Accepted Manuscript

Comparison of intrathecal and local infiltration analgesia by morphine for pain management in total knee and hip arthroplasty: A meta-analysis of randomised controlled trial

Xu-feng Jia, M.D., Yong Ji, M.D., Guang-ping Huang, M.D., Yu Zhou, M.D., Miao Long, M.D.

PII: S1743-9191(17)30184-X
DOI: 10.1016/j.ijsu.2017.02.060
Reference: IJSU 3600

To appear in: International Journal of Surgery

Received Date: 24 December 2016
Revised Date: 15 February 2017
Accepted Date: 17 February 2017


This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
Comparison of intrathecal and local infiltration analgesia by morphine for pain management in total knee and hip arthroplasty: a meta-analysis of randomised controlled trial

Xu-feng Jia, M.D., first author, orthopedics department, Jianyang People's Hospital, Sichuan, R.P.China, 641400;
Yong-Ji, M.D., orthopedics department, Jianyang People's Hospital, Sichuan, R.P.China, 641400;
Guang-ping Huang, M.D., corresponding author, M.D., orthopedics department, Jianyang People's Hospital, Sichuan, R.P.China, 641400;
Email: 1941842317@qq.com; Tel:086-18622273319
Yu-Zhou, M.D., orthopedics department, Jianyang People's Hospital, Sichuan, R.P.China, 641400;
Miao-Long, M.D., orthopedics department, Jianyang People's Hospital, Sichuan, R.P.China, 641400;

Acknowledgements: Thanks Yong Ji for language edit. No funding was received.

Funding: Health and Family Planning Commission of Chengdu (no.2016035)
Comparison of intrathecal and local infiltration analgesia by morphine for pain management in total knee and hip arthroplasty: a meta-analysis of randomised controlled trial

Abstract

Objective: We performed a meta-analysis from randomized controlled trials to evaluate the efficiency and safety between local infiltration analgesia and intrathecal morphine for pain control in total knee and hip arthroplasty.


Results: Four randomized controlled trials (RCTs) involving 242 patients met the inclusion criteria. The meta-analysis showed that there were significant differences in terms of postoperative pain scores at 24 hours during rest (P=0.008) and mobilization (P=0.049) following total knee and hip arthroplasty. Significant difference was found regarding the incidence of nausea (P=0.030), vomiting (P=0.005), and pruritus (P=0.000) between two groups. There was no significant difference between groups in terms of morphine equivalent consumption at postoperative 24 or 48 hours.

Conclusions: Local infiltration analgesia (LIA) provided superior analgesic effects within the first 24 hours compared to intrathecal morphine (ITM) following total knee and hip arthroplasty. There were fewer adverse effects in LIA. Doses of morphine consumption were similar in the two groups.

Key words: Intrathecal morphine, local infiltration analgesia, total knee and hip arthroplasty, meta-analysis
1. Introduction

Total knee arthroplasty (TKA) or total hip arthroplasty (THA) are considered effective procedures for the treatment of the degenerative arthritis, rheumatoid arthritis and traumatic injuries such as displaced femoral neck fractures [1]. However, patients often suffer moderate to severe postoperative pain [2]. Appropriate postoperative pain control is crucial for early ambulation, and better functional outcomes were usually achieved following postoperative rehabilitation. Moreover, optimal pain management may decrease length of stay and the risk of adverse events, such as deep vein thrombosis (DVT) and pulmonary embolism (PE) [3]. Postoperative pain management for these procedures has been a topic of much debate for a few decades and remains controversial Various attempts have been made, including systemic opiates, local infiltration analgesia, femoral nerve block and patient-controlled analgesia with oral narcotics [4-6]. Although it has been proven effective for pain relief, consumption of additional opiates comes along with potential adverse side effects, such as nausea, vomiting, respiratory depression and urinary retention [7-9].

Local infiltration analgesia (LIA) has been promoted for a few decades and shows excellent outcomes for pain relief after total knee and hip arthroplasty [10,11]. A mixture comprised of a long-acting local anesthetic, a non-steroid anti-inflammatory drug and epinephrine is most commonly used. LIA is considered a promising method with few side effects and good prospects for early mobilization without the weakening of quadriceps muscle strength. Intrathecal morphine (ITM) is also an alternative simple method for postoperative analgesia. Previous studies have suggested ITM achieves satisfactory pain control [12-14], but potentially life-threatening-morphine-related side effects were also reported.

To the best of our knowledge, direct comparisons of LIA versus ITM for pain management in joint replacement surgery have seldom been reported, leaving the optimal analgesia method in question. Therefore, we performed a meta-analysis from randomized controlled trials to evaluate the efficiency and safety of local infiltration analgesia and intrathecal morphine for pain control in total knee and hip arthroplasty.
2. Methods

2.1 Search strategy

We systematically search electronic databases including Embase (1980 – 2016.7), Medline (1966 – 2016.7), PubMed (1966 – 2016.7), ScienceDirect (1985 – 2016.7), web of science (1950 – 2016.7) and Cochrane Library for potential relevant articles. Gray academic studies are also identified from the reference of included studies. No language was restricted. The following terms was considered as key words “Total knee replacement and arthroplasty”, “Total hip replacement or arthroplasty”, “local infiltration analgesia”, “intrathecal morphine” and ‘pain control’ were used in combination with Boolean operators “and” or “or”. The retrieval process is presented in Figure 1.

2.2 Inclusion and exclusion criteria

Studies were considered eligible if they met the following criteria: 1) Published clinical randomized control trials (RCTs); 2) Patients undergoing TKA or THA surgery, experiment group received local infiltration analgesia for postoperative analgesia and control group received intrathecal morphine; 3) Reported surgical outcome including postoperative pain scores at rest and mobilization, morphine equivalent consumption, length of stay and drug-related adverse effects including nausea, vomit and pruritus. Dosage and types of local infiltration anesthetics are not limited in our search proceed. Studies would be excluded from present meta-analysis for incomplete data, cases report, conference abstract or review articles.

2.3 Selection criteria

Two reviewers independently review the abstract of the potential studies. After an initial decision, full text of the studies that potentially met the inclusion criteria were reviewed and final decision was made. A senior reviewer is consult in case of disagreement.

2.4 Date extraction

A standard form for date extraction is printed for date extraction. Two reviewers independently extracted the relevant data from the included studies. Details of incomplete data of included articles are received by consulting corresponding author. Following data was extracted: First author names, published year, study design, comparable baseline, anesthesia methods, dosage
and type of anesthetic drug and intervening procedures. Outcome parameters included postoperative pain scores at different periods, the cumulative morphine equivalent consumption, length of stay, and drug-related adverse effects such as nausea, vomit and pruritus. Other relevant data was also extracted from individual studies.

2.5 Quality assessment
Quality assessment of included studies was performed by two reviewers independently. Modified Jadad score (10-points scale) which was based on Cochrane Handbook for Systematic Reviews of Interventions is used for assessment of RCTs. Studies which scores greater than four points was considered high quality. We conducted ‘risk of bias’” table including the following key points: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting and other bias. A consensus is reached through a discussion.

2.6 Data analysis and statistical methods
All calculation was carried out by Stata 11.0 (The Cochrane Collaboration, Oxford, United Kingdom). Statistical heterogeneity was assessed based on the value of P and I² using standard chi-square test. When I² > 50%, P<0.1 was considered to be significant heterogeneity, random-effect model was performed for meta-analysis. Otherwise, fixed-effect model was used. If possible, sensibility analysis is conducted to explore the origins of heterogeneity. The results of dichotomous outcomes were expressed as risk difference (RD) with a 95% confidence intervals (CIs). For continuous various outcomes, mean difference (MD) and standard mean difference (SMD) with a 95% confidence intervals (CIs) was applied for assessment.

3. Results
3.1 Search result
A total of 210 studies were preliminarily reviewed. By reading the title and abstracts, 206 reports were excluded from current meta-analysis followed inclusion criteria. No gray reference was obtained. Finally 4 RCTs [10,15-17] which had been published between 2011 and 2013 were enrolled in present meta-analysis and includes 122 participates in the LIA groups and 120 patients in the ITM groups.
3.2 Risk of bias assessment

Demographic characteristics, the details about the included studies are summarized in Table 1. Modified Jadad score which was based on Cochrane Handbook for Systematic Reviews of Interventions is used for assessment of RCTs (Table 2). All RCTs provide clear inclusion and exclusion criteria and suggest a methodology of randomization, three [15-17] of which described that randomization algorithm was generated from computer. Two of them [10, 17] stated allocate concealment was achieved by sealed envelope. Double blinding was provided in two RCTs [16, 17] and others was single blind. Three of them had attempted to blind assessors [10, 16, 17]. All RCTs demonstrated complete outcome data. None of them performed intent-to-treatment analysis thus a potential risk for type II statistical error would exist.

3.3 Study characteristics

The sample size of the included studies ranged from 50 to 78. All of them compared efficiency and safety between local infiltration analgesia and intrathecal morphine for pain control in TKA or THA. Experimental groups received LIA, while control groups received ITM. There is variation dosage and type of drugs in LIA groups. All patients received spinal anesthesia. Three [10, 16, 17] studies reported that surgical procedure was performed by same surgeons. All articles reported that preoperative oral medication was used for pain prevention and patient-controlled analgesia technique was performed for concomitant pain management. Salmi [10] indicated that cementless prosthesis was used and Tammachote [17] applied cement prosthesis. Others did not provide this information. Only Tammachote conducted sample size analysis. Details of the antithrombotic therapy are presented in Table 1. All of them suggest the outcomes for at least 95% of the patients. The follow-up period ranged from 7 days to 3 months.

3.4 Outcomes for meta-analysis

3.4.1 Postoperative pain scores at 24 hours during rest

Four studies [10, 15-17] reported pain scores at 24 hours during rest following joint
arthroplasty surgery. There was significant heterogeneity ($\chi^2 = 24.54$, df = 3, $I^2 = 87.8\%$, $P = 0.000$); therefore, a random-effects model was used. The result of meta-analysis showed that pain scores at 24 hours during rest was significantly higher in ITM group compared the LIA groups (SMD = -1.065, 95% CI: -1.858 to -0.272, $P = 0.008$; Fig 2).

3.4.2 Postoperative pain scores at 48 hours during rest

Four studies [10, 15-17] reported postoperative pain scores at 48 hours during rest following joint arthroplasty surgery. Statistical heterogeneity was observed in present meta-analysis ($\chi^2 = 26.46$, df = 3, $I^2 = 88.7\%$, $P = 0.000$); therefore, a random-effects model was applied. We found that there was no significant difference between the LIA and ITM groups regarding the postoperative pain scores at 48 hours during rest (SMD = -0.295, 95% CI: -1.077 to 0.488, $P = 0.461$; Fig 3).

3.4.3 Postoperative pain scores at 24 hours during mobilization

Three reports showed postoperative pain scores at 24 hours during mobilization [10, 15, 16]. There was significant heterogeneity and a random-effects model was performed ($\chi^2 = 8.3$, df = 2, $I^2 = 75.9\%$, $P = 0.016$). Current meta-analysis indicated that pain scores at 24 hours during mobilization was significantly higher in ITM group compared the LIA groups (SMD = -0.620, 95% CI: -1.236 to -0.004, $P = 0.049$; Fig 4).

3.4.4 Postoperative pain scores at 48 hours during mobilization

Three studies [10, 15, 16] reported morphine equivalent consumption at 48 hours during mobilization following joint arthroplasty surgery. There was significant heterogeneity ($\chi^2 = 14.02$, df = 2, $I^2 = 85.7\%$, $P = 0.001$); therefore, a random-effects model was used. Present meta-analysis indicated that there was no significant difference between the LIA and ITM groups regarding the morphine equivalent consumption at 48 hours during mobilization (SMD = -0.553, 95% CI: -1.358 to 0.252, $P = 0.178$; Fig 5).

3.4.5 Morphine equivalent consumption at postoperative 24 hours

Morphine equivalent consumption at postoperative 24 hours was presented in four studies [10,
15-17] following joint arthroplasty surgery. There was significant heterogeneity ($\chi^2 = 20.46$, df = 3, $I^2 = 85.3\%$, $P < 0.0001$) and a random-effects model was used. Current meta-analysis showed that there was no significant difference between the LIA and ITM groups in terms of morphine equivalent consumption at postoperative 24 hours (SMD = -0.186, 95% CI: -0.866 to 0.495, $P = 0.592$; Fig 6).

### 3.4.6 Morphine equivalent consumption at postoperative 48 hours

Four studies [10, 15-17] provided morphine equivalent consumption at postoperative 48 hours following joint arthroplasty surgery. Significant heterogeneity was found ($\chi^2 = 23.12$, df = 3, $I^2 = 87.0\%$, $P = 0.00$), therefore a random-effects model was used. Meta-analysis revealed that there was no significant difference between the LIA and ITM groups in terms of morphine equivalent consumption at postoperative 48 hours (SMD = -0.555, 95% CI: -1.289 to 0.180, $P = 0.139$; Fig 7).

### 3.4.7 Length of stay

Three studies [10, 15, 16] showed the data of length of stay. No significant difference was identified ($\chi^2 = 0.03$, df = 2, $I^2 = 0\%$, $P = 0.985$) so that a fixed-effects model was used. The pooled results showed there was no significant difference between groups regarding the length of stay (SMD = -0.016, 95% CI: -0.304 to 0.272, $P = 0.914$; Fig 8).

### 3.4.8 Nausea

Four studies [10, 15-17] provided the incidence of nausea in treatment groups [10-12]. No significant heterogeneity was found in the meta-analysis and a fixed-effect model was applied ($\chi^2 = 0.72$, df = 3, $I^2 = 0\%$, $P = 0.868$). The pooled results showed the incidence of nausea was significant higher in ITM group compared the LIA groups (RD = -0.103, 95% CI: -0.197 to -0.010, $P = 0.030$; Fig 9).

### 3.2.9 Vomiting

Four studies [10, 15-17] reported the incidence of vomiting [11, 13, 15]. No significant heterogeneity was shown in pooled results, therefore a fixed-effects model was used ($\chi^2 = 2.17$, df
$= 3, I^2 =0\%$, $P=0.538$). Current meta-analysis showed the incidence of vomiting was significant higher in ITM group compared the LIA groups (RD = -0.126, 95% CI: -0.215 to -0.037, $P =0.005$; Fig 10).

### 3.2.10 Pruritus

Four studies [10, 15-17] provided the incidence of pruritus. We found no statistical heterogeneity and a fixed-effects model was applied ($\chi^2 = 0.78$, df = 3, $I^2 =0\%$, $P=0.855$). Present meta-analysis showed the incidence of pruritus was significant higher in ITM group compared the LIA groups (RD = -0.153, 95% CI: -0.231 to -0.074, $P =0.000$; Fig 11).

### 4. Discussion

To our knowledge, this is the initial systemic review and meta-analysis from randomized controlled trials to compare the effectiveness and safety between local infiltration analgesia and intrathecal morphine for pain control in joint arthroplasty surgery. The most important finding of the present meta-analysis was that local infiltration analgesia could significantly decrease the pain scores postoperative 24 hours during rest or mobilization. Furthermore, there is a decreased risk of nausea, vomit and pruritus in local infiltration analgesia groups. No significant difference was identified in term of morphine equivalent consumption.

With the aging population, the incidence of osteoarthritis of knee and hip trends to raise, joint replacement surgery is a popular treatment. However, pain suffering that patients faced can be challengeable. A consensus has been reached that early rehabilitation exercise was crucial for functional recovery and a decreased risk for thrombotic events such as deep vein thrombosis (DVT) and pulmonary embolism (PE). It is widely accepted that inappropriate pain control following joint replacement surgery would cause pathological response that influenced postoperative rehabilitation and increased morbidity [18]. Postoperative pain management is an interesting topic for major orthopedic surgery. Multiple strategies has been introduced to minimize postoperative pain.

Periarticular administration has been applied more than 10 years and was first introduced by Bianconi [19]. Since then, LIA was widely used especially in lower limb operation due to ease of injection and lack of motor block which contributes to early mobilization [20,21]. A single
application of bupivacaine and ropivacaine or a mixture was commonly used. There has not reached a consensus regarding the optimal design of the LIA technique or drug mixture. Previous fundamental research has showed periarticular injection could minimize the central response to pain and relieve neuropathic pain [22]. Recently, studies which supports the effectiveness and safety of LIA in major orthopedics surgery has been published. No adverse effects were observed and plasma concentration of anaesthetics below toxic range. However, half-life period of most anaesthetic drugs are no more than 3 hours, therefore the analgesic efficacy is limited [19]. Furthermore, there was a lack of evidence as regards studies comparing LIA with other analgesia technique.

Intrathecal morphine (ITM) is an alternative simple method for pain control, well-established in clinical practice and providing long acting analgesia [12-14]. Previous meta-analysis suggested that intrathecal morphine carried similar postoperative analgesic efficiency compared to femoral nerve block in total knee arthroplasty [23,24]. However, ITM may also be associated with negative side-effects such as nausea, vomiting, urinary retention and respiratory depression. As a result, monitoring systems were at times required, decreasing patients’ satisfaction and increasing treatment costs. There have been numerous efforts to decrease the adverse effects and length of stay by reducing the morphine consumption. Dose-related trials showed that it was safe and effective under low doses of IT morphine (100-300 µg) with additional patient-controlled-analgesia (PCA) opioids in joint replacement surgery [14]. Some reports showed that there was a balance between analgesic efficiency and the profile of side effects by administration of 100µg morphine in TKA [13]. Four included studies provided the data of pain score during rest and mobilization within 24-48 hours after TKA. The present meta-analysis showed that both the rest and mobilization pain score in TIM groups were significantly higher than that in LIA groups in the first 24 hours. No significant difference was found in the second 24 hours. Traditionally, anesthetist was considered to responsible for perioperative analgesia. According to our viewpoint, we can see that surgeon should be also responsible for analgesia following surgical operation. To achieve better analgesic effect, it would depend on the development of multi-disciplinary. This is an important finding of the present meta-analysis.

Opioids, including oral and patient-controlled-analgesia (PCA) administration were usually performed as concomitant postoperative pain management. The consumption of morphine
equivalents is considered as an objective way to measure pain. Besides the side effects above, drug dependence is also an important issue that should be noted. To minimize the opioids consumption could achieve potential better physical outcome [5]. A similar outcome of morphine equivalents consumption has been observed between LIA and ITM groups within postoperative 24 and 48 hours following total joint arthroplasty.

Postoperative pain would result in additional morphine consumption would lead to a long-time bedridden which increased the risk of rehabilitation delay and occurrence of thrombotic events. Multiple factors would influence length of stay following total knee and hip arthroplasty, for instance, body mass index, age, American Society of Anesthesiologists status and postoperative complications [25]. Three studies reported the length of stay between groups and no statistical significance was identified in the length of hospital stay between the treatment groups from present meta-analysis.

Substantial reports have been demonstrated that side effects were frequently associated with intravenous or intrathecal morphine. Current meta-analysis showed the incidence of nausea, vomit and pruritus was significantly higher in ITM groups. We have not performed a dose related exploration because of the small number of included studies. Large sample size and high quality RCTs are needed to further explore the optimal dose of morphine which can balance the analgesic efficacy and side effects. Long-term follow up is also required to confirm the safety of target drugs.

Limitations of current meta-analysis should be noted. (1) Only four studied were included in present meta-analysis, though all of them are recently published RCTs, the sample size are relatively small; (2) Range of motion is a key parameter for postoperative functional outcome. Due to the insufficiency of relevant data, we fail to perform a meta-analysis. (3) Dose of anesthetics are varied and concomitant pain management regime differs from each other, which may influence the results of the meta-analysis; (4) The duration of follow up is relatively short which leads to underestimating complications. (5) Publication bias in present meta-analysis may influenced the results.

Despite the limitations above, this is the first meta-analysis from recently published RCTs to evaluate the effectiveness and safety of intrathecal morphine and local infiltration for pain control in total knee and hip arthroplasty. Future research should focus on the combination of multiple
strategies to achieve satisfied analgesia and low risk of adverse effects.

5. Conclusion

Local infiltration provided superior analgesia effects within the first 24 hours compared intrathecal morphine following total knee and hip arthroplasty. There were fewer adverse effects in LIA groups. Doses of morphine consumption were similar in two groups.

Conflicts of interest: Each author certifies that he has no commercial associations that might pose a conflict of interest with the submitted article.

Reference


<table>
<thead>
<tr>
<th>Studies</th>
<th>Cases</th>
<th>Mean age (LIA/ITM)</th>
<th>Female patient (LIA/ITM)</th>
<th>Anesthesia</th>
<th>Drug dose of LIA</th>
<th>Surgical methods</th>
<th>Drug dose of ITM</th>
<th>IV prophylaxis</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essving 2011</td>
<td>25/25</td>
<td>71/71</td>
<td>16/15</td>
<td>spinal anesthesia</td>
<td>ropivacaine 400mg</td>
<td>TKA</td>
<td>morphine 0.1 mg</td>
<td>Dalteparin 5000 IU</td>
<td>3 months</td>
</tr>
<tr>
<td>Salmi 2012</td>
<td>29/28</td>
<td>65/66</td>
<td>19/17</td>
<td>spinal anesthesia</td>
<td>levobupivacaine 125 mg</td>
<td>THA</td>
<td>morphine 0.1 mg</td>
<td>Low molecular weight heparin, Enoxaparin 5000 IU</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Kuchalik 2013</td>
<td>39/39</td>
<td>67/66</td>
<td>18/16</td>
<td>spinal anesthesia</td>
<td>ropivacaine 300 mg</td>
<td>THA</td>
<td>morphine 0.1 mg</td>
<td>Dalteparin 5000 IU</td>
<td>7 days</td>
</tr>
<tr>
<td>Tammachote 2013</td>
<td>29/28</td>
<td>70/69</td>
<td>26/20</td>
<td>spinal anesthesia</td>
<td>bupivacaine 100mg</td>
<td>TKA</td>
<td>morphine 0.2 mg</td>
<td>NS</td>
<td>3 months</td>
</tr>
</tbody>
</table>

Table 1 Trials characteristics

FNB: Femoral nerve block, LB: Liposomal bupivacaine, ACB: Adductor canal block, IV: Intravenous, NS: not state
<table>
<thead>
<tr>
<th></th>
<th>Tammachote 2013</th>
<th>Salmi 2012</th>
<th>Kuchalka 2013</th>
<th>Essving 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
<tr>
<td>Other bias</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
<td>🟢</td>
</tr>
</tbody>
</table>
Fig. 1 Search results and the selection procedure
NOTE: Weights are from random effects analysis

Overall (I-squared = 87.8%, p = 0.000)

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmi (2012)</td>
<td>-2.01 (-2.70, -1.33)</td>
<td>29.43</td>
</tr>
<tr>
<td>Tammachote (2013)</td>
<td>-2.01 (-2.70, -1.33)</td>
<td>29.43</td>
</tr>
<tr>
<td>Kuchalik (2013)</td>
<td>-1.58 (-2.09, -1.07)</td>
<td>25.43</td>
</tr>
<tr>
<td>Essving (2011)</td>
<td>-0.35 (-0.88, 0.17)</td>
<td>25.42</td>
</tr>
<tr>
<td>ID</td>
<td>-1.07 (-1.86, -0.27)</td>
<td>25.57</td>
</tr>
</tbody>
</table>

Fig. 2 Forest plot diagram showing postoperative pain scores at 24 hours during rest
NOTE: Weights are from random effects analysis

Overall (I-squared = 88.7%, p = 0.000)

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmi (2012)</td>
<td>-0.29 (-1.08, 0.49)</td>
<td>25.06</td>
</tr>
<tr>
<td>Tammachote (2013)</td>
<td>0.57 (0.04, 1.10)</td>
<td>25.17</td>
</tr>
<tr>
<td>Kuchalik (2013)</td>
<td>-0.09 (-0.61, 0.43)</td>
<td>25.95</td>
</tr>
<tr>
<td>Essving (2011)</td>
<td>-0.13 (-0.58, 0.31)</td>
<td>23.82</td>
</tr>
<tr>
<td>Overall (Hedges' p &gt; 0.40)</td>
<td>-1.59 (-2.23, -0.95)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Fig. 3 Forest plot diagram showing postoperative pain scores at 48 hours during rest
NOTE: Weights are from random effects analysis

Overall  (I-squared = 75.9%, p = 0.016)

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essving (2011)</td>
<td>1.84 (0.58, 3.04)</td>
<td>0.36</td>
</tr>
<tr>
<td>Salmi (2012)</td>
<td>0.06 (-0.58, 0.46)</td>
<td>0.27</td>
</tr>
<tr>
<td>Kuchalik (2013)</td>
<td>1.84 (0.58, 3.04)</td>
<td>0.25</td>
</tr>
<tr>
<td>Overall</td>
<td>0.06 (-0.58, 0.46)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Fig. 4 Forest plot diagram showing postoperative pain scores at 24 hours during mobilization
Fig. 5 Forest plot diagram showing postoperative pain scores at 48 hours during mobilization.
Fig. 6 Forest plot diagram showing morphine equivalent consumption at postoperative 24 hours

NOTE: Weights are from random-effects models.
**NOTE:** Weights are from random effects analysis. Overall (I-squared = 87.0%, p = 0.000)

<table>
<thead>
<tr>
<th>Study</th>
<th>ID</th>
<th>SMD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmi (2012)</td>
<td>-0.55 (-1.29, 0.18)</td>
<td>100.00%</td>
<td></td>
</tr>
<tr>
<td>Tammachote (2013)</td>
<td>0.21 (-0.31, 0.73)</td>
<td>25.16%</td>
<td></td>
</tr>
<tr>
<td>Kuchalik (2013)</td>
<td>-0.06 (-0.58, 0.46)</td>
<td>25.56%</td>
<td></td>
</tr>
<tr>
<td>Essving (2011)</td>
<td>-1.24 (-1.73, -0.76)</td>
<td>24.15%</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>-1.14 (-1.74, -0.54)</td>
<td>100.00%</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 7 Forest plot diagram showing morphine equivalent consumption at postoperative 48 hours**
Table 1: Forest plot diagram showing length of stay

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essving (2011)</td>
<td>0.00 (-0.44, 0.44)</td>
<td>100.00</td>
</tr>
<tr>
<td>Salmi (2012)</td>
<td>-0.02 (-0.30, 0.27)</td>
<td>27.02</td>
</tr>
<tr>
<td>Kuchalik (2013)</td>
<td>-0.06 (-0.61, 0.50)</td>
<td>30.81</td>
</tr>
<tr>
<td>Overall</td>
<td>-0.02 (-0.30, 0.27)</td>
<td>116.68</td>
</tr>
</tbody>
</table>

Fig. 8 Forest plot diagram showing length of stay
Fig. 9 Forest plot diagram showing incidence of nausea
Overall (I-squared = 0.0%, p = 0.538)

<table>
<thead>
<tr>
<th>Study</th>
<th>RD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essving (2011)</td>
<td>-0.13 (-0.22, -0.04)</td>
<td>21.88</td>
</tr>
<tr>
<td>Salmi (2012)</td>
<td>-0.18 (-0.33, -0.04)</td>
<td>20.41</td>
</tr>
<tr>
<td>Kuchalik (2013)</td>
<td>-0.15 (-0.34, 0.05)</td>
<td>30.22</td>
</tr>
<tr>
<td>Tammachote (2013)</td>
<td>-0.11 (-0.31, 0.10)</td>
<td>27.14</td>
</tr>
<tr>
<td>Creed (reported ≤ 0%, p ≤ 0.05)</td>
<td>-0.03 (-0.18, 0.12)</td>
<td>3.06</td>
</tr>
</tbody>
</table>

Fig. 10 Forest plot diagram showing incidence of vomiting
Fig. 11 Forest plot diagram showing incidence of pruritus
1. To evaluate the efficiency between local infiltration and intrathecal morphine for pain control in total knee and hip arthroplasty.

2. Only high quality studies were selected.

3. Local infiltration provided superior analgesia effects within the first 24 hours following total knee and hip arthroplasty.
International Journal of Surgery Author Disclosure Form

The following additional information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

Please state any conflicts of interest

Each author certifies that he has no commercial associations that might pose a conflict of interest with the submitted article.

Please state any sources of funding for your research

Health and Family Planning Commission of Chengdu (no.2016035)

Please state whether Ethical Approval was given, by whom and the relevant Judgement’s reference number

All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

Research Registration Unique Identifying Number (UIN)

Please enter the name of the registry and the unique identifying number of the study. You can register your research at http://www.researchregistry.com to obtain your UIN if you have not already registered your study. This is mandatory for human studies only.

reviewregistry187
If you are submitting an RCT, please state the trial registry number – ISRCTN

None

Author contribution
Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing. Others, who have contributed in other ways should be listed as contributors.

Xu-feng Jia and Guang-ping Huang: data collections, revised the manuscript and writing.
Yu Zhou and Miao Long: revised the manuscript and revised figure and data.
Yong Ji: language editing.

Guarantor
The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Guang-ping Huang