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Review

The effect of pregabalin on acute postoperative pain in patients undergoing total knee arthroplasty: A meta-analysis

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HIGHLIGHTS

- We carried on a meta-analysis to identify the efficacy and safety of pain control of pregabalin versus placebo after a TKA.
- Six RCTs were included finally.
- Pregabalin has an analgesic and opioid-sparing effect in acute postoperative pain management.
- Administration pregabalin will decrease the rate of nausea and vomiting.

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ABSTRACT

Objective: The purpose of this systematic review and meta-analysis of randomised controlled trials (RCTs) was to evaluate the effect of pain control of pregabalin versus placebo after a total knee arthroplasty (TKA).

Methods: The electronic databases: Medline, Embase, PubMed, CENTRAL (Cochrane Controlled Trials Register), Web of Science and Google were searched from inception to February 2016. This systematic review and meta-analysis were performed according to the PRISMA statement criteria. The primary endpoint was the visual analogue scale (VAS) after a TKA with rest or mobilization at 24 h and 48 h, which represents the effect of pain control after TKA. The cumulative morphine consumption is also assessed to the morphine-sparing effect. The complications of nausea, vomiting, dizziness and sedation were also compiled to assess the safety of pregabalin. Software Stata 12.0 was used for the meta-analysis. After testing for publication bias and heterogeneity across studies, data were aggregated for random-effects modelling when necessary.

Results: Six clinical trials with 769 patients were used for the meta-analysis. The meta-analysis indicated that pregabalin can decrease the VAS with rest at 24 h (MD = −8.14; 95% CI -12.57 to −3.71; P < 0.001) and 48 h (MD = −7.34; 95% CI -11.65 to −3.02; P < 0.001). Pregabalin can decrease the VAS with mobilization at 24 h (MD = −6.56; 95% CI -10.45 to −2.66; P = 0.001) and 48 h (MD = −9.62; 95% CI -12.80 to −6.44; P < 0.001). The results indicated that perioperative pregabalin can decrease the cumulative morphine consumption at 24 h (SMD = −0.97; 95% CI -1.17 to −0.78; P < 0.001) and 48 h (MD = −2.23; 95% CI -2.48 to −1.97; P < 0.001). Moreover, pregabalin can decrease the occurrence of nausea and vomiting but increase the occurrence of dizziness and sedation.

Conclusion: Based on the current meta-analysis, pregabalin has an analgesic and opioid-sparing effect in acute postoperative pain management without increasing the rate of nausea, vomiting.

1. Introduction

Total knee arthroplasty (TKA) is now one of the most common orthopaedic surgeries and its main indication is for patients with osteoarthritis (OA) or rheumatic arthritis (RA) of the knee; however, TKA has always been associated with a moderate to severe pain after operation [1]. Pang et al. [2] reported that the pain occurrence in TKA is more painful than other orthopaedic surgeries, including total hip arthroplasty. An effective pain control after TKA is important since adequate pain control after TKA allows patients to achieve accelerated recovery and decrease the economic cost [3].

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In recent decades, multiple anaesthesia including morphine has been used to control pain after TKA in order to reduce the side effects of morphine-related complications such as nausea, vomiting and constipation [4]. Methods include regional anaesthesia [5], peri-articular infiltration anaesthesia [6], intra-articular infiltration anaesthesia [7] and anaesthesia with non-steroid drugs such as pregabalin [8].

Perioperative multiple anaesthesia including oral pregabalin may reduce the pain and reduce the morphine-related complications after TKA since the pregabalin can bind to the α2δ subunit of the voltage-gated calcium channel to reduce the calcium influx into the terminal of presynaptic and thus can relieve the sensitisation of peripheral nociceptive nerve terminals and central neurons [9]. However, the effect of pregabalin in reducing the visual analogue scale (VAS) and cumulative morphine consumption after TKA is controversial [10–12]. Base on the current studies, a definite conclusion cannot be drawn, so a meta-analysis was necessary to analyse the effectiveness and safety of pregabalin in TKA.

2. Materials and methods

2.1. Search strategy

The electronic databases Medline, Embase, PubMed, CENTRAL (Cochrane Controlled Trials Register), Web of Science and Google were searched from inception to February 2016. The search strategies were performed based on medical subject headings and the appropriate corresponding terms including pregabalin, total knee arthroplasty, total knee replacement, TKA and TKR. In addition, the reference lists of all of the full-text literature were reviewed to identify any initially omitted studies and no restriction was made on the language of the publication. Two reviewers (Jian Dong, Wenmin Li) independently searched and screened the literature. Any disagreements were resolved by the third reviewer (Yuling Wang) and an examination of the full text to seek the final answer. Since this is a meta-analysis, no ethics committee or institutional review board were required to approve the study.

2.2. Inclusion criteria and study selection

Inclusion criteria are as follows: (1) to have taken part in RCTs; (2) to have undergone a primary TKA; (3) to have received interventions, including pregabalin with a control (placebo or nothing); and (4) to have reported outcomes, including postoperative VAS pain with rest or mobilization at 24 h and 48 h, cumulative morphine consumption for 24 h and 48 h, the incidence of nausea, vomiting, dizziness and sedation. At least one of the outcomes mentioned above had to be included and no language restriction was imposed. Studies on cadaver or artificial models were not take into consideration. Non-RCTs, letters, comments, editorials, practice guidelines and other studies with insufficient data were also excluded for this meta-analysis.

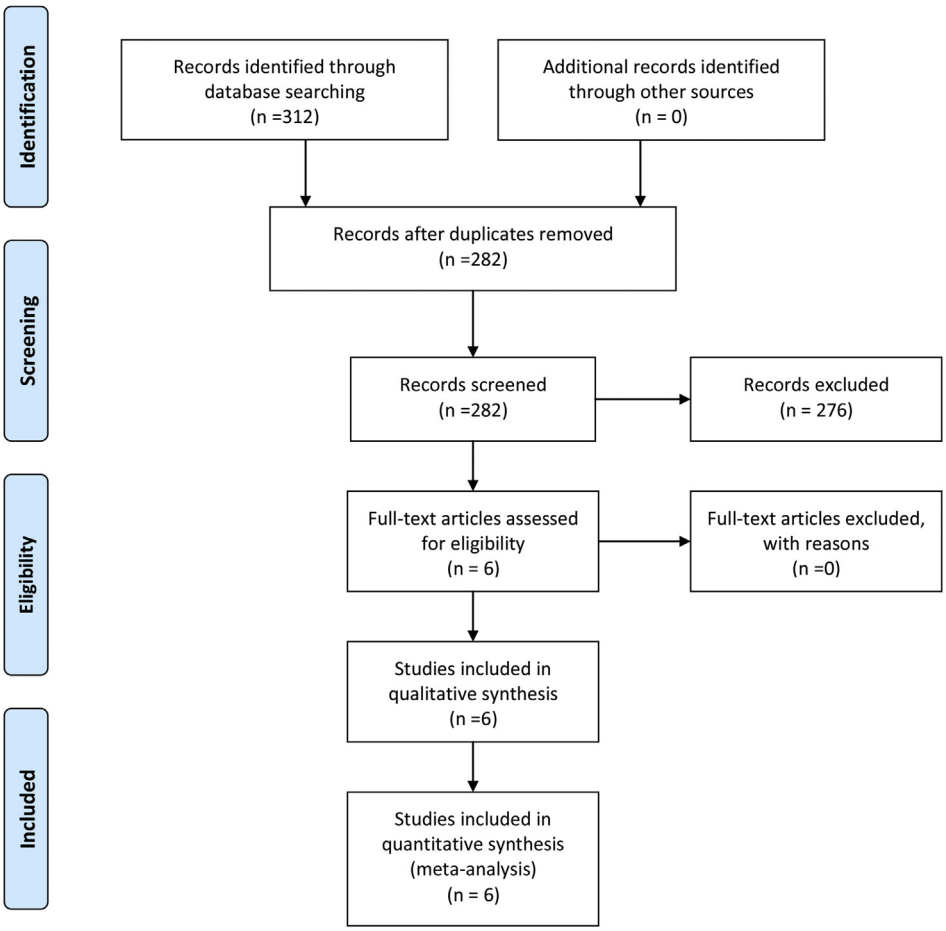

Fig. 1. The flow diagram of the included studies.