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Review

Efficacy and safety of single-dose local infiltration of analgesia in total knee arthroplasty: A meta-analysis of randomized controlled trials

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ABSTRACT

Purpose: To examine the efficacy and safety of single-dose local infiltration of analgesia (LIA) for post-operative pain relief in total knee arthroplasty (TKA) patients.
Methods: A systematic electronic literature search (up to Aug 2013) was conducted to identify the RCTs that address the efficacy and safety of single-dose LIA in the pain management after TKA. Subgroup analysis was conducted to determine changes of visual analog score (VAS) values at six different postoperative time points. Weighted mean differences or relative risks with accompanying 95% confidence intervals were calculated and pooled using a random effect model.
Results: Eighteen trials involving 1858 TKA patients met the inclusion criteria. The trials were liable to medium risk of bias. The VAS values at postoperative 2 h, 4 h, 6 h, 12 h, 24 h, and 48 h per patient were significantly lower in the LIA group than in the placebo group, and the former group also had less morphine consumption and better early functional recovery including range of motion, time to straight leg raise and 90° knee flexion than the latter group. No significant difference in length of hospital stay or side effects was detected between the two groups.
Conclusions: The current evidence shows that the use of single-dose LIA is effective for postoperative pain management in TKA patients, with satisfactory short-term safety. More high-quality RCTs with long-term follow-ups are required for examining the long-term safety of single-dose LIA.
Level of evidence: I, II

Contents

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1. Introduction

Total knee arthroplasty (TKA) is associated with considerable post-operative pain which hinders the ability to participate in early rehabilitation, affects the activity level and satisfaction, and increases the risk of postoperative complications (delay in strength recovery, prolonged knee stiffness, and chronic anterior knee pain) [1]. Therefore, aggressive pain control during the early postoperative period is essential for TKA convalescence [2]. The use of either general anesthesia combined with a peripheral nerve block or spinal anesthesia to provide both operative anesthesia and post-operative pain relief following TKA was supported in a recent systematic review [3], but it can be associated with severe complications such as postoperative headache, intraoperative hypotension, and risk of spinal infection [4,5]. In addition, narcotics routinely administered for pain control may cause nausea, vomiting, somnolence, respiratory depression, decreased gut motility, and urinary retention.

As a measure to reduce pain and severity of side effects, the local infiltration of analgesia (LIA) into soft tissues around the surgical field has been applied in clinical practice [6]. A number of studies have assessed the effectiveness of LIA, especially single-dose LIA, because of the simplicity in concept on post-operative pain relief in patients undergoing TKA. Despite positive reports in some randomized controlled trials (RCTs) and a growing body of evidence [6–8] to support the use of single-dose LIA in pain relief after knee surgery, a number of studies have shown that single-dose LIA during TKA has been of only equivocal benefit [9,10]. Meanwhile, there remain conflicting views on post-operative hospitalization and recovery [8]. Moreover, the safety of single-dose LIA has been questioned. Although simplicity and apparent safety of single-dose LIA were ascertained by some reports, these advantages have not been assessed in detail in large-scale clinical or pharmacokinetic studies [6]. Importantly, the insufficient durations of the follow-ups in these reports do not rule out the possibility of potential narcotic-related side effects and wound complications.

Although good effectiveness of the single infiltration technique was observed in some studies, others did not observe any additional benefit beyond 4 h [10] or up to 24 h only [11] with a single-dose intra-articular injection. Since the pain involved in TKA usually peaks at 3 to 6 h after surgery and continues for the following 72 h [12,13], those who doubt the active duration of single LIA have used continuous intra-articular infusions following TKA to ensure a long enough analgesic effect. As this technique involves catheter placement by the surgeon at the end of the operation under aseptic conditions and the use of bacterial filters and closed infusion systems, it is technically demanding and time-consuming and may be associated with an array of side effects. By contrast, single-dose LIA is still common in clinical practice and reported to be inexpensive and relatively easy to perform and have fewer side effects. We speculated that if the effect of single-dose LIA could last long enough for the pain relief and the potential complications of continuous LIA could be avoided, the single-dose LIA would be really advantageous just because of its sufficient efficacy, simplicity and safety. However, this speculation needs to be clarified by the evidence available to date.

Therefore, this paper intended to assess the effectiveness and safety of single-dose LIA after TKA by a meta-analysis of RCTs that compared single-dose LIA with placebo (or no intervention) in the pain management after TKA, including subgroup analysis of VAS changes at six different postoperative time points to determine the active duration of single LIA. We hope that the findings may improve our understanding of the single-dose LIA for pain relief after TKA.

2. Methods

2.1. Search strategy

PubMed, Cochrane Library, EMBASE, BIOSIS and Ovid databases (up to Aug 2013) were searched to identify RCTs exploring the single-dose

Table 1
Modified Jadad scale with eight items.

Items assessed	Response	Score
Was the study described as randomized?	Yes	+1
	No	0
Was the method of randomization appropriate?	Yes	+1
	No	−1
	Not described	0
Was the study described as blinded?[a]	Yes	+1
	No	0
Was the method of blinding appropriate?	Yes	+1
	No	−1
	Not described	0
Was there a description of withdrawals and dropouts?	Yes	+1
	No	0
Was there a clear description of the inclusion/exclusion criteria?	Yes	+1
	No	0
Was the method used to assess adverse effects described?	Yes	+1
	No	0
Was the method of statistical analysis described?	Yes	+1
	No	0

[a] Double-blind RCT obtains 1 score; single-blind RCT obtains 0.5 score.

Table 2
Selection process for randomized controlled trials included in the meta-analysis.