Patient-controlled epidural analgesia versus conventional epidural analgesia after total hip replacement – a randomized trial

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Aims. Patient-controlled analgesia (PCA) is usually considered a better option for pain management compared to conventional analgesia. The beneficial effect of PCA has been assessed in a number of studies; however, the results are inconsistent. The goal of this study was to compare of patient-controlled epidural analgesia (PCEA) to conventional epidural analgesia after total hip replacement (THR).

Methods. This prospective study was performed at the Department of Anesthesia and Intensive Care Medicine at a tertiary university hospital. After THR, patients were admitted to the intensive care unit (ICU) and randomized to one of two groups (PCEA and non-PCEA). Postoperative pain in the PCEA group was treated using a standardized protocol, while the analgesia in the non-PCEA group was based on physician prescription according to the patient’s clinical condition. The total consumption of analgesics, patients’ satisfaction, pain intensity, and analgesia-related complications were recorded for 24 h after surgery.

Results. The final sample consisted of 111 patients (PCEA group, n=55 and non-PCEA group, n=56). The PCEA group had significantly lower total consumption of analgesic mixtures (0.9±0.3 and 1.3±0.4 mL/kg per day, P<0.001). There was greater patient satisfaction (P<0.001) in the PCEA group. The mean pain intensity over 24 hours postoperatively was similar for both groups (P=0.14). There was no significant difference in rate of analgesia-related complications between the groups (hypotension, P=0.14; bradypnea, P=0.11).

Conclusion. Compared to conventional epidural analgesia based on physician prescription, PCEA led to less total analgesic consumption and greater patient satisfaction after THR.

Key words: patient-controlled analgesia, epidural analgesia, analgesics, drug consumption, total hip replacement, pain relief

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INTRODUCTION

Total hip replacement (THR) is usually followed by significant postoperative pain. Postoperative analgesia is therefore a fundamental part of postoperative management after THR, and may affect postoperative outcomes. Poorly managed postoperative pain increases the risk of developing chronic pain, postoperative morbidity, complications, costs, and length of hospital stay 1,2. In contrast, adequate analgesia has a positive effect on patient comfort, including early mobilization 3. With respect to the mode of analgesia, intravenous (i.v.) patient-controlled analgesia (PCA) or fixed interval i.v. administration of strong opioids should be preferred to on-demand administration according to the Procedure-Specific Postoperative Management (PROSPECT) recommendations 4. However, the results of comparisons between PCA and conventional methods of analgesia have been inconsistent 5,6. In patients undergoing THR, patient-controlled epidural analgesia (PCEA) may be considered an appropriate alternative for managing postoperative pain (ref. 7). However, other studies on postoperative pain management with PCEA used morphine despite the fact that sufentanil is a highly effective lipophilic opioid analgesic currently used more often in clinical practice 8. Only a few studies have to date investigated the use of sufentanil for PCEA.

The primary goal of this prospective, randomized study was to compare the effects of two different sufentanil-based methods of analgesia; patient controlled (PCEA) and conventional non-PCEA) where the drug is delivered according to the physician’s prescription. The main goal was to determine the difference in total use of analgesic mixture. The secondary goals were 1) patient satisfaction during the first 24 h postoperatively; 2) the degree of pain intensity; and 3) to assess the safety of the methods of analgesia based on the occurrence of analgesia-related complications including hypotension, bradypnea, heart rate abnormalities, itching, and postoperative nausea and vomiting (PONV).
PATIENTS AND METHODS

Trial design and patients
This prospective, randomized controlled trial was approved by the Ethics Committee of the University Hospital of Ostrava (Ref: 713/2013) and registered at clinicaltrial.gov (ID: NCT03599024). Patients were informed in person and written informed consent was then obtained from all participants prior to enrollment in the study in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects. The trial was conducted between September 2014 and March 2016 at the Department of Anesthesia and Intensive Care Medicine, University Hospital of Ostrava. All eligible participants were adult patients of both genders aged 18 years or older, and scheduled for elective orthopedic surgery (THR). A detailed list of inclusion and exclusion criteria is given in Table 1.

Randomization procedure
The enrolled patients underwent per-protocol randomization into one of two groups (PCEA or non-PCEA group) using the envelope method giving the participant a 50% chance of being assigned to either study or control group. Randomization was performed immediately after ICU admission by an independent physician who was not involved in the data collection or management of the study subjects.

Variables and time intervals of measurement
Following randomization, patients were admitted to the ICU. Data for the analyses were collected for 24 h after THR.

The baseline demographic and preoperative characteristics (age, gender, weight, body mass index, and American Society of Anesthesiologists [ASA] physical status) were obtained at the time of admission.

The degree of motor block was assessed using the modified Bromage Score. The level of sedation due to the residual effect of anesthetics at the time of admission was assessed using a sedation score (1 = awake; 2 = tired, sleepy, but easy to wake up; 3 = somnolent; and 4 = coma) (ref.10). The Visual Analogue Scale (VAS) values were determined at hourly intervals and 30 min after administration of analgesics to determine the effect of the analgesic dose. The other parameters evaluated at hourly intervals were: a) the presence of hypotension defined as a decrease in systolic blood pressure below 90 mmHg or a greater than 30% decrease from the baseline value; b) bradypnea measured on a numeric scale: (1= normal respiratory rate [RR]; 2 = RR ≤ 12/min; and 3 = RR ≤ 8/min); c) bradycardia defined as heart rate ≤ 50/min and tachycardia defined as heart rate ≥ 120/min; d) the presence of PONV as determined using a numerical scale (0 = no nausea; 1 = mild nausea; 2 = antiemetic given; 3 = nausea despite antiemetic; and 4 = vomiting) (ref.11); and e) skin itching (yes/no).

At the time of discharge from the ICU, the total use of analgesics was recorded, and patients’ satisfaction was evaluated using Likert scale (5-point version) (ref.12).

Protocol for administration of anesthesia and analgesia
The patients were given 7.5 mg of midazolam orally one hour before surgery. Patients weighing more than 70 kg received 2 mg of bisulepin. Prior to surgery, subarachnoid blockade was established with 2-4 mL of levobupivacaine 0.5% at the L2-L3 spinal interspace. Subsequently, a catheter for postoperative analgesia was inserted into the epidural space. If the subarachnoid blockade was insufficient for surgery, epidural levobupivacaine 0.5% was provided to a maximum of 10 mL, after which the patient underwent general anesthesia and was excluded from the study. During surgery, patients were sedated with a target-controlled infusion of propofol (dose of 1-2 mg/kg body weight per hour) so that they were asleep but aroused when spoken to. After surgery, patients received a mixture of levobupivacaine 0.1% and sufentanil 1 µg/mL. Postoperatively, patients were moved to the ICU. Immediately after ICU admission, continuous monitoring of vital functions and pain was initiated. When the pain intensity exceeded ≥ 4 points, analgesic...
therapy was initiated by administration of a mixture containing levobupivacaine 0.1% and sufentanil 1 μg/mL. The PCEA group was initially given a bolus of 10 mL of the mixture then a basal infusion at a rate of 3 mL/h. A bolus was set on 4 mL, a lockout interval of 20 min, and a maximum dose of 40 mL/4h according to the literature recommendation\textsuperscript{13}. The non-PCEA group was initially administered 5 mL of the analgesic mixture followed by a basal infusion at 5 mL/h. If pain developed, a bolus of 8 mL of the mixture was administered according to the physician’s prescription. If analgesia was insufficient after one hour of maximal dosing in both groups, the patient table 2. The baseline demographic and presurgical characteristics.

| Characteristics                  | PCEA group (n=55) | non-PCEA group (n=56) | P      |
|----------------------------------|-------------------|-----------------------|--------|
| Age, years, mean±SD              | 65.5 ± 9.4        | 69.7 ± 10.3           | 0.032  |
| Males % (n)                      | 49.1 (27)         | 36 (15)               | 0.015  |
| Females (n) %                    | 50.9 (28)         | 64 (41)               |        |
| Body weight, kg, mean±SD         | 83.8 ± 15.3       | 78.3 ± 14.8           | 0.065  |
| BMI, kg/m\(^2\), mean±SD         | 29.1 ± 4.1        | 28.4 ± 5.2            | 0.493  |
| ASA I, % (n)                     | 1.8 (1)           | 3.6 (2)               | 1.000  |
| ASA II, % (n)                    | 92.7 (51)         | 94.7 (53)             | 0.716  |
| ASA III, % (n)                   | 5.5 (3)           | 1.8 (1)               | 0.364  |

Nominal values are reported as relative frequencies (in %) and absolute numbers; numeric values are reported as means ± standard deviation (SD). The p values indicate differences between the patient-controlled epidural analgesia (PCEA) group and the non-patient-controlled epidural analgesia (non-PCEA) group.

BMI, Body mass index; ASA, American Society of Anesthesiologist

Fig. 1. CONSORT 2010 Flow Diagram.
was given adjunctive analgesic therapy including one or a combination of the following drugs: i.v. paracetamol, i.v. metamizole, or i.v. tramadol. Patients requiring systemic adjunctive medication were excluded from the final analysis.

Statistical analysis

A power analysis based on the authors’ pilot data was performed prior to the study start. Continuous variables were expressed as means and standard deviation (SD) and categorical variables as proportions. Selected variables (anaesthetic mode) were compared using the nonparametric Mann-Whitney test and chi-square test or, where necessary, Fisher’s exact test. Some data were graphically depicted as box plots. To address the baseline differences between groups, a regression analysis was performed including the influence of age, sex, and randomization. The level of significance was set at 5%. The analyses were performed by a certified statistician using Stata 13 software.

RESULTS

During the study period, 175 patients undergoing THR were assessed for eligibility. The final analysis included data from 111 patients divided into the PCEA (n=55) and non-PCEA (n=56) groups. The CONSORT 2010 flow diagram of the patient selection process is shown in Fig. 1. The PCEA group was significantly younger ($P=0.032$) and consisted of fewer males than females ($P=0.015$). Other baseline and preoperative characteristics were not significantly different between the groups (Table 2).

Total use of analgesics

The total use of the analgesic mixture during the first 24 h after ICU admission was significantly lower in the PCEA group. The mean sum of the continuous and bolus doses was 0.9±0.3 mL/kg in the PCEA group and 1.3±0.4 mL/kg per day in the non-PCEA group ($P<0.001$); i.e., 73.0±17.1 mL per day in the PCEA and 97.9±25.0 mL per day in the non-PCEA groups ($P<0.001$; Fig. 2). A bolus of the analgesic mixture was administered to 50 patients (91%) in the PCEA group and 46 patients (82%) in the non-PCEA group ($P=0.18$).

Patient satisfaction during postoperative pain management

The use of a Likert scale showed that the PCEA group was considerably more satisfied than the non-PCEA group, with mean satisfaction scores of 4.3±1.0 and 2.8±0.7, respectively ($P<0.001$; Fig. 3). According to gender, the median satisfaction was higher in males (3.9±1.2) than in females (3.3±1.2), $P=0.014$.

Pain intensity

The assessment of pain intensity using the VAS showed that mean VAS scores were similar in the PCEA and non-PCEA groups (1.1±0.6 and 1.2±0.4, respectively, $P=0.14$) during the first 24 h postoperatively. Mean VAS scores were less than 2 in the entire sample (both groups). We found that the PCEA group had lower intensity of pain for 16 hours of the following 24 h compared to 8 h, where the VAS was non-significantly higher in the PCEA group. Significantly higher VAS scores in the non-PCEA group were found at only three time points: 6 h ($P=0.02$), 14...
10 h ($P=0.01$), and 23 h ($P=0.03$) after the initiation of analgesic therapy (Fig. 4).

**Analgesia-related complications**

Hypotension was noted in a total of 37 patients. The occurrence of hypotension in the PCEA group was 40% ($n=22$), while it was 26.8% ($n=15$) in non-PCEA group ($P=0.14$). Bolus-related hypotension was found in 20.0% ($n=10$) of cases in the PCEA group and 8.7% ($n=4$) of cases in the non-PCEA group ($P=0.15$). Bradypnea developed in 20.7% ($n=23$) of cases in the entire sample; 14.5% ($n=8$) of cases in the PCEA group and 26.8% ($n=15$) of cases in the non-PCEA group ($P=0.11$). No heart rate abnormalities (i.e. bradycardia and/or tachycardia), PONV, or any form of itching were observed in the whole group.

**DISCUSSION**

Individualized therapeutic management of patients is currently recommended in a majority of health care fields, and postoperative pain relief is an essential priority for all patients undergoing surgical procedures of any kind. In the field of hip arthroplasty the PROSPECT recommendations prefer PCA over analgesia on patient request.\textsuperscript{4} The primary aim of our study was to compare the PCEA modality with standard pain management in patients undergoing THR. THR is a frequent and challenging orthopedic procedure usually followed by high levels of postoperative pain. We found lower total consumption of an analgesic mixture in the PCEA group during the first 24 h after THR. Moreover, higher subjective patient satisfaction...
was also found in the PCEA group. Both methods were effective in decreasing the pain intensity. There was no significantly different rate of analgesia-related complications between the two groups. Patients in the PCEA group tolerated the method well.

Seventy two percent of patients undergoing orthopedic surgery experience moderate to severe pain at rest, and 89.3% experience pain during early mobilization. Untreated or poorly managed pain can delay the initiation of rehabilitation, ambulation, and basic self-care. Therefore, it significantly limits patients’ return to normal daily routines. Patients who are in pain are also at risk of developing health complications due to prolonged bed rest such as thromboembolic diseases and pulmonary dysfunction. Patients undergoing THR are usually treated by administration of strong opioids, sometimes in combination with non-opioid analgesics. The currently recommended and generally accepted modality for pain management in this group of patients is drug administration in the epidural space. It is associated with a better analgesic effect and a lower risk of complications compared to systemically administered analgesics.

Concerning patients’ active involvement in pain management, i.v. PCA was considerably more effective in reducing pain after cardiac surgery than nurse-controlled analgesia. In acute traumatic pain in the emergency department, i.v. PCA with morphine was associated with faster pain relief and greater patient satisfaction than standard analgesia. However, the current study was more concerned with a comparison among local anesthetics during PCA, and only a few studies have compared the effects of i.v. PCA (or PCEA) to the conventional mode of analgesia in patients undergoing THR. For instance, the effect of mixtures of sufentanil and ropivacaine 0.165% or levobupivacaine 0.125% was compared during PCEA after orthopedic surgery. Patients receiving sufentanil and levobupivacaine required lower doses of analgesics and were more satisfied due to greater pain relief. Similar results were found in a randomized study comparing the effects of levobupivacaine 0.125%, bupivacaine 0.125%, and ropivacaine 0.2% administered via a PCEA mode (5 mL/h basal infusion, 2 mL bolus, 20 min lockout) in patients undergoing orthopedic surgery. With regard to pain intensity and optimal recovery of motor function, levobupivacaine appeared to be the most effective. According to these results, the combination of levobupivacain and sufentanil was chosen for PCEA in our study.

The total consumption of analgesic is an important clinical end point because of the potential adverse effects of high doses of opioids. Moreover, decreasing the dose of analgesics can also lead to a reduction in treatment costs and shorter time spent bedside by medical staff. We found that the PCEA modality of drug delivery significantly decreased the overall amount of analgesics necessary for required pain relief. To date, no study has compared the effect of PCEA on analgesic consumption after THR.

Postoperative pain management using i.v. PCA versus conventional methods of pain control was compared in a study that investigated patient satisfaction after surgical intervention. The duration of PCA pump use and patients’ age, gender, marital status, educational level, type of surgery, and work status were identified as significant predictors of patient satisfaction (P < 0.001) (ref. ). Our findings also demonstrated higher satisfaction with the PCEA method of drug delivery. In another study, an association between satisfaction and a decrease in pain intensity was proposed. However, satisfaction is subjective and objective measurement of it is controversial. For example, patient satisfaction surveys tend to yield positive results since patients are reluctant to criticize the treatment process, and even though many patients experience high levels of pain, they still report satisfaction with pain management. Assessment of satisfaction is often considered an important parameter of how patients perceive the efficacy of their treatment. However, in agreement with our results, a prospective study assessing patient satisfaction and outcome after general surgery concluded that PCEA was associated with higher satisfaction independent of the maximum pain intensity assessed by VAS score after orthopedic and gynecological surgery. We presume that higher satisfaction ratings in our PCA group are related mostly to perceived possibility of higher control over pain relief given by PCA.

The results of studies addressing pain intensity are heterogeneous. The studies from 2001 concluded that the perception of pain by surgical patients who receive various types of analgesia is essentially identical. However, PCA helps patients feel more secure and less anxious. In our study, the estimated pain intensity by VAS score showed generally lower VAS scores (16 of 24 postoperative hours) in the PCEA group versus the non-PCEA group during their 24-hour stay in the ICU. However, the overall VAS score did not exceed a value of 2, and no statistical significance in mean VAS scores was found between the groups. These results suggest that pain management was successful using both modalities of analgesic administration. This highlights the importance of the decreased amount of analgesics used in the PCEA group, while the difference in pain intensity was insignificant between the groups.

The continuous administration of opioids requires constant monitoring of physiological functions. Opioid-based drugs cause more than 60% serious postoperative side effects, especially respiratory depression, which can lead to cardiac arrest and death (ref. ). The use of PCEA offers easier pain management and decreases the time spent on patient care by qualified nursing staff. To evaluate the incidence of analgesia-related complications, we monitored the occurrence of hypotension, bradypnea, heart rate abnormalities such as bradycardia and/or tachycardia, PONV, and postoperative itching. We expected that especially hypotension and bradypnea might follow the administration of a bolus dose of an analogic. Although the bolus dose was more frequently administered in the PCEA group, we found no significant difference in the occurrence of hypotension and bradypnea between groups. This result shows that PCEA is as safe as the conventional mode of epidural analgesia.
We are aware of several study limitations including the relatively small sample size and differences in baseline characteristics (age, gender). However, the differences between groups were assessed by multivariate regression analysis, providing an opportunity for randomization, age, and sex to influence the results. Only randomization had a significant influence on the variables of interest including total analgesic consumption and patient satisfaction. The PCEA group consisted of more males than the non-PCEA group. This could affect patients’ overall satisfaction because males were significantly more satisfied with pain management than females.

CONCLUSION

The PCEA modality of delivery is associated with less total analgesic consumption, more satisfaction, and similar rates of adverse analgesia-related complications compared to the conventional mode of epidural analgesia after THR. Our results suggest that PCEA should be considered the method of first choice for analgesia in patients after THR.

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