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Review

Intravenous acetaminophen as an adjunct to multimodal analgesia after total knee and hip arthroplasty: A systematic review and meta-analysis

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HIGHLIGHTS

- To perform a meta-analysis to investigate the impact of acetaminophen for pain management after TJA.
- Intravenous acetaminophen to multimodal analgesia could significantly reduce pain after TJA.

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ABSTRACT

Background: This meta-analysis aimed to perform a meta-analysis to investigate the impact of additional intravenous acetaminophen for pain management after total joint arthroplasty (TJA).
Methods: We conducted electronic searches of Medline (1966–2017.07), PubMed (1966–2017.07), Embase (1980–2017.07), ScienceDirect (1985–2017.07) and the Cochrane Library. Randomized controlled trials (RCTs) and non-RCTs were included. The quality assessments were performed according to the Cochrane systematic review method. The primary outcomes were postoperative pain scores and opioid consumption. Meta-analysis was performed using Stata 11.0 software.
Results: A total of four studies were retrieved involving 865 participants. The present meta-analysis indicated that there were significant differences between groups in terms of pain scores at POD 1 (WMD = −0.954, 95% CI: −1.204 to −0.703, P = 0.000), POD 2 (WMD = −1.072, 95% CI: −2.072 to −0.073, P = 0.000), and POD 3 (WMD = −0.883, 95% CI: −1.142 to −0.624, P = 0.000). Significant differences were found regarding opioid consumption at POD 1 (WMD = −3.144, 95% CI: −4.142 to −2.146, P = 0.000), POD 2 (WMD = −5.665, 95% CI: −7.383 to −3.947, P = 0.000), and POD 3 (WMD = −3.563, 95% CI: −6.136 to −0.991, P = 0.007).
Conclusion: Additional intravenous acetaminophen to multimodal analgesia could significantly reduce pain and opioid consumption after total joint arthroplasty with fewer adverse effects. Higher quality RCTs are required for further research.

1. Introduction

Total knee arthroplasty (TKA) and total hip arthroplasty (THA) are successful surgical procedures to replace the weight-bearing surfaces of the joint to relieve pain and disability for patients suffering from osteoarthritis. Recent data indicated that more than 700 thousand TKAs and 330 thousand THAs were operated in the US, which predicting an increasing trend and requirement for the next few years [1–3]. However, the surgical procedures were associated with acute pain from mild to severe which influenced functional restoration and the quality of life [4]. Adequate analgesia regime can contribute to early rehabilitation and less postoperative complications.

Pain control after major orthopedic surgery has become a serious clinical problem. Numerous analgesic method has been applied including periarticular injection, oral form of opioid, blockade of the femoral nerve, and epidural analgesia [5–8] However, each method has its limitations. Periarticular injection

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was unable to provide a long duration of action; Oral opioid was criticized for the frequent adverse effects such as nausea, vomiting, urinary retention, pruritus, and respiratory depression. Femoral nerve block (FNB) has been advised for pain control after total joint arthroplasty (TJA). It has many advantages over oral opioid and epidural analgesia. However, FNB may cause the weakness of quadriceps muscle strength which results in an increased risk of postoperative falls and affect the early mobilization [9,10]. Currently, multimodal analgesia regimens was recommended in the setting of the postoperative pain after TJA.

Acetaminophen is a kind of non-steroidal anti-inflammatory drugs (NSAIDs) which is widely used for mild to moderate pain control [11]. It exerts its analgesic effect through inhibiting the synthesis of prostaglandins in the central nervous system and works peripherally to block pain impulse generation [12]. Whether the addition of acetaminophen to a multimodal analgesia regimen would improve pain control in patients undergoing TJA remains controversial. Thus, we performed a systematic review and meta-analysis to investigate the impact of intravenous acetaminophen for pain management after TJA.

2. Methods

This meta-analysis was performed in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. All analyses were based on previous studies, therefore, no ethical approval are required.

2.1. Search strategy

We conducted electronic searches of Medline (1966–2017.7), PubMed (1966–2017.7), Embase (1980–2017.7), ScienceDirect (1985–2017.7) and the Cochrane Library. The following key words were used on combination with Boolean operators AND or OR: “total knee replacement OR arthroplasty”, “total hip replacement OR arthroplasty”, “acetaminophen” and “pain control”. References of the included articles were also scanned for potentially relevant studies. No restrictions were placed on the publication language.

2.2. Inclusion criteria and study selection

(1) Participants: Published literatures enrolling adult patients that with a diagnosis of end-stage of joint osteoarthritis and prepared for TJA; (2) Interventions: The intervention group received the multimodal analgesia regimen and intravenous acetaminophen for postoperative pain management; (3) Comparisons: The control group received multimodal analgesia regimen without intravenous acetaminophen; (4) Outcomes: Pain scores at postoperative POD 1–3, opioid consumption, length of stay and postoperative complications such as opioid-related adverse effects; (5) Study design: randomized controlled trials (RCTs) and non-RCT were regarded as eligible in the study. Articles would be excluded from the present meta-analysis for case reports, conference abstract or review articles. Two reviewers independently scanned the abstracts of the potential articles identified by the above searches. Subsequently, the full text of the studies that met the inclusion criteria was screened, and a final decision was made. A senior author had the final decision in any case of disagreement regarding which studies to include.

2.3. Date extraction

The included studies were examined by two investigators and key data were extracted including first author name, samples size, published year, baseline characteristics, intervention of each groups and other outcome parameters. The primary outcomes were pain scores and opioid consumption at POD 1–3. The secondary outcomes were length of stay and opioid-related adverse effects.

2.4. Assessment of methodological quality

A quality assessment of each RCT was performed by two reviewers based on the Cochrane Handbook for Systematic Reviews of Interventions. Disagreement was resolved by consulting a senior reviewer. We created a “risk of bias" table that included the following elements: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting and other bias. Methodological Index for Non-Randomized Studies (MINORS) scale, which assigns scores ranging from 0 to 24, was used to assess the methodological quality of the included studies in the present meta-analysis which was based on the twelve main items.

The quality of the evidence for the main outcomes in present meta-analysis were evaluated using the Recommendations Assessment, Development and Evaluation (GRADE) system including the following items: risk of bias, inconsistency, indirectness, imprecision and publication bias [13]. The recommendation level of evidence is classified into the following categories: (1) high, which means that further research is unlikely to change confidence in the effect estimate; (2) moderate, which means that further research is likely to significantly change confidence in the effect estimate but may change the estimate; (3) low, which means that further research is likely to significantly change confidence in the effect estimate and to change the estimate; and (4) very low, which means that any effect estimate is uncertain.

2.5. Data analysis and statistical methods

The data were pooled using Stata 12.0 (The Cochrane Collaboration, Oxford, UK). After extracting the data from the included studies, we exported the means, SDs and sample sizes of groups into Stata 12.0 to determine the heterogeneity. Statistical heterogeneity was assessed based on the P and I^2 values using the standard Chi-square test. When $I^2 \geq 50\%$ or $P < 0.1$, significant heterogeneity was indicated and a random-effects model was applied for the meta-analysis. Otherwise, a fixed-effects model was used. Dichotomous outcomes (i.e., complications) were expressed as risk differences (RDs) with 95% confidence intervals (CIs). For continuous outcomes (i.e., pain scores), weighted mean differences (WMDs) and 95% confidence intervals (CIs) were calculated.

3. Results

3.1. Search result

A total of 316 studies were identified through the initial search. By scanning the abstracts, 312 reports that did not meet inclusion criteria were excluded from the current meta-analysis. No gray studies were included. Finally, three RCTs [14–16] and one non-RCTs [17] which published between 2016 and 2017 were included in the present meta-analysis which contained 534 patients in acetaminophen groups and 331 patients in control groups.

3.2. Study characteristics

Only patients with end-stage joint osteoarthritis and prepared to undergo TJA were included in our study. The sample sizes ranged from 66 to 609 and average age ranged from 57 to 74. In these articles, the experimental groups received intravenous acetaminophen and the control groups received placebo or normal saline. The