Observational Studies

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Intravenous patient-controlled analgesia vs nurse administered oral oxycodone after total knee arthroplasty: a retrospective cohort study

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Abstract

Objectives: Severe post-operative pain is common after total knee arthroplasty. Patient-controlled analgesia is an alternative method of pain management, whereby a patient administers his or her own pain medication. Patients seem to prefer this method over nurse-administered analgesia. However, it remains unclear whether patients using patient-controlled analgesia devices use higher or lower doses of opioids compared to patients treated with oral opioids.

Methods: This retrospective study examined 164 patients undergoing total knee arthroplasty. Post-operatively, 82 patients received oxycodone via intravenous patient-controlled analgesia devices, while the pain medication for 82 patients in the control group was administered by nurses. The main outcome measure was the consumption of intravenous opioid equivalents within 24 h after surgery. Secondary outcome measures were the use of anti-emetic drugs and the length of stay. Furthermore, we evaluated opioid-related adverse event reports.

Results: The consumption of opioids during the first 24 h after surgery and the use of anti-emetic drugs were similar in both groups. The median opioid dose of intravenous morphine equivalents was 41.1 mg (interquartile range (IQR): 29.5–69.1 mg) in the patient-controlled analgesia group and 40.5 mg (IQR: 32.4–48.6 mg) in the control group, respectively. The median length of stay was 2 days (IQR: 2–3 days) in the patient-controlled analgesia group and 3 days (IQR: 2–3 days) in the control group (p=0.02). The use of anti-emetic drugs was similar in both groups.

Conclusions: The administration of oxycodone via intravenous patient-controlled analgesia devices does not lead to increased opioid or anti-emetic consumptions compared to nurse-administered pain medication after total knee arthroplasty. Patient-controlled analgesia might lead to shortened length of stay.

Keywords: acute pain; opioid use; oxycodone; patient-controlled analgesia; postsurgical pain; total knee arthroplasty.

Introduction

Total knee arthroplasty (TKA) is a surgical procedure, which relieves pain and discomfort in degenerative knee joints and significantly improves patient mobility in long-term follow-ups [1–3]. It is one of the most common inpatient operations in Finland and many other countries, and the annual number of procedures is constantly growing [4–6].

Nearly 20% of TKA patients are dissatisfied after surgery with post-operative pain being one of the main causes [7–9]. Adequate pain management and thus lower pain scores after surgery appear to be key factors in ensuring patient satisfaction, preventing persistent pain, facilitating early mobilisation and shortening the hospital length of stay (LOS) [10–12]. The recommended systemic analgesia for high-intensity post-operative pain is oral multimodal analgesia [13–14]. In addition, intraoperative periarticular multimodal drug injection (local infiltration anaesthesia, LIA) is an effective way to treat early post-operative pain [15].

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Oxycodone is the most used post-operative opioid in Finland and a host of other countries, and its use increases worldwide [16–18]. In HUS Helsinki University Hospital, patients undergoing TKA usually receive post-operative oral opioids (oxycodone) as a part of multimodal analgesia unless they are incapable of swallowing due to nausea or vomiting. In these cases, other modes of administration, such as intramuscular or intravenous routes, are used.

Patient-controlled analgesia (PCA) is a method of pain management whereby patients can administer their own pain medication. One commonly used form of PCA is a device with which patients receive a predetermined intravenous dose of opioids by pushing a button. PCA is associated with better pain control, and patients seem to prefer it to other methods [19–20]. It has been suggested that PCA might encourage patients to use more opioids compared to conventional methods of administration, but the evidence is inconclusive due to the heterogeneity of the relevant studies [19, 20].

In order to improve patient satisfaction after TKA, we have increased the use of PCA devices as part of multimodal post-operative pain management in our hospital. We also used PCA in a randomised clinical trial on the effects of anaesthesia and surgical tourniquets on TKA [21] as a measure of acute post-surgical pain, as has previously been commonly used in pain research [22]. Before incorporating PCA devices into the routine TKA pain management protocol, we wanted to ensure that the devices would not lead to safety problems, and especially to an excessive use of opioids. In this study, we aimed to investigate whether there were any differences in opioid consumption, incidence of post-operative nausea and vomiting and LOS between patients who were using PCA and those who were not. We also evaluated adverse event reports associated with opioid medication from the study period.

Methods

Ethics

The study design was approved by the HUH Ethics Committee (ref. HUS/1831/2017). The study was funded by a HUS Helsinki University Hospital government science grant (no. TYH2017239).

Patients

This retrospective cohort study comprised 164 patients who underwent TKA as a treatment for osteoarthrosis at HUS between 2016 and 2017. In the PCA group, 82 patients received post-operative opioid medication via intravenous PCA devices, while 82 patients in the control group received oral medication administered by nurses. Patients in the PCA group were recruited in a randomised controlled trial comparing the possible effect of general and spinal anaesthesia with and without a tourniquet on the outcomes of total knee arthroplasty (EudraCT 2016-002035-15, ClinicalTrials.gov NCT03364088) [21]. The control group consisted of consecutive patients selected retrospectively amongst patients who had undergone primary TKA with patellar resurfacing.

We included patients with an American Society of Anesthesiologists (ASA) Physical Status classification level between I and III who were 75 years old or younger and did not use strong opioids before surgery. Exclusion criteria were renal insufficiency, liver failure, bilateral TKA and the use of epidural catheter or femoral nerve block in post-operative pain management. The criteria were the same for both the PCA and the control group.

Intra- and post-operative care

All procedures were performed by the same experienced arthroplasty surgeons according to our standard operating protocol under spinal anaesthesia with isobaric bupivacaine (Bicain Spinal, Orion, Espoo, Finland), and patients were lightly sedated with propofol infusion. During the surgery, before wound closure, all patients received LIA with ropivacaine, epinephrine and ketorolac.

Post-operative pain medication after TKA included non-steroidal anti-inflammatory drugs and paracetamol. PCA devices were provided to intervention group for the first 24 post-operative hours. The devices were programmed to allow a maximum of four oxycodone doses of 0.04 mg/kg of ideal body weight/hour. The lockout intervals between doses were 10 min. After the PCA, the intervention group received one oral dose of prolonged-release oxycodone (5–15 mg), and immediate-release oxycodone tablets (5–15 mg) on demand [21]. The control group received postoperatively three doses of oral prolonged-release oxycodone (5–15 mg) twice a day, and 5–15 mg of immediate release oxycodone on demand, according to the anaesthesiologists' instructions. To prevent the common side effects of pain medication, the patients also received daily doses of proton-pump inhibitors, laxatives and anti-emetics as needed. If analgesia was insufficient for high-intensity pain, oral pregabalin, femoral nerve block or epidural analgesia were used as rescue analgesia.

Study outcomes

The primary outcome was the total consumption of opioids during the first 24 post-operative hours, as measured by intravenous morphine-equivalent doses. All opioids, which patients received according to the electronic patient record, were converted to equivalent doses using conversion tables from the literature and summaries of product characteristics [Table 1, 23–25].

Table 1: Conversion ratios of opioid doses.

Oxycodone hydrochloride	Oxycodone	1: 0.9
Oxycodone hydrochloride trihydrate	Oxycodone	1: 0.78
Oxycodone oral	Oxycodone intravenous	1: 0.6
Oxycodone intravenous	Morphine intravenous	1: 1.5
Pethidine intravenous	Morphine intravenous	1: 0.1

Secondary outcomes were the use of anti-emetic medication and the LOS after the operation. We also evaluated adverse events reported during the study period.

Data and analysis

For sample size calculations, we used two-tailed tests, alpha 0.05, 80% power, and parametric methods to compare the mean differences between groups and expanded the results by 16% to adjust for possible non-parametric analyses. We used data by Harsten and colleagues [26] to approximate opioid consumption of TKA patients. In order to detect a 20% clinically significant difference in opioid consumption, a minimum sample size of 73 patients per group was required.

After forming the groups, we collected data from the electronic patient record and tabulated variables using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). The obtained data included age, gender, body weight and height, ASA scores, intraoperative variables, post-operative use of analgesics and anti-emetics, LOS and in-hospital post-operative complications (deviations from standard care recorded in electronic patient records, comprising e.g. anaesthetists' consultations, deviations from protocol medication or care, new symptoms and diagnoses, medical emergency team calls, transfers to intensive care unit, resuscitations). In addition, we identified all opioid-related notifications from our postanaesthesia care unit and surgical wards included in the Finnish patient safety reporting system HaiPro in 2016–2017.

All analyses were performed with the help of an independent biostatistician. To compare the variables between the study groups, we used independent-samples t-test, Mann–Whitney U-test and Pearson's chi-square test. The variables were tested for normality with Q–Q plots. A permutation test using 100 000 permutations was used to test the difference in interquartile ranges between the groups. As we did not detect any missing values, they were not imputed. A value of $p \leq 0.05$ was considered statistically significant. For continuous variables, the results were expressed as median and interquartile range (IQR) when the data were not normally distributed; otherwise, means with standard deviations were reported.

Results

The characteristics of the 164 patients in the PCA (82) and control (82) groups are presented in Table 2. The median values of opioid consumption expressed as intravenous morphine equivalents did not differ: 41.1 mg (IQR: 29.5–69.1 mg) in the PCA group and 40.5 mg (IQR: 32.4–48.6 mg) in the control group (p=0.35) (Figure 1). The interquartile range of opioid doses was significantly wider in the PCA group compared to the control group (p=0.005).

We did not find a statistically significant difference in the use of anti-emetic drugs between the two groups (p=0.86). In the PCA group, 22 patients (26.8 %) received anti-emetics within the first 24 post-operative hours; the respective number in the control group was 23 (28.0 %). The median LOS was 2 days (IQR: 2–3 days) in the PCA group and 3 days (IQR: 2–3 days) in the control group, with a statistically significant difference (p=0.02).

Table 2: Patient characteristics.

	PCA-group (n=82)	Control group (n=82)	p-Value
Age (years)[a]	64.1 ± 7.6	62.2 ± 8.3	0.13
Female gender, n (%)	54 (65.9)	52 (63.4)	0.74
Height (cm)[a]	169 ± 9	171 ± 9	0.29
Weight (kg)[a]	88.5 ± 15.7	85.4 ± 16.7	0.22
Body mass index (kg/m^2)[a]	30.7 ± 4.5	29.2 ± 4.8	0.031
Pre-operative ASA score, n (%)			0.94
1	8 (9.8)	9 (11.0)	
2	43 (52.4)	41 (50.0)	
3	31 (37.8)	32 (39.0)	

Mean ± SD. Control group = Nurse administered analgesia; PCA = Patient controlled analgesia; ASA = American Society for Anesthesiologists' Physical Status Classification System.

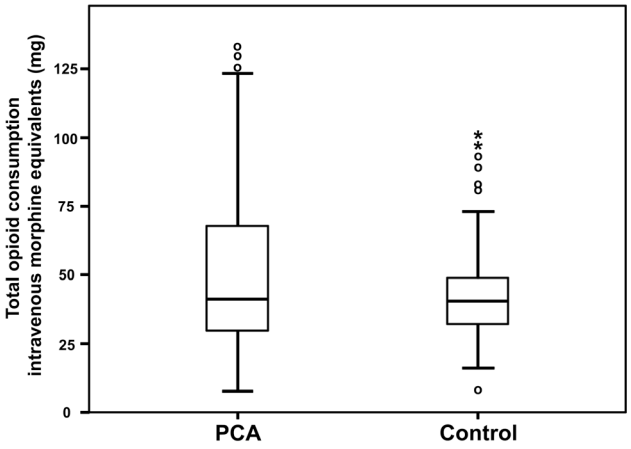

Figure 1: Total opioid consumption in intravenous morphine equivalents. Control = conventional nurse-administered analgesia. PCA = patient-controlled analgesia. Outlying values are marked as circles (values < lower quartile +1.5 × interquartile range [IQR] and values > upper quartile +1.5 × IQR) and stars (values > upper quartile +3 × IQR).

In this patient cohort, we identified few post-operative complications. Two patients in the control group were diagnosed with pneumonia. One patient in the control group required a Medical Emergency Team consultation due to hypotension, but no further interventions were needed. In the PCA group, one patient developed delirium after surgery. No acute thromboembolic complications were recorded. We identified three HaiPro patient safety reporting system notifications concerning PCA devices and oral opioid medication during the study period. Two reports related to PCA were made due to incorrect connection of infusion catheters in the post-anaesthesia care unit (PACU). Personnel reported one case where the patient accidentally received a wrong dose of oral long-release oxycodone.

Discussion

Our results indicate that TKA patients' post-operative opioid consumption is not affected by the method of administration (PCA vs oral). This is in line with a Cochrane Review [19, 20], although the studies included therein were not observing TKA patients but mostly patients undergoing abdominal and cardiothoracic surgery. While nowadays misuse and abuse of prescribed opioids is a real concern [27], and patients could use more opioids than needed through PCA, our results suggest that the post-operative use of an intravenous PCA device does not lead to heavier in-hospital opioid consumption among opioid-naïve patients.

We found that the variation in the total doses of opioids used in the first 24 h was wider in the PCA group. The wide variation in the opioid demand, which we detected in the PCA group, is previously shown to be linked to patients age and genetic predisposition [28–30]. The difference in variations between the PCA and nurse-administered groups may indicate that some patients do not receive sufficient pain medication when it is delivered by a nurse, whereas some patients might take unnecessarily large doses of opioids. Better identification of patients who require either very small or large doses of analgesics for adequate pain control could promote more individualised care. It is notable that patients in the control group had to request additional short-acting opioids. As this can sometimes cause significant delays, some patients may have requested but not received additional pain medication within the first 24 h. The elimination of delays in opioid administration via PCA has been suggested as of the major reasons for the greater patient satisfaction in previous studies [19–20].

Patients who used PCA did not consume more antiemetics than patients who received oral opioids. In agreement, a Cochrane Review by McNicol and colleagues on postoperative pain showed no differences in nausea, vomiting or both between the PCA or non-PCA groups [19]. Also, a meta-analysis by Ballantyne and colleagues showed better pain relief with PCA without an increase in adverse events such as nasea and vomiting [20].

In our patient cohort, there was a small but statistically significant difference in the LOS in favour of the PCA group. It has been suggested that older age and higher body mass index (BMI) or ASA scores are predictors of longer LOS after TKA [31–33]; however, in our study these factors do not explain the difference. While PCA itself does not shorten the LOS [19], better pain control might do so [10]. The observed shortened LOS might be due to better pain control through PCA or other unidentified factors.

Although PCA offers important advantages over the traditional oral administration of opioids, safety concerns are obvious. In the period 2000–2004, approximately 1% of registered medication errors in the USA were related to PCA analgesia, and the majority of medication mistakes were caused by human factors [34]. During our one-year study period, we found two PCA-related risk event notifications about misconnected infusion catheters. Additional employee education and training in the operation of PCA devices could prevent these errors. However, there was also one registered notification about an incorrect dose of oral oxycodone, a reminder that medical errors also happen with oral medication, not only with devices.

As a retrospective study, this study has limitations, among which the possibility of selection bias due to lack of randomization is the most important one. The patients of the intervention group were part of another randomized trial. Due to same exclusion criteria used in this study it is likely that the control group patients were not included to the randomized trial due to organizational reasons or unwillingness to participate in the randomized trial. Due to the participation in the randomized trial, however, patients in the intervention group could have had a more standardized treatment regime than the control group despite the standard operating protocols of our clinic. Neither the participants nor the caregivers were blinded. Moreover, we were not able to measure all key variables, such as intensity of pain, nausea, and patient satisfaction. Unfortunately, the number of patients was not sufficient for making conclusions about rare adverse events.

In summary, our results suggest that the administration of oxycodone via intravenous PCA does not lead to increased opioid or anti-emetic consumption compared to nurse-administered oral oxycodone medication after total knee arthroplasty. There is more variation in oxycodone consumption in the PCA group compared to the nurse-administered oral oxycodone group. PCA analgesia might lead to shortened length of stay. A prospective randomised study is needed to confirm the results, and to identify the patients who might benefit from the use of a PCA device the most.

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Conflict of interest: Authors state no conflict of interest.

Informed consent: According to the approval by the HUH Ethics Committee (ref. HUS/1831/2017), no informed consent was required for this retrospective database study, covering the period 2016–2017.

Ethical approval: The study was approved by the HUH Ethics Committee (ref. HUS/1831/2017).

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