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Influence of fentanyl-based Patient-Controlled Intravenous Analgesia (PCIA) with and without background infusion on postoperative pain intensity in patients following total hip replacement

Nirvana Ahmed Elshalakany

Anaesthesia and Intensive Care Unit, Faculty of Medicine, October 6 University, Cairo, Egypt

ABSTRACT

Objective: The goal of this trial was to determine if fentanyl PCIA and background infusion are effective for post-total hip replacement analgesia.

Methods: This trial examined two groups of patients receiving PCIA who had total hip replacements: group A ($n = 35$) with no background infusion, lockout time of 6 min; group B ($n = 35$) with background infusion 2 mL/h infusion, lockout time of 10 min. The fentanyl dose in each group was diluted with 100 mL normal saline. Primary outcome was VAS scores at rest after 24 hr. The secondary outcomes included VAS scores at rest at 6, 12, and 18 hr, fentanyl consumption, injection to attempt ratio, blood pressure, and heart rate.

Results: Neither background infusion nor no background infusion showed significant differences in VAS scores at 24 hr. Background infusion groups exhibited lower VAS pain levels at 6, 12, and 18 hr. At 24 hr after surgery, attempts, injections, and fentanyl consumption were significantly different between the two groups ($P < 0.001$). While BP and HR did not differ significantly between groups, pain control effectiveness showed statistically significant differences between groups.

Conclusion: Background infusion increased the overall quantity of fentanyl consumed within 24 hr after total hip replacement. The background infusion considerably decreased the pain at 6, 12, and 18 hr, but it had little effect on hip replacement pain at 24 hr. Importantly, it did not increase the incidence of BP, and HR. However, there were no significant differences in BP or HR between both groups, Fentanyl Background infusion was effective for post-total hip replacement analgesia.

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Fentanyl; hip replacement; Background infusion PCIA; VAS scores

1. Introduction

Acute pain treatments have been implemented in several hospitals during the past 20 years as a consequence of important efforts to improve the control of postoperative pain, including the design and implementation of pain-dealing guidelines [1]. Recent research, however, suggests that postoperative pain is still poorly controlled [2].

Hip replacement procedures are prevalent among the elderly, and they are significantly more painful [3]. The patient may suffer greatly as a result of the pain, which can also affect physiological functioning caused by hormonal fluctuations caused by sympathetic nervous system initiation [4]. Anesthesiologists and patients alike are concerned about pain management following major surgery. It should also be mentioned that every pain management medication has certain side effects, especially when an opioid is utilized [5].

In the clinical ICU, patient-controlled intravenous analgesia (PCIA) has been familiarised with improving post-operative pain management. It typically affords superior pain management and increases patient satisfaction when compared to "on-demand" opioid injections [6]. Instruction of PCIA comprises the settings automated into the PCIA machine, for instance, the bolus dosage, lockout interval, dose limitations, and background infusion. Both of these variables could affect the protection and effectiveness of PCIA [7].

A new fentanyl-based PCIA therapy has been developed to overcome limitations associated with PCIA provided by IV, such as programming mistakes, mobility limits, and the danger of needle stick injuries [8]. Prommer and colleagues demonstrated that a fentanyl dosage delivered through PCIA caused a C-max of 1.954 µg/L of fentanyl per 10 min/dose supply time [9].

Therefore, the aim of this randomized-controlled research (RCT) was to evaluate the effectiveness of fentanyl-PCIA and background infusion in patients receiving analgesia for total hip replacement.

CONTACT Nirvana Ahmed Elshalakany nirvanaelshalakany@yahoo.com Anaesthesia and Intensive Care Unit, Faculty of Medicine, October 6 University, Cairo, Egypt

2. Methods

2.1. Study design

From March 2021 to February 2022, we conducted the present study on October 6 University Hospital conducted this study with a two-arm parallel-group design. Patients were screened before surgery. Participants were primarily assessed for suitability up to 3 weeks preceding enrolment, providing their medical history, a physical examination, an informed consent form, and established preoperative instruction on how to use the PCIA pump, as well as instructions to switch on the button whenever they felt pain. Patients who were qualified for the study were ≥40 years old; with American Society of Anesthesiologists [10] (ASA) grade I, or II; were planned for a total hip replacement; a 24 hr hospital stay was anticipated following the procedure, and moderate to severe postoperative pain was predicted.

Patients who met any of the following criteria were not included in the study: a history of mental or neurological complaints, opioid and local anesthetic allergies, opioid tolerance, local infection, preoperative deep vein thrombosis (DVT), renal and hepatic insufficiency, and anticoagulant therapy-induced hemorrhage.

The ethics committee of October 6 University Hospital approved the study. The trial was conducted in accordance with the GCP guidelines and the principles of the Helsinki Declaration. The trial was registered under the clinical Trials registry NCT05429567.

2.2. Intervention

All patients received conventional monitoring prior to regional anesthesia, including electrocardiograms, non-invasive blood pressure measurements, and pulse oximetry. The patients were given a preload of 500 ml of ringer solution through an intravenous (IV) line fitted with an 18-gauge IV cannula. The patients were supported in their sitting position on a horizontal table by an assistance. In the lumbar region, an aseptic technique was used to prepare it and drape it. An intervertebral gap was identified between L3 and L4. A 2% lignocaine solution was injected into the prick point in a volume of 2 mL. In all patients, for rapid onset, good anesthesia and muscle relaxation effect combined spinal and epidural anesthesia (CSEA) was performed using 3–4 ml of 0.5% hyperbaric bupivacaine and 25 ug fentanyl administered using a 27-gauge Whitacre spinal needle and an 18-gauge Tuohy epidural needle. By applying the loss of resistance method, we were able to determine the epidural space. As soon as the medication was injected into the cerebral spinal fluid (CSF), the spinal needle was removed, and an epidural catheter was inserted and secured. The patient was then gradually positioned supine. The unblocked segments were tested by pin prick test 1.0–1.5 ml of 0.5% isobaric bupivacaine was administrated through the epidural route until the block was extended to T10.

A dose of 6 mg of ephedrine hydrochloride was administered intravenously to treat hypotension (if the blood pressure was <20% from base line). Bradycardia, which was defined as a drop-in heart rate of more than 20% of base line, it was treated with 0.6 mg of atropine intravenously. All patients got 4 L of oxygen per minute during surgery using a disposable face mask. Once the patient's vital signs had stabilized and their sensory block did not exceed T8, they were transported to their respective ward. All of the participants' PCIA pumps were shut off after 24 hr.

100 mL of fentanyl diluent was prepared for infusion, and each fentanyl diluent was prepared according to body weight of 0.25 µg/kg per 1.0 mL of diluent, using normal saline. PCIA analgesia protocol was started with a 0.5 mL bolus (2ug/kg fentanyl) in 70 patients, who were then randomized to either no background infusion, 6-minute lockout time (Group A), or background infusion 2 mL/h infusions, 10-minute lockout time (Group B). All PCIA devices were labelled with the study number of the patient, so the investigators could not tell which PICA regimen they were on. The patients were shown how to use the PCIA pump and to press the button whenever they experienced discomfort. Patients were allowed to get slow intravenous injection of 100 mg tramadol if their pain score was more than 7, if the inclusive satisfaction score was fair or poor and the procedure could be repeated if required. The patients who complained of nausea and vomiting received intravenous granisetron 40 µg/kg as a rescue antiemetic. PCIA was stopped for two hr in case of severe nausea persisted after antiemetics administration, and then reintroduced after the symptoms subsided.

As the main endpoint measurements, visual analog scale (VAS) scores [11] at 24 hr were evaluated. The VAS ratings at 6, 12, and 18 hr and the total quantity of fentanyl consumed was determined at the same time points, the injection/attempt (I/A) ratio, and fentanyl side effects were the secondary endpoints. The I/A ratio measures the number of analgesic doses administered with the number of analgesic requests (attempts). 24 hr following surgery, the inclusive satisfaction score [12] consistent with PCIA was recorded using a 4-point category numeric scale as follows: excellent (4): no complaint, good (3): patient complaint from minor pain but no need for analgesia, fair (2): patient complaint from moderate pain and need analgesics, poor (1): patient cannot tolerate. Basic demographics included age, body mass index (BMI, kg/m2), operation time (min), hospital stay, and ASA classification were measured.

2.3. Sample size calculation

We inspected the primary endpoints of pain levels assessed by VAS to define the optimal dose of fentanyl in post-operative PCIA. In the overall patient population, the predicted standard deviation of the means for VAS was 6.9 mm, 16, 21, and 22, while the participants' SD was 20 mm [13]. For each group, 35 individuals are required to have a power of 90% and a 95% confidence interval with alpha error was 0.05.

2.4. Data statistical analysis

SPSS 20 was used to conduct statistical analysis (IBM, NY, USA). Continuous data were presented as mean, SD, or mean difference with a 95% confidence interval (95% CI). Cases and frequency were used to show categorical data. The Kolmogorov – Smirnov test was used to determine if the data were normal. Repeated measures of ANOVA analysis and independent sample t-test were used to determine the differences between the two groups. P-values below 0.05 were considered statistically significant.

3. Results

3.1. Baseline features of the patients

A total of 81 patients were evaluated for eligibility; eleven ($n = 11$) were ineligible because they did not follow the research protocol. Therefore, 70 patients were randomized, as revealed in Figure 1. Thirty-five patients were in the no background infusion group (A = 35); 35 patients were in the background infusion group (B = 35). The starting point demographic data are revealed in Table 1. Throughout the trial, the hemodynamic data values were within the normal range.

4. Determination of the primary and secondary endpoints between the studied patients

4.1. Primary endpoint

VAS scores at 24 h were assessed as the primary endpoint measures. VAS scores included wound pain at rest (VAS-R) scores and during movement (VAS-M) scores. The intensity of pain was recorded with a 10-cm VAS, which ranged from 0 (no pain) to 10 (the worst pain imaginable) in Table 2. There were no significant

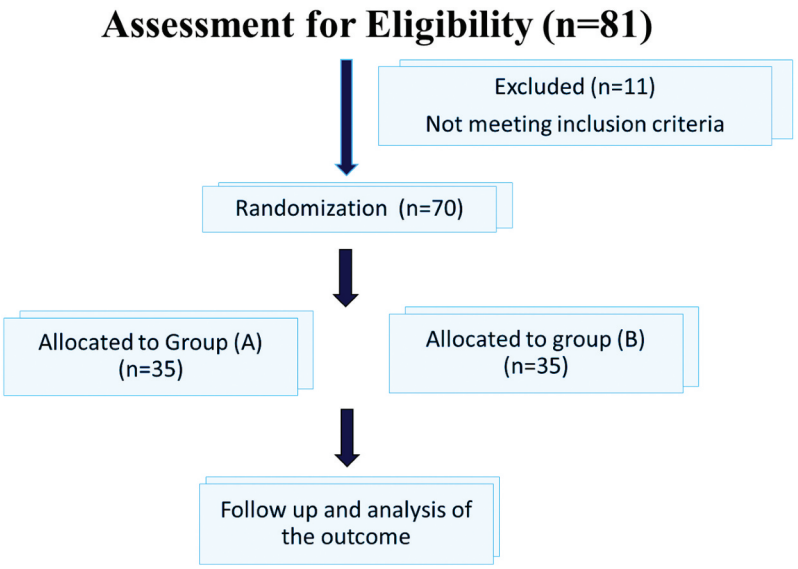

Figure 1. Study CONSORT flow diagram.

Table 1. Baseline characteristics among all patients.

Parameters	Group A ($n = 35$) (no background infusion)	Group B ($n = 35$) (background infusion)	*P*-value
Age (years)	47.8 ± 1.62	48.2 ± 3.72	0.48
BMI (kg/m^2)	29.3 ± 2.62	28.0 ± 1.55	0.37
Operation time (min)	88 ± 9	74 ± 10	0.35
Hospital stays (day)	6.5 ± 0.9	5.6 ± 1.0	0.09
ASA classification (n)	11	9	0.14
I	24	26	0.28
II			

Note: **BMI**, body mass index.

Table 2. VAS pain score between the studied groups 24 hr after surgery.

Primary outcome	Group A (no background infusion) ($n = 35$)	Group B (background infusion) ($n = 35$)	*P*-value
VAS-R 24 hr	2.10 ± 0.79	1.76 ± 0.71	0.26
VAS-M 24 hr	1.93 ± 0.34	1.73 ± 0.49	0.58

Note: Values are given as means (mean±SD). Abbreviations: VAS-R, visual analog scale – rest; VAS-M, visual analog scale – movement.

Table 3. VAS pain score for post-surgery among the studied groups 6, 12, 18 hr.

Outcome of VAS-R	Group A (no background infusion) ($n = 35$)	Group B (background infusion) ($n = 35$)	P-time	*P*-value (time#)
VAS				
– 6 hr	6.26 ± 0.87	4.12 ± 1.01	-	<0.001
– 12 hr	5.76 ± 1.17	3.27 ± 1.02	<0.001	<0.001
– 18 hr	4.21 ± 0.13	3.24 ± 1.06	<0.001	<0.001

Note: Values are given as Mean±SD. *P time: all time points compared with 6 h. #time: no background infusion compared to the background infusion group at 6 h, 12 h, 18 h, and 24 h. **VAS**, visual analog scale.

differences in VAS at 24 hr between the no background infusion and background infusion groups ($p > 0.05$).

4.2. Secondary endpoint

Regarding the VAS score at 6, 12, and 18 hr in Table 3 the data revealed that there were significant differences between two groups ($p < 0.05$) it was lower in background infusion group (B). Furthermore, Table 4 reveals the evaluations of attempts, injections, and total fentanyl administration at 6, 12, 18, and 24 hr. The two groups had different attempts, injections, and overall fentanyl administration. The background infusion group (B) had considerably fewer attempts and injections than the group (A) no background infusion group; nevertheless, fentanyl consumption was higher in group (B).

Furthermore, at 24 hr after surgery, there were no significant differences ($p > 0.05$) (in I/A, BP, or HR between the two groups). However, Group (B) was significantly more satisfied regarding pain control than group (A) ($P < 0.01$) as revealed in Table 5.

Table 4. Attempts, injections, and total fentanyl required after surgery for two groups.

	Group A (no background infusion) ($n = 35$)	Group B (background infusion) ($n = 35$)	P-time	*P*-value (time#)
Attempts				
6 h	0.94 ± 0.92	0.23 ± 0.12	-	0.03
12 h	27.58 ± 12.02	5.23 ± 1.58	<0.01	<0.01
18 h	33.56 ± 4.56	4.89 ± 2.16	<0.01	<0.01
24 h	61.39 ± 17.25	6.99 ± 2.35	<0.01	<0.01
Injections				
6 h	0.87 ± 0.56	0.31 ± 0.25	-	<0.01
12 h	21.32 ± 5.02	3.01 ± 1.01	<0.01	<0.01
18 h	37.52 ± 4.23	4.92 ± 1.13	<0.01	<0.01
24 h	47.13 ± 14.25	5.21 ± 2.03	<0.01	<0.01
Total fentanyl administration (mcg)				
6 h	47.25 ± 3.21	81.20 ± 4.25	-	<0.01
12 h	52.33 ± 5.78	82.31 ± 3.99	<0.01	<0.01
18 h	62.32 ± 3.56	89.34 ± 6.19	<0.01	<0.01
24 h	47.56 ± 8.25	79.52 ± 11.23	<0.01	<0.01

Note: Values are given as Mean±SD. *P time: all time points compared with 6 h. #time: no background infusion compared to background infusion at 6 hr, 12 hr, 18 hr, and 24 hr.

Table 5. I/A and satisfaction and hemodynamic changes 24 hr. after surgery among the groups.

	Group A (no background infusion) ($n = 35$)	Group B (background infusion) ($n = 35$)	95% CI	*P*-value
I/A	0.9 ± 0.11	1.23 ± 0.21	(–0.11, 0.21)	0.52
Satisfaction	5.12 ± 0.78	4.41 ± 0.32	(–1.11, –0.45)	<0.01
BP	116.0 ± 7.46	119.0 ± 8.52	–7.15, 4.04	0.06
– Systolic	74.0 ± 3.23	70.0 ± 2.31	–5.2, 3.02	0.11
– Diastolic				
HR	81.23 ± 1.23	80.79 ± 0.87	–2.97, 1.12	0.56

Note: Values are given as mean ± standard deviation. *$P < 0.05$ compared with no background infusion group. **CI**; confidence interval.

Table 6. Assessment of the pain control effectiveness between the groups.

Parameters	Group A (No background infusion) ($n = 35$)	Group B (Background infusion) ($n = 35$)	*P*-value
Excellent	13 (37.1%)	21 (60%)	*<0.001
Good	11 (31.4%)	13 (37.1%)	*<0.001
Fair	8 (22.9%)	1 (2.9%)	*<0.001
Poor	3 (8.6%)	0 (0%)	*<0.001

Note: Values are the numbers of patients (%).

Regarding the assessment of pain control effectiveness, there were statistically significant variances ($p < 0.05$) in the degree of pain control effectiveness between the two groups, and they were better in background infusion group Table 6.

5. Discussion

Patients who had hip replacement arthroplasty, in general, suffered acute pain following surgery [14]. Postoperative pain in the elderly might induce or worsen respiratory and cardiovascular problems [15]. As a result, pain management is crucial. As a result, the goal of this trial was to see if fentanyl PCIA and background infusion helped patients with post-total hip replacement analgesia.

PCIA minimizes the pathophysiological alterations allied with surgery, promotes quicker rescue of gastrointestinal function, lowers cardiac ischemia, and diminishes lung problems in older patients [16]. Furthermore, PCIA is more efficient for pain treatment than intravenous PCA, and it reduces the need for opioids, leading to higher patient contentment [17].

For moderate-to-severe postoperative pain, opioids are effective analgesics. Opioids like morphine, fentanyl, and sufentanil are ordinarily utilized in PCIA [18]. Morphine has long been recognized as the chief-line treatment for PCIA and is the utmost commonly used and studied drug in this condition [19]. Nonetheless, morphine's effectiveness is usually risked by its vigorous metabolite (morphine-6-glucuronide), which yields respiratory depression, particularly in people with renal inadequacy [20].

As a consequence, the findings revealed that patients are typically satisfied with PCIA as qualified pain control. It has been shown that pain management improved following common surgical operations. Pain assessment was the primary postoperative outcome as determined by VAS. Firstly, at 24 hr, there were no statistically significant variations in the VAS between the groups. Furthermore, 6, 12, and 18 hr VAS pain scores were analysed as secondary clinical outcomes after surgery. At 6 hr after surgery, the VAS was greater in both groups, which could be related to how challenging it is to effectively treat pain with fentanyl alone. This result was in accordance with Nie et al., who revealed that 2 μg/kg sufentanil boosted the potency of morphine PCIA by reducing pain levels [21].

A lower I/A ratio indicates that more patient attempts are made for each injection. It can be an indication of inadequate pain treatment. Furthermore, Abu-Zaid et al. [22] speculate that decreased I/A ratios may indicate a delay in achieving the peak analgesic effect. In this study, the I/A ratio did not fluctuate meaningfully between the groups.

This study was restricted by the small sample sizes of each group. As a result, we are unable to distinguish differences in side effect frequency. So, based on the results for each group's level of pain, we calculated a sample size, but it was too small to detect uncommon side effects.

6. Conclusion

In conclusion, PCIA was utilized to treat postoperative pain after hip replacement using fentanyl. Group (Background infusion) consumed more fentanyl at 24 hr postoperatively than group (No Background infusion). Furthermore, Background infusion did not improve hip replacement pain at 24 h; however, it did significantly reduce pain at 6, 12, and 18 hr. Likewise, after 24 hr, patient satisfaction has been elucidated.

Disclosure statement

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ORCID

Nirvana Ahmed Elshalakany http://orcid.org/0000-0002-3834-8032

Availability of data and materials

The original contributions presented in the study are included in the article and further inquiries can be directed to the corresponding author.

Ethics Committee Approval

Ethical committee approval was received from the ethics committee of October 6 University Hospital.

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