

**ORIGINAL****Postoperative nausea and vomiting following lower limb surgery : a comparison between single-injection intraarticular anesthesia and continuous epidural anesthesia**

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**Abstract :** Study Objective : the incidence of postoperative nausea and vomiting (PONV) following single-injection intraarticular anesthesia was compared to that following continuous epidural anesthesia. Design : Prospective, double-blind, randomized study. Setting : University-affiliated teaching hospital. Patients : Forty-eight patients finally participated in this study, and each group contained twenty-four patients. Interventions : Patients scheduled to undergo lower limb surgery under general anesthesia were randomly allocated into two groups, to receive either single-injection intraarticular or continuous epidural anesthesia for postoperative analgesia. Measurements : The incidence and severity of PONV, complete response rates (i.e., no vomiting or rescue antiemetic use), and pain scores were recorded 2, 24, and 48 h postoperatively. Main results : No significant differences between groups were observed in the incidence and severity of PONV, rescue antiemetic use, or complete response rate at any of the time points, but only the use of rescue analgesics was significantly less in continuous epidural anesthesia group during the 2-24h postoperative period (P=0.04). Conclusion : While the use of single-injection intraarticular anesthesia following lower limb surgery did not prevent PONV more than continuous epidural anesthesia in this study, the intraarticular technique still provides greater simplicity, safety, and cost-effectiveness. *J. Med. Invest.* 66:303-307, August, 2019

**Keywords :** PONV, intraarticular injections, epidural anesthesia

**INTRODUCTION**

Postoperative nausea and vomiting (PONV) is a distressing complication that can adversely affect patient recovery ; it frequently delays patient discharge from the post-anesthesia care unit and is the leading cause of unexpected hospital admission following planned ambulatory surgery (1). PONV is considered by many patients to be more distressing than postoperative pain (2). The general incidence of PONV is approximately 50% and in a subset of high-risk patients, PONV rates can be as high as 70% (3, 4, 5, 6). The four main risk factors of PONV include the female sex, a history of PONV or motion sickness, being a non-smoker, and the use of postoperative opioids (7).

Immediate postoperative pain following lower limb surgery can be severe and sometimes difficult to manage. Postoperative pain relief can be achieved using a variety of techniques, such as intravenous analgesia, epidural analgesia, peripheral nerve blocks, and local anesthetic infiltration. Effective treatment of postoperative pain and controlling side effects are important to enable early rehabilitation and hospital discharge following lower limb surgery (8). Continuous epidural analgesia has been shown to provide better pain relief than systemic opioid administration, but is associated with significant side effects, including nausea, urinary retention, hypotension, and delayed mobilization.

Furthermore, use of epidural analgesia may delay initiation of anticoagulant thromboprophylaxis due to the potential risk of epidural hematoma (8, 9). Local infiltration of analgesics combined with a single-injection or continuous infusion of local anesthetics at the surgical site has been reported as an alternative method for achieving effective postoperative pain relief (10, 11). Additionally, various combinations of drugs and local infiltration techniques (i.e., drug mixture, and the use of a wound catheter) have been evaluated (11,12,13). Among them, use of the intraarticular analgesic method has been shown to potentially reduce the occurrence of side effects while maintaining adequate pain relief and maximum muscle control. However, these studies have provided conflicting results owing to their differing study designs (14, 15, 16,17,18).

Since intraarticular anesthesia is administered by the surgeon intraoperatively and acts locally, we predicted that the rate of complications following intraarticular anesthesia may be less than that of other methods. Therefore, the purpose of this study was to compare the incidence of PONV following the use of intraarticular local anesthesia to that following continuous epidural anesthesia, after lower limb surgery.

**PATIENTS AND METHODS**

The current prospective study was approved by the Human Research Ethics Committee of Tokushima University Hospital and registered in the clinical trials database (UMIN000019978). Informed consent was obtained from all patients, and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

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Patients aged 30–85 years, with an American Society of Anesthesiologists (ASA) physical status of I–III, that were scheduled to undergo lower limb surgery (total knee arthroplasty, total hip arthroplasty, or rotational acetabular osteotomy) under general anesthesia were enrolled in this prospective study between November 2015 and July 2016. The patients' information, including their sex, history of PONV and/or motion sickness, and smoking status, was recorded. The exclusion criteria were as follows: an ASA physical status of IV, abnormal liver and/or renal function, or use of antiemetics.

No preanesthetic medication was administered. All patients were monitored using electrocardiography, noninvasive arterial blood pressure, pulse oximetry, and capnography. General anesthesia was induced with remifentanyl, propofol, and rocuronium to facilitate endotracheal intubation, and was maintained using volatile anesthetics (sevoflurane 1–2% and desflurane 4–6%) in oxygen, with a mixture of remifentanyl 0.1–0.5 µg/kg/min and fentanyl 0–100 µg. Incremental doses of rocuronium were administered, as necessary, for neuromuscular blockade, the effects of which were reversed using sugammadex 2 mg/kg upon surgery completion.

Prior to undergoing surgery, the patients were randomly allocated into one of two groups according to which postoperative analgesia method they were to receive: single-injection intraarticular anesthesia or continuous epidural anesthesia. The patients that received intraarticular anesthesia (i.e., Group I) were administered ropivacaine 200 mg and dexamethasone 6.6 mg, mixed with sterile normal saline to comprise a combined volume of 40 mL. Patients that were to receive continuous epidural anesthesia (i.e., Group E) underwent epidural catheter placement at either L2–3 or L3–4, followed by epidural administration of fentanyl 0.1 µg/kg/ml, total 10 µg/kg and local anesthetic (0.125% levobupivacaine, 2–4 ml/h); this was maintained for > 48 h. A rescue analgesic (diclofenac sodium 25 mg sup. or loxoprofen sodium 60 mg p.o.) was administered upon patient request for both groups. Intravenous metoclopramide (10 mg) was administered as a rescue antiemetic when necessary.

The incidence and severity of PONV, complete response rate, and the patients' pain scores (using a visual analog scale [VAS]) were recorded 2, 24, and 48 h after surgery by blinded observers. The severity of nausea was recorded using the following scale: 0, absence of nausea; 1, mild nausea; 2, moderate nausea; or 3, severe nausea. The complete response rate was defined as no occurrence of vomiting and no rescue antiemetic use. The patients' analgesic demands were also recorded.

#### Statistical analysis

Statistical analyses were performed using SPSS software, version 22 (SPSS Inc., Chicago, IL, USA). The data are expressed as the mean ± standard deviation (SD). *P* values < 0.05 were considered statistically significant without any adjustment for multiplicity of testing.

The t-test,  $\chi^2$  test, and Fisher's exact test were used to analyze the patient demographics, cumulative incidence of vomiting at each time point, rescue antiemetic use, complete response rate, and VAS pain scores. The Mann-Whitney U test was used to analyze the nausea severity scores.

## RESULTS

Of 53 patients considered eligible for the study, 3 refused and 50 agreed to participate. One patient was excluded due to the operation being called off and one patient was excluded to occlusion of the epidural catheter (Figure 1). Twenty-four patients received intraarticular anesthesia (Group I), and 24 received continuous epidural anesthesia (Group E). The demographic data were similar for both groups with respect to age, sex, weight, ASA physical status, smoking status, and history of motion sickness and PONV. Similarly, there were no differences in the durations of anesthesia or surgery, or the amount of blood loss (Table 1).

There were no significant differences observed in the incidence of PONV, nausea severity scores, rescue antiemetic use, or complete response rate between the two groups at any time point

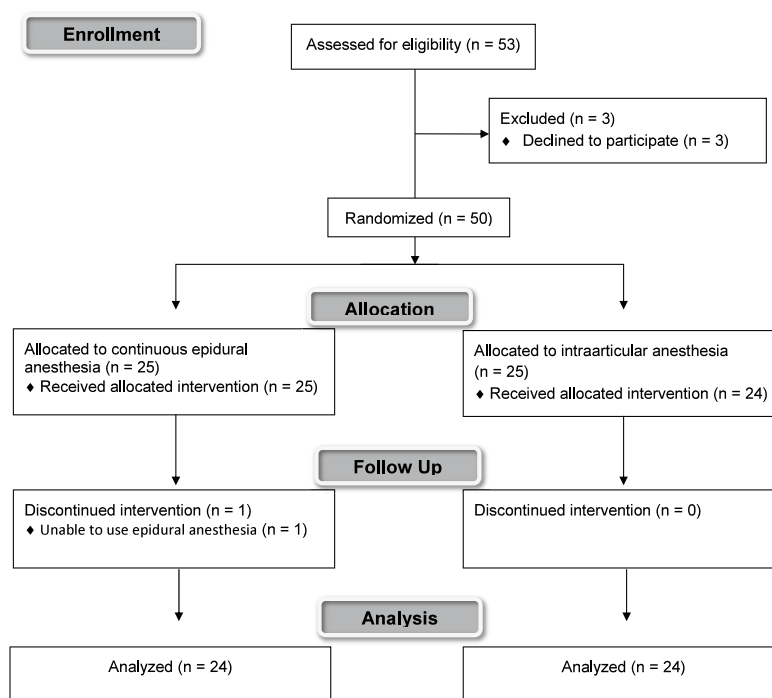


Figure 1. CONSORT flow chart showing the selection process for patients.

(Table 2). The VAS pain scores were also not significantly different between the groups ; however, the use of rescue analgesics was significantly less in Group E during the 2–24-h postoperative period (Table 3).

**Table 1.** Patient demographic and perioperative data

	Group I (n = 24)	Group E (n = 24)
<b>Patients</b>		
Age (years)	67.1 ± 9.6	60.5 ± 13.9
Sex (Male : Female)	8:16	7:17
Height (cm)	154.0 ± 7.1	157.6 ± 7.2
Weight (kg)	58.6 ± 11.0	60.7 ± 13.3
ASA physical status (I/II/III)	3/19/2	7/16/1
<b>Risk factors</b>		
Smoker	1	1
History of motion sickness	2	3
History of PONV	3	4
<b>Surgery-/anesthesia-related parameters</b>		
Duration of anesthesia (min)	248.5 ± 57.8	256.3 ± 49.8
Duration of surgery (min)	180.1 ± 59.4	189 ± 66.0
Blood loss (ml)	429.5 ± 393.6	487.0 ± 442.8
Type of surgery (Hip : Knee)	18 : 6	22 : 2
Total hip arthroplasty	17	20
Rotational acetabular osteotomy	1	2
Total knee arthroplasty	6	2

Data are presented as the mean ± standard deviation, or number (n).

Group I, intraarticular anesthesia group ; Group E, continuous epidural anesthesia group ; ASA, American Society of Anesthesiologists ; PONV, postoperative nausea and vomiting.

**Table 2.** Postoperative parameters

	Group I (n = 24)	Group E (n = 24)	P-value
<b>0–2-h Postoperative period</b>			
PONV	5	6	P = 0.36
Vomiting (no. of episodes)	4	8	P = 0.37
Nausea scores (0/1/2/3)	19/1/0/4	18/0/1/5	P = 0.71
Rescue antiemetic use	4	2	P = 0.33
Complete response (%)	20 (83%)	19 (79%)	P = 0.5
<b>2–24-h Postoperative period</b>			
PONV	2	6	P = 0.12
Vomiting (no. of episodes)	0	4	P = 0.10
Nausea scores (0/1/2/3)	22/0/1/1	18/1/3/2	P = 0.14
Rescue antiemetic use	1	2	P = 0.5
Complete response (%)	23 (96%)	21 (88%)	P = 0.3
<b>24–48-h Postoperative period</b>			
PONV	1	4	P = 0.17
Vomiting (no. of episodes)	0	2	P = 0.16
Nausea scores (0/1/2/3)	23/0/1/0	20/2/0/2	P = 0.16
Rescue antiemetic use	1	1	P = 0.76
Complete response (%)	23 (96%)	22 (92%)	P = 0.5

Data are presented as the number of patients (percentile), unless otherwise stated.

Group I, intraarticular anesthesia group ; Group E, continuous epidural anesthesia group ; PONV, postoperative nausea and vomiting. Nausea scores : 0, absence of nausea ; 1, mild nausea ; 2, moderate nausea ; or 3, severe nausea.

**Table 3.** Postoperative pain data

	Group I (n = 24)	Group E (n = 24)	P-value
<b>0–2-h Postoperative period</b>			
Rescue analgesic use (%)	9 (38%)	10 (42%)	P = 0.5
VAS pain score	4.4 ± 3.5	4.5 ± 4.1	P = 0.91
<b>2–24-h Postoperative period</b>			
Rescue analgesic use (%)	13 (54%)	6 (25%)	P = 0.04#
VAS pain score	2.3 ± 2.0	2.3 ± 2.7	P = 0.9
<b>24–48-h Postoperative period</b>			
Rescue analgesic use (%)	9 (38%)	7 (29%)	P = 0.38
VAS pain score	1.4 ± 1.9	2.5 ± 2.6	P = 0.10

Data are presented as the number of patients (percentile) or the mean ± standard deviation.

Group I, intraarticular anesthesia group ; Group E, continuous epidural anesthesia group ; VAS, visual analog scale (0, no pain ; to 10, the worst pain imaginable).

## DISCUSSION

In this study, we compared the intraarticular injection technique with continuous epidural infusion for postoperative analgesia, and found no significant differences in the incidence or severity of PONV, complete response rate, or the use of rescue antiemetics between the two methods. The benefits of intraarticular analgesia have been evaluated previously, primarily with patients having undergone knee surgery ; a systematic review of previous studies demonstrated evidence of reduced pain during the immediate and early postoperative periods following intraarticular local anesthesia after knee surgery (15, 18). However, some studies have demonstrated the effectiveness of intraarticular analgesia following hip surgery (11,12). In the current study, we included patients undergoing knee or hip surgery, and found that intraarticular analgesia was effective for pain management following both types of surgery.

We noted that there was a significant difference between the two study groups regarding the use of rescue analgesics during the 2–24-h postoperative period. Since single-injection intraarticular analgesia only remains effective short period (19,20), it is reasonable that patients in Group I required rescue analgesia more often than those in Group E. However surgical site, knee or hip, and the invasiveness, i.e. total knee arthroplasty > total hip arthroplasty, may influence on the results for the use of rescue analgesics. Although, there was no statistically significant difference, Group I tended to have more knee surgery than Group E. Use of continuous wound catheters may reduce the need for rescue analgesics ; however, we chose not to utilize them in the present study owing to concerns regarding the possible increased risks of infection and delayed wound healing (8, 21). Previous studies investigating the efficacy of local infiltration analgesia after knee surgery did not demonstrate an increased frequency of infections, but the follow-up periods in these studies were very limited (10, 22, 23). Therefore, it should be further investigated whether combining intraarticular injections and continuous infusion of local anesthesia to surgical sites can provide more effective pain control than traditional methods.

Ropivacaine is a relatively new, long-acting, aminoamide local anesthetic agent (24) that is chemically homologous to bupivacaine and mepivacaine (25). It demonstrates similar clinical efficacy to racemic bupivacaine, but is less cardio- and neurotoxic, and induces less vasodilation. The peak plasma concentration of ropivacaine following intraarticular administration has been

shown to be proportional to the dose administered, and remains below the recognized toxicity level after administration of 200 mg (19,20). Therefore, we chose to administer 200 mg of ropivacaine for intraarticular anesthesia in our study.

A few previous studies have quantified the incidence of PONV after intraarticular analgesia; Lykoudi *et al.* (26) found no significant difference between ropivacaine and a placebo, and Rautoma *et al.* (27) reported that the incidence PONV for patients that received ropivacaine was lower than that of those who received a placebo. However, intraarticular ropivacaine and morphine administration has been associated with a higher incidence of PONV (16), but these study participants were only observed for a short period (24-h). In the present study, we did not observe any significant reduction in PONV during the 48-h postoperative period.

This study had several limitations. First, we did not define the dose of fentanyl for continuous epidural anesthesia, which may have affected the study's results. Second, dexamethasone was used as an adjuvant drug in the intraarticular analgesia group. Dexamethasone is a potent and highly selective glucocorticoid with minimal mineralocorticoid effects. It inhibits nociceptive impulse transmission along myelinated C-fibers, and when combined with local anesthetics, it increases the duration of regional blocks (28, 29). Intraarticular ropivacaine has only been shown to be effective when it is administered with other drugs, not when used alone (15); therefore, dexamethasone was used in this study to increase analgesic efficacy. The corticosteroid dexamethasone effectively prevents nausea and vomiting in postoperative patients. However, in this study, it may have acted locally *via* steroid receptors, it could not have acted systemically; therefore, it could not prevent PONV. Finally, antiemetic use was restricted to only metoclopramide in this study; however, use of other antiemetics may have reduced PONV.

In conclusion, the use of single-injection intraarticular anesthesia following lower limb surgery did not prevent PONV more than continuous epidural anesthesia in this study. However, the greater simplicity, safety, and cost effectiveness of the intraarticular technique is apparent. Therefore, further studies are needed to further decrease the incidence of PONV.

## CONFLICTS OF INTEREST

Each author declares that they have no conflicts of interest associated with this study or manuscript.

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