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Is gabapentin effective and safe in open hysterectomy? A PRISMA compliant meta-analysis of randomized controlled trials

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ABSTRACT

Background: Pain management after open hysterectomy has been investigated for years. Owing to the effect of significant analgesic, gabapentin was often administrated for pre-emptive analgesia. However, the relationship between gabapentin and postoperative pain after open hysterectomy is still controversial. This meta-analysis was applied to assess the efficacy of pre-emptive use of gabapentin in open hysterectomy.

Methods: This meta-analysis of randomized controlled trials (RCTs) was performed to compare the use of gabapentin with placebo in open hysterectomy regarding (1) the mean difference (MD) of postoperative opioid requirements; (2) the changes of visual analogue scale (VAS) scores in two groups; and (3) incidence rate of adverse effects. Systematic searches of all related literatures was conducted using the following databases: MEDLINE, EMBASE, ClinicalTrials.gov and Web of Science. Only randomized controlled trials (RCTs) for open hysterectomy were included. The MD of postoperative opioid requirements and VAS scores, relative risk (RR) of incidence rate of adverse effects in the gabapentin group *versus* placebo group were extracted throughout the study.

Results: Fourteen trials were included in this meta-analysis. The total opioid consumption at 24 h was a less in gabapentin group. (MD = −11.61, 95% CI: −16.71 to −6.51, $P = 0.00$) The visual analogue scale (VAS) score at 4, 12 and 24 h were less in the gabapentin group. (MD = −16.83, 95% CI: −22.88 to −10.77, $P = 0.00$), (MD = −17.45, 95% CI: −21.83 to −13.08, $P = 0.00$), (MD = −9.83, 95% CI: −13.31 to −6.35, $P = 0.00$) The incidence rate of vomiting and nausea were significantly less in gabapentin groups. (RR 0.13, 95% CI 0.45 to 0.73, $P = 0.00$), (RR 0.67, 95% CI 0.49 to 0.93, $P = 0.02$). Compared with placebo, gabapentin achieved higher patient satisfaction. (MD = 20.43, 95% CI: 12.42 to 28.44, $P < 0.00$).

Conclusion: This meta-analysis suggested that the employment of gabapentin was efficacious in reduction of postoperative opioid consumption, VAS score and some side effects after open hysterectomy.

Contents

Abbreviations: VAS, Visual analogue scale scores; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCTs, Randomized controlled trials; MD, Mean difference; CI, Confidence intervals; RR, Relative risk.

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1. Background

Open hysterectomy is a common operation in modern medicine, but it is particularly prone to postoperative pain with large surgical incision and relatively long operation times [1]. Trying to improve the surgical techniques and perioperative period management may be a good approach to ease pain, but the majority of patients undergoing open hysterectomy still experience intense pain after the operation. Poor analgesia may have negative effects on the cardiovascular and cerebrovascular system, and further affect the final operation outcomes [2]. Under such circumstances, how to reduce postoperative pain is an urgent issue for many surgeons, the pre-emptive analgesia seems provide a feasible way in clinical practice [3].

The pain management in open hysterectomy is frequently directed to reduce the pain score, the narcotic requirement as well as adverse effect by multimodal analgesia techniques [4]. Even the multimodal approach had been provided, the persistent postoperative pain may also occur in many patients [5,6]. Considering the various adverse effects of opioid analgesics, the use of some non-opioid agent, such as gabapentin, is often recommended [7]. As a third-generation anticonvulsant agents, gabapentin can selectively affects the nociceptive process by inhibiting calcium influx *via* voltage-gated calcium channels [8]. It not only played a key role in assist to alleviating pain, but also had less side effects [9].

During the past years, the roles of gabapentin in analgesia have been evaluated by a few of studies [10–13]. Although some conclusions had been made, rare meta-analysis was made for the assessment of pre-emptive use of gabapentin alone in open hysterectomy. Trying to reveal the effect of the gabapentin in reduction of opioid consumption and visual analogue scale (VAS) score from randomized controlled trials (RCTs) is our major purpose. Further explorations of the adverse effects of gabapentin are also discussed as well.

2. Methods

This meta-analysis followed the guidelines of the PRISMA statement [14]. Because this was a meta-analysis of former published literatures, ethical approval was not required. All literatures identified from different electronic-based search, including MEDLINE (1966–Present), EMBASE (1966–Present), and Cochrane Central Register of Controlled Trials. The following keywords combined with MeSH terms, and their combinations were used to maximize the search accuracy: “pain management, postoperative pain, open hysterectomy and gabapentin.” The search was limited to randomized controlled trials (RCTs) in humans up to June 2017. PRISMA Flow Diagram (Fig. 1).

2.1. Inclusion criteria

Literatures were regarded eligible for inclusion if the following criteria were fulfilled: Types of studies: RCTs with placebo, report in English. Population: Patients with open hysterectomy, general anesthesia only. Types of interventions: gabapentin and placebo. Types of outcomes: at least one of the following items was reported: cumulative consumption of morphine at 24 h; visual analogue scale (VAS) score, and adverse effects.

2.2. Exclusive criteria

Patients were excluded from this work if they had bone neoplasms, serious osteoporosis, infection, metal sensitivity, or mental diseases.

2.3. Selection criteria

An eligibility assessment was carried out independently by two reviewers. Disagreements between reviewers were settled by discussion; if there was no consensus could be made, the third reviewer made the final decision as the adjudicator. The risk of bias was assessed according the Cochrane collaboration's tool, and the quality of the RCTs was evaluated by funnel plots [15].

2.4. Data extraction

Data from the included studies were pooled by two authors independently. The following data were extracted and analysed: first author's name; publication year, number of patients, type of open hysterectomy, gabapentin regimen and dose, types and methods of narcotics, pain assessment methods and adverse reactions. In studies in which data were unclear or incomplete, attempts were made to contact the authors for the missing data.

2.5. Statistical analysis

RevMan5.3 was conducted to analyse the pooled data (The Cochrane Collaboration, Oxford, United Kingdom). By the usage of chi-square test, heterogeneity was evaluated by the value of P and I^2. $P > 0.10$ and $I^2 < 50\%$ were defined as having no significant heterogeneity. Then, a fixed-effects model was applied for data analysis. A random-effects model was used when the significant heterogeneity was found. For continuous outcomes, such as VAS scores and narcotic consumption, the mean difference (MD) and 95% confidence intervals (CIs) were pooled to express the results. Relative risk with 95% CIs were calculated