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Perioperative steroid administration improves knee function and reduces opioid consumption in bilateral total knee arthroplasty

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ABSTRACT

Introduction: The benefits of steroid usage have been well described for unilateral total knee arthroplasty (TKA), however its benefits in bilateral TKA has not been well published in the literature. We describe the impact of perioperative steroid administration in a cohort of bilateral TKAs (74 knees) with regard to immediate post-operative knee function, postoperative knee strength and opioid consumption.

Materials and methods: We report on a single-surgeon consecutive case series of simultaneously-performed bilateral TKAs. Eighteen patients received 2 doses of 8 mg IV dexamethasone in the perioperative setting. There were 19 patients in the control group. Primary outcome measures were day 1 postoperative knee flexion (degrees), knee strength and postoperative analgesic requirements (mg/mcg). Morphine dose equivalents (MDE) were calculated to compare all opioid-based analgesics. Secondary outcomes included post-operative pain according to the VAS (at 24, 48 and 72 h), anti-emetic requirements (mg) and length of stay (days).

Results: The mean knee flexion achieved day 1 in the steroid group was 70.1° ($\sigma = 17.64$, 95% CI 64.1–76.0) compared to 55.8° in the non-steroid group ($\sigma = 19.8$, 95% CI 49.2–62.3) ($p = 0.0008$). Regarding the straight leg raise, 88.9% of the steroid group were able to achieve this compared to only 55.2% of the non-steroid group ($p = 0.002$). There was a reduction in the MDE requirement per patient across all medications for the 'steroid' group. Both Targin® ($p = 0.03$) (Prolonged-Release Oxycodone) and Fentanyl ($p = 0.01$) requirements were significantly reduced in the 'steroid' group.

Conclusion: We recommend the use of perioperative steroids in bilateral TKA to allow accelerated rehabilitation, improved immediate knee function and an overall reduction in the consumption of potentially problematic opioid-based analgesics.

1. Introduction

Total Knee Arthroplasty (TKA) is a common orthopaedic procedure. Some 1.2% of all TKAs are performed as part of bilateral procedures.¹ Performing simultaneous procedures has shown to be more cost-effective for hospitals and patients over staged procedures.^{2–4} In addition, the need for only 1 recovery period for bilateral TKAs compared to 2 recovery periods for staged TKAs is very desirable from the patient's perspective.

Enhanced acute recovery after bilateral TKAs is achievable with certain perioperative measures such as steroid administration. Enhanced recovery and early engagement with postoperative physiotherapy is already known to improve functional outcomes post unilateral TKA.⁵ The use of perioperative steroid administration has been effective in this regard for unilateral TKAs.^{6–11} The benefits of steroid administration in

unilateral TKA also include a reduced length of stay and a reduced postoperative readmission rate.^{12–14} The benefits of steroids in simultaneous bilateral TKAs have not been well described in the literature.

In light of the growing concerns around the perioperative opioid consumption in arthroplasty patients, measures are now being taken to restrict patient exposure to these highly addictive and potentially lethal medications.^{15–18} Perioperative steroid administration is one such measure and so we explore the impact of perioperative steroid administration in a cohort of bilateral TKAs with regard to immediate post-operative knee function, postoperative knee strength and overall opioid consumption.

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2. Methods

2.1. Study design

This was a single-surgeon consecutive case series of simultaneously-performed bilateral TKAs from November 2014 through to September 2019. All patients received a fixed-bearing posterior stabilised prosthesis using gap balancing techniques (Attune® Knee System, DePuy Synthes, Warsaw, Indiana, USA) (Fig. 1). From 2014 to 2016, all bilateral TKAs were performed without the administration of any corticosteroid. These patients comprised the ‘non-steroid’ group. In May 2016, a protocol was introduced specifying that all patients undergoing bilateral TKAs receive 8 mg of IV dexamethasone intraoperatively followed by 8 mg of IV dexamethasone 24 h postoperatively. This consecutive prospective patient cohort comprised the ‘steroid group’. All procedures across both cohorts were performed under spinal anaesthesia supplemented with a regional nerve block, intra-operative peri-capsular local anaesthetic and tranexamic acid. All patients received standardised post-operative anti-coagulation and foot-pumps.

2.2. Analgesic protocol

All patients in the immediate post-operative period were prescribed regular prolonged-release oxycodone (Oxycontin® and Targin®), with additional immediate-release oxycodone (Oxynorm®) available as requested by the patient for break-through pain. Other opioid medications such as fentanyl, morphine, tapentadol and tramadol were used at the discretion of the prescribing physician. A direct comparison of all opioid-based analgesics was possible by converting all prescribed opioid medications into ‘morphine dose equivalents’ (MDE). It was then possible to objectively assess and compare the amount of opioid based analgesia all patients were requiring.

Non-steroidal anti-inflammatory drugs (NSAIDs) prescribed included diclofenac, ibuprofen and naproxen. Other miscellaneous analgesics used included paracetamol, parecoxib, pregabalin, clonidine, pethidine and diazepam. Paracetamol was prescribed for all patients. All others were prescribed based on the prescribing physician’s discretion. The three main types of anti-emetics used were ondansetron, prochlorperazine and cyclizine. Physiotherapy was commenced as soon as patients were able to engage on the same day of surgery when possible.

2.3. Selection criteria

Inclusion criteria were all bilateral total knee arthroplasty patients with complete datasets pertaining to objective ROM, analgesic

requirements and subjective VAS scores. Patients were excluded if already administering corticosteroids preoperatively or if datasets were incomplete. Patients were identified using theatre operating logs for the respective time frame. Data was then extracted from their clinical charts and recorded for statistical analysis.

2.4. Outcomes

The primary outcomes were day 1 postoperative knee flexion (degrees), knee strength and postoperative analgesic requirements (mg/mcg). The straight leg raise with the patient in the supine position was taken as a surrogate marker for knee strength in this instance. Knee flexion was assessed using a goniometer by a specialist musculoskeletal physiotherapist. Secondary outcomes included post-operative pain according to the VAS (at 24, 48 and 72 h), anti-emetic requirements (mg) and length of stay (days).

2.5. Statistics

Descriptive statistics were used to assess patient demographics and intergroup variability. Patient age, gender and BMI were all recorded. In order to analyse the impact of steroid administration on interval outcome variables, the *two-sample t-test with equal variances* was used. The relationship between two categorical variables was analysed using the *chi-squared test* when all groups had a sample size of at least 5. If this criterion was not met, *Fisher’s exact test* was used. A p-value of 0.05 was taken to be statistically significant. All statistical analyses were performed using the software Stata/IC 13.1 for Mac (64-bit Intel).

3. Results

3.1. Demographics

Nine patients were excluded due to regular preoperative steroid administration. Thirty seven patients (74 knees) were eligible for inclusion. In total, there were 19 patients in the ‘non-steroid’ cohort and 18 in the ‘steroid’ cohort. Mean patient age was 61.1 years ($\sigma = 9.16$, 3.9–77.8). The mean age in the ‘steroid’ group was 63.4 years compared to 58.4 in the ‘non-steroid’ group. In the ‘steroid’ group, there were 12 females and 6 males compared to 8 females and 11 males in the ‘non-steroid’ group. The overall mean BMI was 31.3 ($\sigma = 4.76$, 23.7–41.6), with a mean BMI of 30.2 in the ‘steroid’ group and 32.4 in the ‘non-steroid’ group. The operative indication in all cases was osteoarthritis except for 1 patient in the ‘non-steroid’ group where the indication for surgery was rheumatoid arthritis.

Fig. 1. Postoperative radiographs of bilateral TKA.

3.2. Knee function

When considering all 74 knees, the 'steroid' group had significantly improved knee flexion and knee strength on the first day after surgery. The mean knee flexion achieved day 1 in the 'steroid' group was 70.1° ($\sigma = 17.64$, 95% CI 64.1–76.0) compared to 55.8° in the 'non-steroid' group ($\sigma = 19.8$, 95% CI 49.2–62.3) ($p = 0.0008$). For right knees exclusively, the mean flexion was 71.3° ($\sigma = 17.5$, 95% CI 62.6–80.0) in the 'steroid' group compared to 56.3° ($\sigma = 19.9$, 95% CI 46.7–65.9) in the 'non-steroid' group ($p = 0.01$). For left knees exclusively, the mean flexion was 68.8° ($\sigma = 18.1$, 95% CI 59.8–77.9) in the 'steroid' group compared to 55.2° ($\sigma = 20.3$, 95% CI 45.4–65.0) in the 'non-steroid' group ($p = 0.019$) (Fig. 2).

Of the 36 knees in the 'steroid' cohort, 32 were able to straight leg raise on day 1. Of the 38 knees in the 'non-steroid' cohort, 21 were able to straight leg raise on day 1. There was a significant difference in outcome with 88.9% of the steroid group being able to achieve a straight leg raise compared to only 55.2% of the non-steroid group ($p = 0.002$).

3.3. Analgesic requirements and VAS

Regarding opioid analgesic medications, we noted a reduction in the MDE requirement per patient across all medications for the 'steroid' group. Both Targin® ($p = 0.03$) (*Prolonged-Release Oxycodone*) and Fentanyl ($p = 0.01$) requirements were significantly reduced in the 'steroid' group. The mean Targin® requirement in the steroid group was 96.8 mg ($\sigma = 45.5$, 95% CI 58.7–134.9) in the 'steroid' group compared to a significantly higher mean requirement in the 'non-steroid' group of 170 mg ($\sigma = 14.1$, 95% CI 42.9–97.0) ($p = 0.031$). Regarding fentanyl requirements, the mean fentanyl requirement in the 'steroid' group was 66.25 mcg ($\sigma = 13.7$, 95% CI 44.3–88.1) in the steroid group compared to a significantly higher mean requirement in the 'non-steroid' group of 100 mcg ($\sigma = 0$, 95% CI 100) ($p = 0.015$). Oxycotin® (PR Oxycodone), Oxynorm® (IR Oxycodone), Morphine and Tramadol all showed a trend toward reduced requirement in the 'steroid' group (Table 1). On analysis of antiemetic requirements, there were no significant differences noted between the two groups.

VAS analysis demonstrated no difference between the 2 groups at any timepoint. At 24 h, the mean 'steroid' group VAS was 4.88 ($\sigma = 2.72$, 95% CI 3.53–6.24) compared to 4.73 ($\sigma = 2.23$, 95% CI 3.66–5.81) in the 'non-steroid' group ($p = 0.57$). At 48 h, the mean 'steroid' group VAS was 3.94 ($\sigma = 2.6$, 95% CI 2.65–5.23) compared to 3.89 ($\sigma = 2.9$, 95% CI 2.49–5.29) in the 'non-steroid' group ($p = 0.52$). At 72 h, the mean 'steroid' group VAS was 2.77 ($\sigma = 2.41$, 95% CI 1.57–3.97) compared to 2.89 ($\sigma = 2.05$, 95% CI 1.90–3.88) in the 'non-steroid' group ($p = 0.43$).

3.4. Length of stay

For the entire group, the mean length of stay was 4.9 days ($\sigma = 1.18$,

2–8). The 'steroid' group did have a slightly lower total LOS at 4.7 days compared to 5.1 days in the 'non-steroid' group ($p = 0.16$).

4. Discussion

In the context of lower limb arthroplasty, prolonged opioid usage in the perioperative period has been associated with opioid dependence, higher rates of revision arthroplasty surgery and an increase in mortality rate.¹⁵ International experience would also suggest that the use of perioperative opioids increases the rate of hospital readmission post lower limb arthroplasty and the length of stay in hospital after these procedures.^{16,17} Numerous efforts have been made to both understand and mitigate the factors contributing to opioid abuse in the context of lower limb arthroplasty.^{18–20}

One method of reducing the reliance on opioids has been to administer perioperative corticosteroids. The use of corticosteroids in unilateral lower limb arthroplasty has been demonstrated to reduce patient opioid consumption and postoperative pain^{6,9,10,21,22}. The impact of steroid usage on bilateral TKA has been explored by Jules-Elysee et al. in 2 separate studies.^{23,24} Using three doses of IV hydrocortisone in 68 knees demonstrated a reduction in patient reliance on their epidural PCA.²⁴ Neither of these studies directly described the impact of corticosteroids on the amount of opioids required however, and so we demonstrate this effect in bilateral TKA for the first time.

For the six opioid-based medications prescribed in this cohort, we noted a reduction in the dosage required by the 'steroid' group across every medication whilst still achieving a comparable VAS to the 'non-steroid' group. Although there were no differences noted in the VAS across the two groups, we can infer that, since the 'steroid' group required less analgesia overall to achieve a similar VAS to the 'non-steroid' group, the pain experienced by the 'steroid' group was less severe. Using morphine dose equivalents, we were able to measure the reduction in opioid prescriptions received by the 'steroid' group. Two of these (Targin® and Fentanyl) were noted to have a significantly reduced MDE per patient in the 'steroid' group compare to the 'non-steroid' group. The remaining 4 medications were all trending towards lower dosage in the 'steroid' group. Our speculation is that increased power in future studies will likely demonstrate a similar effect across all opioid-based medications. The impact of steroid administration on reducing the opioid requirements for patients undergoing bilateral TKA is homogenous in this cohort and may provide a real solution to the current issue of opioid-related issues in the field of arthroplasty.

The precise mechanism through which steroid administration improves knee function and reduces subjective pain post TKA is still being researched. IL-6 is suggested to play an important role in this process by reducing inflammation at the operative site.²⁴ We describe a two-dose 8 mg IV dexamethasone protocol over 24 h that results in excellent rates of knee flexion in the patients receiving steroid over those that did not. We corroborate the results in this regard reported by Jules-Elysee et al.²⁴

Fig. 2. Left and right knee mean flexion.

Table 1

Morphine Dose Equivalents for all opioid-based analgesics
(*MDE = Morphine Dose Equivalent).

Medication	Non-Steroid V Steroid	Potency ratio to PO Morphine	Sum Total MDE* administered	MDE per patient	Steroid-induced MDE reduction per patient	p-value
Oxycontin® (PR Oxycodone)	Non-Steroid	2	3,660 mg	215 mg		0.29
	Steroid	2	3,400 mg	188 mg	- 28 mg	0.29
Oxynorm® (IR Oxycodone)	Non-Steroid	2	2,850 mg	158 mg		0.21
	Steroid	2	2,360 mg	131 mg	-27mg	0.21
Targin® (PR Oxycodone)	Non-Steroid	2	680 mg	340 mg		0.03
	Steroid	2	1,550 mg	193.75 mg	-146.25 mg	0.03
Fentanyl	Non-Steroid	100	20 mg	10 mg		0.01
	Steroid	100	27 mg	6.75 mg	-3.25 mg	0.01
Morphine	Non-Steroid	1	4 mg	4 mg		–
	Steroid	1	7 mg	3.5 mg	-0.5 mg	–
Tramadol	Non-Steroid	0.15	221 mg	36.8 mg		–
	Steroid	0.15	15 mg	15 mg	-21.8 mg	–

Unlike Jules-Elysee et al., we also proceed to investigate the improvement in knee strength as suggested by the patient's ability to straight leg raise in the supine position on postoperative day 1. In the 'steroid' group, 88.9% of patients were able to straight leg raise compared to 55.2% in the 'non-steroid' group. This is a significant finding and leads us to the conclusion that perioperative steroid administration not only improves knee flexion and reduces opioid consumption, but it also significantly improves the patient's strength on the first day after surgery. Improving the patients ability to engage with physiotherapists in an accelerated rehabilitation pathway has been shown to reduce the patient's length of hospital stay and reduce the cost of providing TKA by the relevant institution.²⁵

Limitations include our sample size. Although this is the largest bilateral TKA cohort assessing the role of corticosteroid usage in bilateral TKA, larger numbers may have demonstrated significant reductions in the MDE per patient for all 6 opioid-based medications prescribed. This study was not contemporaneous in nature, resulting in the steroid cohort TKAs being performed later in the primary surgeons career at a time when they would have had more operative experience. The time frame for the entire study was short enough however so as to ensure that this learning curve effect is likely to be minimal. We did not record any infections in either cohort. Longer follow-up of this cohort will be necessary to detect any issue with infection in future.

5. Conclusion

Whilst corticosteroid usage has been shown to be of benefit in unilateral TKA, there is a paucity of published literature demonstrating its effectiveness in bilateral TKA. Perioperative corticosteroid use in bilateral TKA significantly improves day 1 knee flexion, knee strength and reduces opioid requirements. We recommend the use of perioperative steroids in bilateral TKA to allow accelerated rehabilitation, improved immediate knee function in the postoperative period and an overall reduction in the consumption of potentially problematic opioid-based analgesics.

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Declaration of competing interest

No competing interests are noted from any of the authors in relation to this research.

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