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Comparison of the postoperative analgesic efficacies of intravenous acetaminophen and fascia iliaca compartment block in hip fracture surgery: A randomised controlled trial

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ABSTRACT

Background: Managing pain during movement after hip fracture surgery is important for achieving earlier hip mobilisation and for preventing postoperative complications. In the present study, we tested the hypothesis that the fascia iliaca compartment block (FICB) would improve postoperative pain on movement compared with intravenous acetaminophen.

Methods: In this prospective, randomised, controlled, parallel trial, patients were assigned to either the intravenous acetaminophen or the ultrasound-guided FICB group. Visual analog scale (VAS) pain scores were evaluated at 6, 9, 12, 18, 24 h, 2 days, and 7 days postoperatively. The primary outcome was VAS scores on movement at 24 h after surgery. The secondary outcomes were VAS scores on movement at the other time points, VAS scores at rest, the total number of rescue analgesics required and incidence of delirium during the first 24 h postoperatively, potential drug or block-related complications, and the time to first standing.

Results: VAS scores on movement at 24 h after surgery were significantly lower in the FICB group than in the intravenous acetaminophen group [median (the 25th to 75th percentiles), 20 (10–30) vs 40 (30–53); $P < 0.01$]. The VAS scores on movement at any other time point and the scores at rest at 12 h after surgery were also significantly lower in the FICB group than in the intravenous acetaminophen group. The two groups did not differ in terms of the total number of rescue analgesics required or the incidence of delirium during the first 24 h postoperatively; complications; or the time to first standing.

Conclusions: FICB improved postoperative pain on movement compared with intravenous acetaminophen without increasing the complication rate. However, the total number of rescue analgesics required and the time to first standing were not significantly different between the two groups.

Introduction

Postoperative pain management after hip fracture surgery, especially with regard to pain on movement, is important for earlier hip mobilisation and restoration of function, and for preventing postoperative complications. Non-steroidal anti-inflammatory drugs (NSAIDs) increase the risk of bleeding and can exacerbate underlying gastrointestinal problems in geriatric patients. Intravenous acetaminophen is a viable alternative to NSAIDs, especially considering the low incidence of adverse effects [1–5]. Patients with opioid use disorders are at higher risk for adverse events such as respiratory depression, hypotension, mental status changes, and mortality after hip fracture surgery [6,7]. According to some systematic reviews and the guidelines, peripheral nerve blocks can be valuable for maintaining a reasonable opioid dosage [5,8,9]. The fascia iliaca compartment block (FICB) has been shown to provide postoperative analgesia for hip fracture pain in geriatric patients [9–12].

So far, no study has compared the efficacy of intravenous acetaminophen and FICB following hip fracture surgery. Therefore, we conducted a randomised controlled trial (RCT) to compare the

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postoperative analgesic efficacy of intravenous acetaminophen with that of FICB in patients undergoing hip fracture surgery. We hypothesised that FICB would improve postoperative pain on movement compared with intravenous acetaminophen.

The study was approved by the institutional review board and registered as a RCT with the University Hospital Medical Information Network Clinical Trial Registry (Code JPRN-UMIN000024147).

Patients & methods

Study design

This prospective, two-arm, parallel-group, RCT that compared intravenous acetaminophen and FICB for the management of postoperative pain following hip fracture surgery, was conducted at a single general hospital (Unnan City Hospital in Shimane, Japan). The study focused on postoperative pain on movement in the first 24 h following hip fracture surgery.

Participants

Consecutive patients diagnosed as acute proximal hip fracture at our hospital from October 2016 to January 2018 were screened for inclusion in the study. Inclusion criteria were age over 50 years, the ability to provide written informed consent and stand on their own before the fracture, American Society of Anesthesiologists physical status I-II, and planned surgery for proximal hip fracture under spinal anaesthesia. Eligible patients had the ability to cooperate for the study. Exclusion criteria were poorly-controlled diabetes mellitus, defined as hemoglobin A1c level over 7.0% [13]; neurologic disease; history of allergy to the study drugs; serious systemic comorbidities; bleeding disorders; previous surgery in the affected hip; regular opioid therapy; infection at the injection site; open fractures; multiple injuries requiring pain medications or other surgeries; impaired cognition or dementia, and delirium at admission.

After written informed consent was obtained, patients were enrolled in the study and divided into two groups by randomisation.

Randomisation and blinding

In stratified block randomisation, randomisation was stratified by sex (female, male), age (<70, 71–79, 80–89, ≧90 years), fracture type (pertrochanteric fracture, femoral neck fracture), and type of surgery (internal fixation, bipolar hemiarthroplasty [BHP]). Randomisation within each stratum was performed by a permuted block randomisation with a block size of 4 and a 1:1 allocation [14] with a random number list generated by a computer software (Excel 2010, Microsoft, Redmond, Washington). The allocation sequence was prepared by an independent operator not otherwise involved in the trial. Both researchers and patients were not blinded. The medication used for each individual patient was prepared by a nurse not otherwise involved with the collection of patient data.

Interventions

The interventions used in the study were intravenous acetaminophen and FICB. Each patient was aware of the group allocation because we believed that a placebo injection in the inguinal area was not acceptable for hip fracture patients.

Patients allocated to the intravenous acetaminophen group received 1000 mg intravenous acetaminophen (Acelio; TERUMO, Tokyo, Japan) 6 and 12 h postoperatively. According to the drug manufacturer's recommendations, the dose is 1000 mg for patients weighing more than 50 kg and 15 mg/kg for patients weighing less than 50 kg [15].

Patients allocated to the FICB group were administered the FICB as originally described by Dalens et al. [16] before spinal anaesthesia by an orthopedic surgeon with extensive experience in this block procedure. The patient was placed in the supine position without premedication or adjunctive sedation. Standard noninvasive monitors were applied. A line was drawn from the pubic tubercle to the anterior superior iliac spine, and after dividing this line into three equal sections, the puncture site was marked 1 cm caudal to the point dividing the lateral third and medial two thirds of this line. After sterilisation of the skin, a short bevel 100-mm, 21-gauge insulated nerve block needle (B. Braun Melsungen AG, Melsungen, Germany) was inserted perpendicular to the

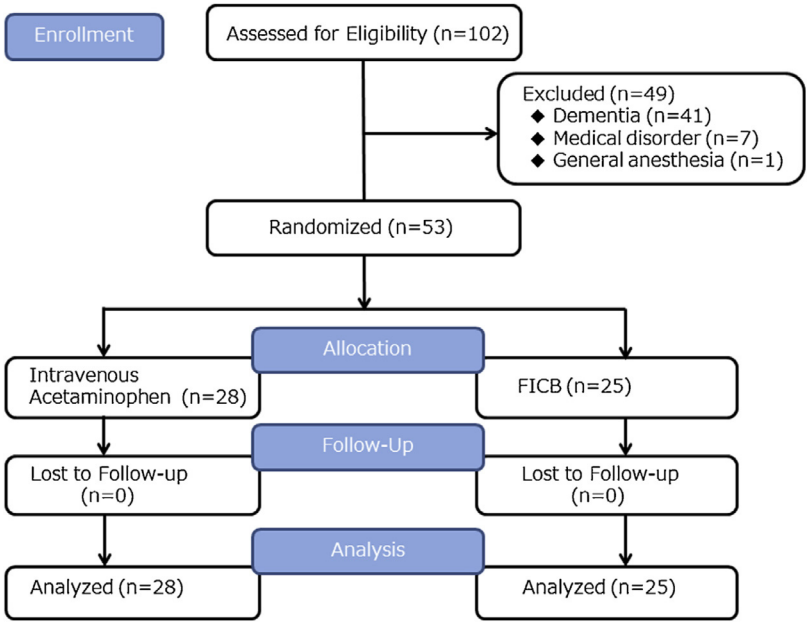

Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Table 1
Patient demographics and baseline clinical characteristics.

	Intravenous acetaminophen (n = 28)	FICB (n = 25)	*P*-value
Age, years	84.6 ± 7.8	84.7 ± 6.5	0.95
Gender (Female/Male)	23/5	22/3	0.55
Height, cm	150.7 ± 7.4	150.0 ± 8.3	0.65
Weight, kg	47.5 ± 8.2	47.6 ± 9.7	0.96
Body mass index, kg/m^2	20.9 ± 3.0	21.1 ± 3.2	0.63
Preoperative diagnosis (N/P)	11/17	10/15	0.96
Surgical procedure (B/I)	5/23	3/22	0.55

Results are shown as mean ± standard deviation.
FICB, fascia iliaca compartment block; N, femoral neck fracture; P, pertrochanteric fracture; B, bipolar hemiarthroplasty; I, internal fixation.

skin until two "pops", corresponding to the puncture of the fascia lata and fascia iliaca, were felt. Insertion of the needle was performed under real-time ultrasound guidance with a handheld ultrasound device (Noblus ultrasound system, Hitachi, Ltd, Tokyo, Japan) with a high-frequency, 5–18 MHz, linear-array transducer (L64) to facilitate accurate needle placement. After confirming that the needle had perforated the iliac fascia and negative aspiration, a total of 40 mL of 0.25% levobupivacaine (Maruishi Pharmaceutical Co, Tokyo, Japan) was injected below the iliac fascia slowly, and the adequacy of the deposition was confirmed by the ultrasound device.

Surgery and rehabilitation

All the patients received spinal anaesthesia with 2.0–2.5 mL of 0.5% isobaric bupivacaine (AstraZeneca, Osaka, Japan). All the surgeries were performed by one of three orthopedic surgeons (N.Y., A.N., or T.D.). The surgical procedure for internal fixation was performed on a traction table with the patients placed in the supine position, while the BHP surgery was performed in the lateral decubitus position. No additional local anaesthetics or opioids were administered during the surgery. Only after BHP, a normal suction drain was used postoperatively.

The postoperative rehabilitation regimen was the same for both groups and was started the day after surgery. Early mobilisation, quadriceps setting exercise, transfer to wheelchair, and standing at the bedside were started from the first day after surgery. Ambulatory training with weight bearing as tolerated was started 2 days after surgery.

Preoperative and postoperative protocols

Before surgery, all patients were instructed in the use of the visual analog scale (VAS). Postoperatively, patients received loxoprofen sodium (Daiichi-Sankyo, Tokyo, Japan) 60 mg orally and/or diclofenac sodium suppository (Adefuroniczupo; Teva, Nagoya, Japan) 25 mg, on request. Regular parenteral analgesia was not prescribed. Vital parameters such as blood pressure, heart rate, and oxygen saturation were monitored in all patients. Blood tests were performed on day 1 and day 7 postoperatively.

Outcome measurements

Most of the data were collected by a nurse not involved in the trial. When data were not collected by the nurse at the scheduled time for any reason, an investigator involved in the trial collected the data at the scheduled time as an exceptional situation. Measurements included intensity of pain, which was evaluated using a 100-mm horizontal VAS ranging from 0 mm (no pain) to 100 mm (worst imaginable pain) at rest and on movement at 6, 9, 12, 18, 24 h (when the patient was awake during these times), 2 days, and 7 days postoperatively. Pain on movement was elicited by passively elevating the fractured leg to 15° [17].

The primary outcome was the VAS score on movement at 24 h after surgery. The secondary outcome measures included the following evaluations. The postoperative VAS scores at rest and on movement (other than the primary outcome) were compared between the groups. The total number of rescue analgesics required during the first 24 h was evaluated. Delirium occurring within 24 h after surgery was diagnosed by the confusion assessment method [18]. Patients were also evaluated for potential drug or block-related complications during the course of the trial. The time to first standing or performing walking exercises was noted by the physiotherapist.

Sample size calculation

Based on previous studies of pain management in acute hip fractures [19], a sample size of 42 patients (21 patients per treatment group) were needed for this study to have 80% power to detect a 30% difference in VAS scores on movement at a type I error of 5% [17]. Finally, 25 patients were enrolled in each group to accommodate for patient dropouts.

Statistical analysis

For missing data, we replaced scores either by linear interpolation in cases where the missing scores fell between two valid scores or with the median scores of other patients at the same point in time in the same treatment group [14]. Data are presented as mean ± standard deviation unless otherwise stated. The comparisons between the study groups were performed using chi-square test or Fisher exact-test for categorical variables, and Student's *t*-test or Mann-Whitney U test for continuous variables according to the data distribution; normality of data was confirmed by the Kolmogorov-Smirnov test. All tests were 2-sided, and a *P* value of <0.05 was considered statistically significant. All statistical analyses were performed by an investigator using EZR software (Saitama Medical Centre, Jichi Medical University, Saitama, Japan).

Table 2
Visual analog scale scores for postoperative pain on movement.

	Intravenous acetaminophen (n = 28)	FICB (n = 25)	*P*-value
6 h after surgery	50 (30–60)	20 (10–30)	< 0.01
9 h after surgery	40 (29–56)	30 (14–35)	0.01
12 h after surgery	40 (30–50)	30 (15–36)	0.01
18 h after surgery	50 (38–53)	25 (10–40)	< 0.01
24 h after surgery	40 (30–53)	20 (10–30)	< 0.01
2 days after surgery	30 (28–40)	20 (10–30)	< 0.01
7 days after surgery	30 (20–33)	10 (10–10)	< 0.01

Visual analog scale score was rated using a 100-mm horizontal scale.
The values are given as the median and the 25th to 75th percentiles.
FICB, fascia iliaca compartment block.

Table 3
Visual analog scale scores for postoperative pain at rest.

	Intravenous acetaminophen (n = 28)	FICB (n = 25)	*P*-value
6 h after surgery	20 (10–50)	20 (10–30)	0.98
9 h after surgery	17.5 (4–33)	10 (4–20)	0.21
12 h after surgery	22.5 (10–36)	10 (4–20)	0.03
18 h after surgery	10 (0–30)	0 (0–20)	0.26
24 h after surgery	20 (8–40)	10 (10–20)	0.45
2 days after surgery	10 (8–30)	10 (5–20)	0.62
7 days after surgery	20 (10–23)	10 (5–20)	0.20

Visual analog scale score was rated using a 100-mm horizontal scale.
The values are given as the median and the 25th to 75th percentiles.
FICB, fascia iliaca compartment block.

Source of funding

There was no external source of funding for this study.

Results

Of the 102 patients eligible for the study, 49 patients were excluded: 41 due to dementia, seven due to medical disorders, and one due to general anaesthesia. Fifty-three patients were randomised to two groups (Fig. 1). No patients were excluded after allocation. Of the 56 included participants, 45 were female; the mean age was 84.6 (±7.2) years. The baseline characteristics were similar in both groups (Table 1).

Primary outcome

VAS scores on movement at 24 h after surgery were significantly lower in the FICB group than in the intravenous acetaminophen group (median and the 25th to 75th percentiles, 20 (10–30) vs 40 (30–53); $P < 0.01$) (Table 2).

Secondary outcome

VAS scores at rest were significantly lower in the FICB group than in the intravenous acetaminophen group only at 12 h after surgery (Table 3). VAS scores on movement at any time point were significantly lower in the FICB group than in the intravenous acetaminophen group (Table 2). The total number of rescue analgesics and incidence of delirium during the first 24 h postoperatively, complications, and the time to first standing were not significantly different between the two groups (Table 4).

Discussion

In this RCT that compared the postoperative analgesic efficacy of intravenous acetaminophen with that of FICB in patients who had undergone hip fracture surgery, we observed that FICB improved postoperative pain on movement compared with intravenous acetaminophen without increasing the complication rate. The difference in the primary outcome VAS scores between the two groups was 20, which is above the level of clinical significance as indicated by the threshold value of the minimum clinically important difference (MICD) of 12 [20]. However, the total number of rescue analgesics required and the time to first standing were not significantly different between the two groups.

It has been suggested that peripheral nerve block provides better pain relief during movement than intravenous medication administered at regular intervals. In a study that compared intravenous patient-controlled analgesia (PCA) and femoral nerve PCA after pertrochanteric fracture surgery, patients administered femoral nerve PCA experienced significantly less pain on movement and had faster ambulation [21]. Our study supports these results as we observed that peripheral nerve block provided better pain relief during movement than intravenous medication.

So far, no study has evaluated both postoperative pain on movement and the time to first mobilisation using FICB for hip fracture surgery. In the present study, although the VAS scores on movement were significantly lower in the FICB group, no significant difference was observed between the two groups with regard to the time to first standing. In a RCT that studied multimodal pain management following BHP, the time until the patient started walking was marginally, but not significantly, different between the two groups (mean, 2.9 days in Group I, which received preemptive pain medication and intraoperative periarticular injections, and 3.9 days in Group II, which did not receive any medication), although multimodal pain management significantly reduced the postoperative pain [22]. This is again similar to the results of the present study. The earlier standing during rehabilitation might probably be due to the significant reduction in pain during movement or other factors besides the VAS scores, such as pre-injury walking ability, extent of systemic disease, and the timing of surgery.

Several methods have been described for achieving reduction of pain on movement. Preoperative continuous FICB has been shown to provide effective analgesia in the perioperative period after hip fracture surgery [23,24]. However, a recently published Cochrane review article reported that there was no difference between continuous femoral nerve block and single shot FICB with regard to the pain scores on movement at 24 h [25]. In the present study, we avoided placing a continuous infusion catheter in the groin area, as we felt that it would be helpful in terms of safety for starting anticoagulants and early rehabilitation. Furthermore, the usefulness of a multimodal pain approach for hip fractures has been reported [10,22]. A combination of preemptive medication, postoperative medication [10], another peripheral nerve block, local anaesthetic injections at the surgical site intraoperatively [26], and intraarticular injections [27] might be a key to effective pain control in the multimodal approach.

There were several limitations to this study. First, most importantly, the study design was open-label. A sham FICB injection was not approved by our institutional review board. An open-label design in randomised controlled trials can cause overestimation of the results [28]. Second, the present study was conducted in a single centre and only three surgeons were involved; hence, generalising and applying these findings to community settings should be done cautiously. Third, the sample size of the present study was calculated on the basis of the primary outcome measure. Although the present study showed a significant difference between

Table 4
Secondary outcomes.

	Intravenous acetaminophen (n = 28)	FICB (n = 25)	*P*-value
Total number of rescue analgesics during the first 24 h postoperatively	0.5 ± 0.6	0.6 ± 0.8	0.65
Complications (yes/no)	0/28	0/25	N/A
Delirium (yes/no)	4/24	2/23	0.49.
Time to first standing (days)	3.1 ± 1.4	3.0 ± 0.8	0.91

FICB, fascia iliaca compartment block; N/A, not applicable.

groups in terms of the primary outcome, the sample size may not have sufficient power to make definitive conclusions with regard to secondary outcomes. Though there were some potential sources of bias in the present study, our results draw attention to the potential impact of FICB, particularly since these would lead to improved postoperative outcomes, and consequently have an impact on public health and economics. Further research is needed to improve walking ability, time to discharge from hospital, and medical cost.

Conclusions

FICB improved postoperative pain on movement compared with intravenous acetaminophen without increasing the complication rate. However, FICB did not reduce the total number of rescue analgesics nor the time to first standing after the surgery.

Funding

No funds were received in support of this work.

Conflict of interest

There are no conflicts of interest to declare.

Consent

Informed consent was obtained from the patients for the publication of this study.

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