcrystals induce the production of cyclooxygenase-2 (COX-2) in human monocytes. NSAIDs include traditional NSAIDs and selective COX-2 inhibitors (COXIBs) – the former inhibits both COX-1 and -2 enzymes whereas the latter specifically antagonizes COX-2. The efficacy of COXIBs is comparable to that of traditional NSAIDs; however, COXIBs have fewer adverse effects, particularly gastrointestinal adverse effects.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 April 2020 and was last updated on 04 April 2020 (registration number INPLASY202040025).

INTRODUCTION

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non-steroidal anti-inflammatory drugs (NSAIDs), and corticosteroids. The deposition of monosodium urate microcrystals in the articular and periarticular tissues elicits acute or chronic inflammatory responses that are known as gouty arthritis.There is evidence that monosodium urate microcrystals induce the production of cyclooxygenase-2 (COX-2) in human monocytes. NSAIDs include traditional NSAIDs and selective COX-2 inhibitors (COXIBs) – the former inhibits both COX-1 and -2 enzymes whereas the latter specifically antagonizes COX-2. The efficacy of COXIBs is comparable to that of traditional NSAIDs; however, COXIBs have fewer adverse effects, particularly gastrointestinal adverse effects.

METHODS

Participant or population: Adult patients (age≥18 years) with a diagnosis of acute gout defined by the American Rheumatology Association diagnostic criteria.

Intervention: Traditional non-selective NSAIDs or selective cycloxygenase-2 inhibitor.

Comparator: Traditional non-selective NSAIDs or selective cycloxygenase-2 inhibitor.

Study designs to be included: Randomized controlled trial.

Eligibility criteria: Trials that compared COXIBs with traditional non-selective NSAIDs or compared the various COXIBs.

Information sources: Biomedical databases, including Medline, Web of Science, China National Knowledge Infrastructure (CNKI), and Wanfang Data

Main outcome(s): Primary outcomes: Pain assessed using a visual analog scale (VAS) score and 5-point Likert scale for days 2–8. Secondary outcomes were: i) response rate (defined as the proportion of patients who achieved improvement in clinical symptoms) for days 2–8; ii) onset of efficacy (hours); iii) post-treatment serum C-reactive protein level; iv) patient's global assessment of response; v) investigator's global assessment of response; and vi) inflammatory swelling.

Quality assessment / Risk of bias analysis: Two authors assessed the risk of bias of the included studies using the methods recommended by the Cochrane Collaboration for the following items. We scored each study on six domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other sources of bias. The risk of bias was graded as high, low, or unclear risk of bias. Furthermore, the quality of evidence across pooled studies (risk of bias, inconsistency, indirectness, imprecision, and publication bias) was assessed by two researchers as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and using the online version of GRADEpro GDT software (www.gradepro.org, McMaster University, 2016). Disagreements were resolved, first, by discussion and, then, by consulting a third senior author for arbitration.

Strategy of data synthesis: Traditional meta-analyses were conducted for studies that directly compared COXIBs and traditional non-selective NSAIDs and those that compared between etoricoxib, celecoxib, and meloxicam. Odds ratios (OR) and standardized mean difference (SMD) with corresponding 95% confidence intervals (CIs) were used for dichotomous and continuous outcomes, respectively.

Subgroup analysis: Comparative efficacy of traditional non-selective NSAIDs and COXIBs. Comparative efficacy of COXIBs

Sensibility analysis: In order to check the stability of the result, sensitivity analysis was performed by sequential delete single study if suitable.

Countries involved: China

Keywords: Acute gout, NSAIDs, selective cycloxygenase-2 inhibitors, efficacy.