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ORIGINAL PAPER

# Peri-articular injection of an analgesic mixture in primary total hip arthroplasty: an effective strategy for pain control during the first post-operative day

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## Abstract

**Background** Previous studies of soft tissue infiltration in hip arthroplasty present variable results. The purpose of this study is to identify whether injection of an analgesic mixture improves pain management during the immediate post-operative period.

**Materials and methods** This cohort study compared 129 patients that received peri-articular soft tissue injection with 20 ml of 0.25% bupivacaine and 2 ml of ketorolac (30 mg/1 ml) in 28 ml of saline solution, with 71 patients who did not received injections. Pain intensity in the Verbal Analog Scale (VAS), opioid titration, and consumption (mg morphine equivalents) in the post-anaesthetic care unit (PACU) and during the first post-operative day were assessed for both groups. All patients received the same analgesia protocol.

**Results** Median VAS score in the PACU was 4 (IQR 2–7) in the injection group and 7 (IQR 4–8) in the non-injection group ($p = 0.001$). Median opioid titration was 0 mg for the injection group and 2.6 mg for the non-injection group ($p = 0.011$). In the first post-operative day, the difference in VAS scores between groups was statistically significant ($p = 0.009$), but there was no difference in opioid consumption.

**Conclusion** Soft tissue injection with local anesthetics and non-steroidal anti-inflammatory drugs allows adequate pain control in the immediate post-operative period and reduces the requirement for opioid consumption. We recommend the implementation of this safe and effective strategy in post-operative pain management after primary hip arthroplasty.

Level of evidence: Level II, cohort study.

**Keywords** Hip arthroplasty · Hip replacement · Pain · Post-operative · Pain management · Local anaesthesia

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## Introduction

Adequate pain control during the post-operative period of hip arthroplasty allows early mobilization and rehabilitation, decreases the rate of complications, reduces the length of hospitalization [1–3], and is associated with patients' satisfaction with the procedure [4, 5].

Over the years, different strategies for pain control after major orthopaedic surgery have been implemented. These include the use of multimodal analgesia, in which both local anesthetics and systemic analgesics with different mechanisms of action are combined [6–8]. This concept is based on combining medications with additive or synergistic effects, to effectively reduce post-operative pain, with a minimum consumption of opioids and minimal side effects associated with its use [9, 10].

More recently, the use of analgesics and anaesthetics for peri-articular soft tissue infiltration or intra-articular injection has increased significantly [11, 12]. This is a simple and safe procedure [12] that has demonstrated to be effective in post-operative pain control [13] and reduces the costs associated with health care [14].

However, the evidence available up to date is limited [11] due to the low external validity of the published studies, defects in the design of randomized control trials, and to the lack of standardization of the post-operative pain management approaches [10, 12]. Therefore, the need of a standardized protocol, which is able to isolate the effect of the local injection, arises.

The aim of this study is to determine whether an analgesic mixture injected both in peri-articular and subcutaneous soft tissues improves pain control during the first 24 hours after total hip arthroplasty.

## Materials and methods

This non-randomized cohort study included all hip arthroplasty patients between February 2015 and March 2016. In our institution, every patient who undergoes hip arthroplasty is enrolled in an institutional arthroplasty register and clinical outcomes are collected prospectively including pain intensity during in-hospital stay and after discharge. Although this information was collected in real time, the design and analysis of this study was conducted after inclusion and outcome measurement, which makes it a retrospective cohort.

Internal Review Board approval was granted to this protocol before it was initiated.

Before surgery, all patients received standard non-operative management of osteoarthritis according to the NICE guidelines [15]. Patients who underwent hip arthroplasty for oncologic pathology, hip arthritis secondary to radiation, hip fractures, and hip arthroplasty through an anterior approach were excluded. In addition, patients who did not receive patient controlled analgesia were excluded due to the limitation to determine the amount of opioid consumption.

From the prospectively collected data of the Institutional Arthroplasty Register, two groups of patients were identified: (1) the study group, including all patients from a single surgeon, who received injection with 20 ml of 0.25% bupivacaine and 2 ml of ketorolac (30 mg/1 ml) in 28 ml of normal saline, and (2) the control group, comprising of consecutive patients from three different surgeons, who did not receive soft tissue injection.

All hip arthroplasties were performed through a posterolateral mini-incision approach. In the study group, after the reattachment of the external rotators (piriformis muscle tendon) and the joint capsule, 20 $cm^3$ of the analgesic/anaesthetic mixture was injected in the posterior capsule and short external rotators as shown in Fig. 1. During this procedure, permanent irrigation and suction is used in order to prevent anesthetic to make contact with sciatic nerve. After this procedure was completed and the fascia sutured, 20 ml of the remaining mixture was injected in the subcutaneous tissue prior to skin closure.

Aside of the infiltration for the study group, all patients in both groups were prescribed with a standard analgesic protocol. The post-operative pain management protocol implemented included the administration of transitional intravenous analgesia with opioids and acetaminophen. In the PACU, opioid titration was initiated according to pain intensity (Verbal Analog Scale (VAS) score), the therapeutic response, and the absence of side effects associated with opioid consumption. During hospitalization, patients received combined oral analgesia with acetaminophen and intravenous opioids through patient-controlled analgesia, as determined by the pain physician. Adequate pain control (analgesic goal) was defined as VAS score less than or equal to 4.

Outcomes assessed were pain intensity reported by patients according to the VAS, opioid titration in the PACU, VAS score

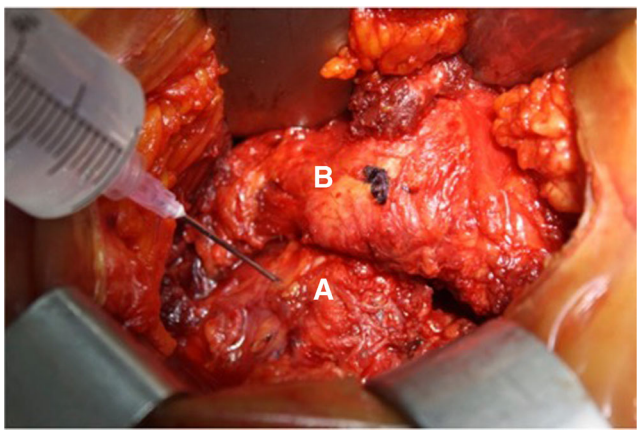


**Fig. 1** Intra-operative picture of the injection of the external rotators and posterior capsule (**a**) after their reattachment to the greater trochanter (**b**)

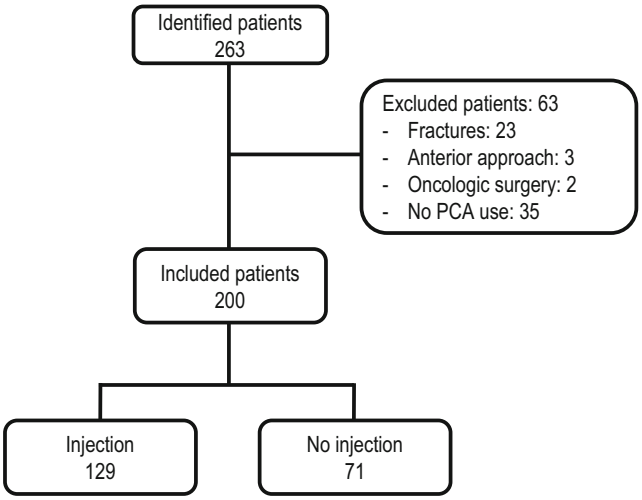


**Fig. 2** Flow diagram of the process of identification and selection of patients included in each study group

and opioid consumption in the first post-operative day, and side effects associated with opioid use. The amount of opioid consumption is expressed in milligram of morphine equivalents. These data were obtained from the Institutional Arthroplasty Register, which collects pain control follow-up information in real time.

The distribution of variables was determined by the Kolmogorov-Smirnov test. For demographic characteristics, type of opioid administered and side effects, frequencies, and averages were used. As pain intensity in the VAS score and opioid consumption are variables of asymmetric distribution, they are presented as medians and interquartile ranges (IQRs). Differences in pain intensity and opioid consumption between groups (injection vs. non-injection) were determined by Mann-Whitney *U* test. Statistical significance was defined as a $p$ value $< 0.05$. Data was processed using the statistical software IBM® SPSS® Statistics version 21 (IBM Corporation, Armonk, NY, USA).

**Table 1** Demographic data of the patients included in the study and details of the anesthetic technique used

| Variable | Total ($N = 200$) | Injection ($N = 129$) | No injection ($N = 71$) |
|---|---|---|---|
| | *n* (%) | | |
| Gender | | | |
| Female | 137 (68.5%) | 81 (62.8%) | 56 (78.9%) |
| Male | 63 (31.5%) | 48 (37.2%) | 15 (21.1%) |
| Anesthetic technique | | | |
| General | 197 (98.5%) | 127 (98.5%) | 70 (98.6%) |
| Regional | 3 (1.5%) | 2 (1.5%) | 1 (1.4%) |
| Tranexamic acid | 151 (75.5%) | 103 (79.8%) | 44 (70%) |
| Transitional analgesia | 198 (99%) | 128 (99.2%) | 70 (98.6%) |
| Hydromorphone | 157 (79.3%) | 92 (71.9%) | 65 (92.2%) |
| Morphine | 15 (7.6%) | 13 (10.2%) | 2 (2.9%) |
| Oxycodone | 22 (11.1%) | 21 (16.4%) | 1 (1.4%) |
| Fentanyl | 1 (0.5%) | 0 | 1 (1.4%) |
| Ketamine | 3 (1.5%) | 2 (1.6%) | 0 |
| | Mean (range) | | |
| Age (years) | 65 (28–90) | 66 (28–90) | 63 (29–85) |
| Surgical time (min) | 111 (59–295) | 114 (74–295) | 104 (59–257) |
| | Mean ± standard deviation | | |
| BMI (kg/m$^2$) | 25.73 ± 3.5 | 25.68 ± 3.1 | 25.81 ± 4.1 |

## Results

During the period of study, 263 hip arthroplasty patients were identified. Of these, 201 patients with diagnosis of primary or secondary osteoarthritis were included in the analysis. One-hundred and twenty-nine (65.2%) patients received injection and 71 (35.9%) patients did not. The patient selection process is represented in Fig. 2.

The 68.5% of the patients were females, the average age was 65 (range 28–90) years old, and the mean body mass index (BMI) was 25.73 ± 3.5 kg/m$^2$. The 98.5% of patients received general anesthesia, which in our hospital is at discretion of the anaesthesiologist, given the general status of health of the patient. Mean surgical time was 111 minutes and 151 patients received intravenous tranexamic acid according to the institutional protocol. Ninety-nine percent of patients received transitional analgesia (Table 1).

For patients in the injection group, the median (and interquartile range) of the VAS score in PACU was 4 (IQR 2–7), while patients in the non-injection group had a median VAS score of 7 (IQR 4–8) ($p = 0.001$) (Fig. 3). From the total of patients in the injection group, 55.8% had adequate pain control (VAS score ≤ 4), whereas only 36.6% form the non-injection group reached analgesic goals.

Of all patients included in the analysis, 79 required opioid titration in the recovery room. Of these, 37 patients were from the injection group and 42 were from the non-injection group. Median opioid consumption in the injection group was 0 mg and the median for the non-injection group was 2.6 mg ($p = 0.002$) (Fig. 4).

In the first postoperative day, the median VAS score of patients in the injection group was 3 (IQR 1–4) and 4 (IQR 2–6) in the non-injection. The difference in these VAS scores between both groups was statistically significant ($p = 0.001$) (Fig. 5). In contrast, there were no statistically significant differences in opioid consumption among groups; the median of opioid use in the injection group was 2.68 mg (morphine equivalents) and 4 mg in the non-injection group ($p = 0.350$) (Table 2).

During the first 24 h after surgery, 18% of all patients ($N = 200$) presented with side effects possibly associated with

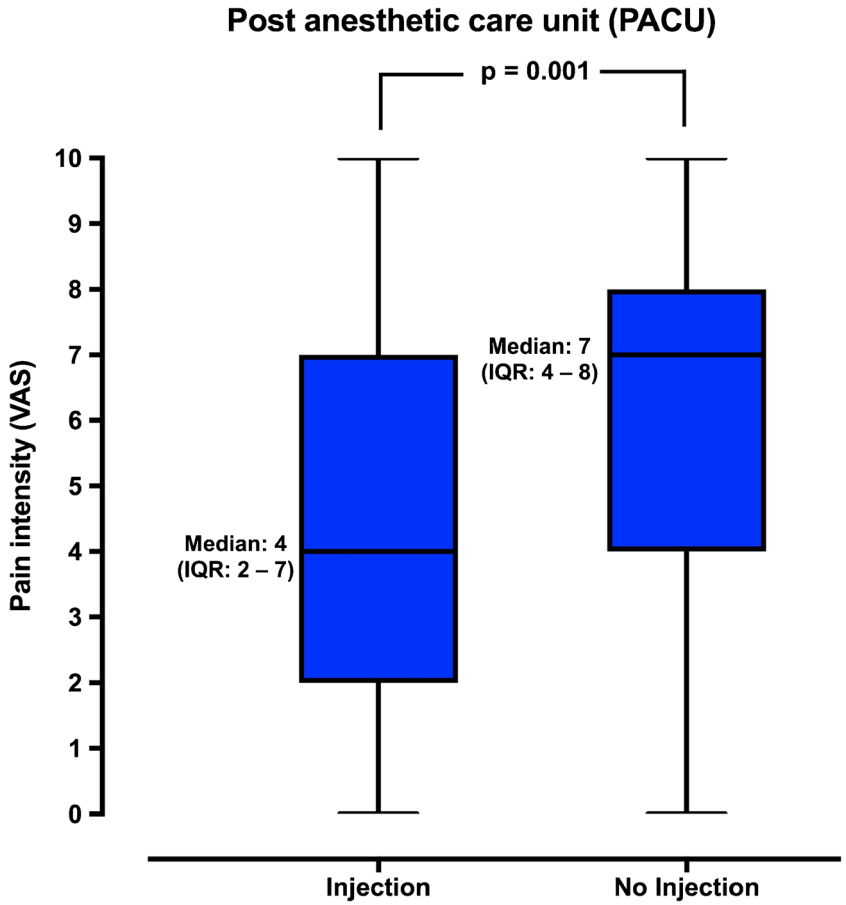


**Fig. 3** Box plot of the median and interquartile range (IQR) of pain intensity according to the verbal analogue scale assessed during the immediate postoperative period in the postanesthetic care unit for patients who received the injection and those who did not, and the *p* value calculated for this difference

opioid consumption. In the soft tissue injection group, 3.8% (26/129) presented with these side effects and 14.0% (10/71) in the non-injection group ($p = 0.28$). There were no neurovascular injuries in either group.

As long as only three patients received spinal anesthesia, no analysis was performed in order to establish differences in pain scores and opioid consumption related to this variable.

## Discussion

Hip arthroplasty is a painful procedure [16]. Despite the fact that different analgesic strategies have been implemented [6–8], most patients still have inadequate postoperative pain control [17], which significantly impacts their outcomes in both medium and long term [1, 3, 18].

Protocols of multimodal analgesia have shown to be effective for pain control [19], and in recent years, injection of soft tissues around the joint has become an adequate option for pain management in patients undergoing hip arthroplasty [12–14]. Nevertheless, the results published to this point are heterogeneous [10, 11]; moreover, the high variability in the mixture of drugs used, the method of injection, and the postoperative analgesia protocols [10–12] limit the applicability of these results. To our knowledge, this is the first time that the effect of the injection of an analgesic mixture in the posterior capsule and short external rotators, in combination with a standardized protocol for post-operative analgesia, is described.

In the present study, it was found that patients who received soft tissue injection had less pain and opioid consumption during the first 24 hours after surgery, compared to those who did not receive the injection, and the differences were statistically significant.

Even though different authors conclude that local injection in hip surgery may not be as effective for pain control as in knee replacement surgery [11], Parvataneni et al. [17], Busch et al. [20], and Kerr et al. [12] showed favourable results with the use of this strategy, and the results obtained in our study evidenced that it is an effective strategy for pain control, at least for the first 24 postoperative hours after primary total hip arthroplasty. A previous study by Villatte et al. did not demonstrated

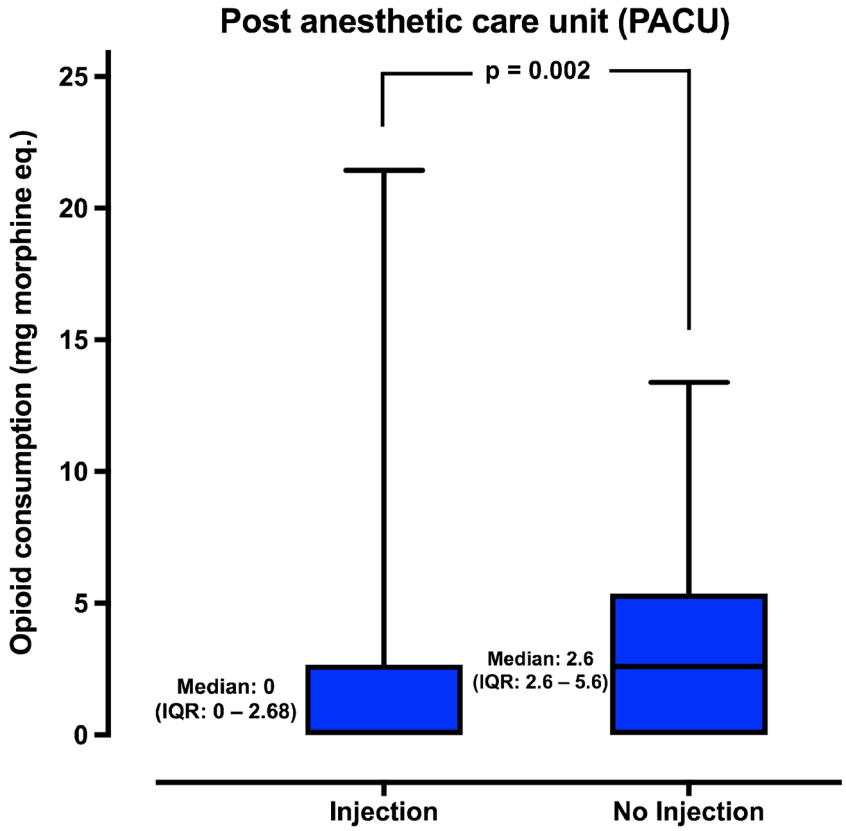


**Fig. 4** Box plot of the median and interquartile range (IQR) of opioid consumption in milligrams of morphine equivalents during the immediate postoperative period in the postanesthetic care unit for patients who received the injection and those who did not, and the *p* value calculated for this difference

differences in favor of peri-articular injection in terms of opioid consumption. However, these results might be due to the fact that the mixture for soft tissue injection did not contained NSAIDs; in addition, authors did not report opioid consumption in the immediate post-operative period when this strategy could represent the highest benefit [21]. In addition, the decrease in opioid consumption during the first hours after surgery is comparable to that reported by Busch et al., where consumption of morphine in 32 patients randomized to receive infiltration was significantly lower compared with patients that did not receive infiltration ($p = 0.0093$) [20].

Other strategies such as the use of continuous analgesic infusion during 24 hours after the procedure do not show significant differences in pain scale scores [19, 22], even when patients undergoing bilateral hip arthroplasty were assessed comparing pain scores in one hip to the contralateral one, thus eliminating the subjective nature of pain [23]. Similarly, Andersen et al., in a randomized controlled trial of the use of intra-articular drug injection during surgery, reported no statistically significant differences in opioid consumption between patients who received intra-articular drug injection during surgery and those who did not [24].

The main limitation of this study is that even though a control group was evaluated, patients were not randomly assigned to either group and the use of placebo was not considered. Additionally, we were unable to determine which patients were consuming narcotics previously, and this might be a shortcoming of this study, given the fact that patients who received opioids before surgery tend to require higher doses after the procedure [25]. Finally, this study only assesses the outcomes during the first 24 hours after surgery, compared with other studies that evaluate mid-term results [11, 21]. However, considering the half-life of the injected drugs and the lack of differences in the results after the first post-operative day, the assessment of outcomes beyond this point does not seem relevant.

On the other hand, the main strengths of this study are the highly standardized post-operative pain management protocol, that data was collected by a third party, blind to injection assignment, and the ability to obtain a systematic and free of biases follow-up. Even though patients from the injection group were from a single surgeon and all of the control patients were from different surgeons, this study was carried out within the framework of a Clinical Care Center with standardized clinical processes, it is very unlikely that subtle differences, if any, the surgical technique produce different results.

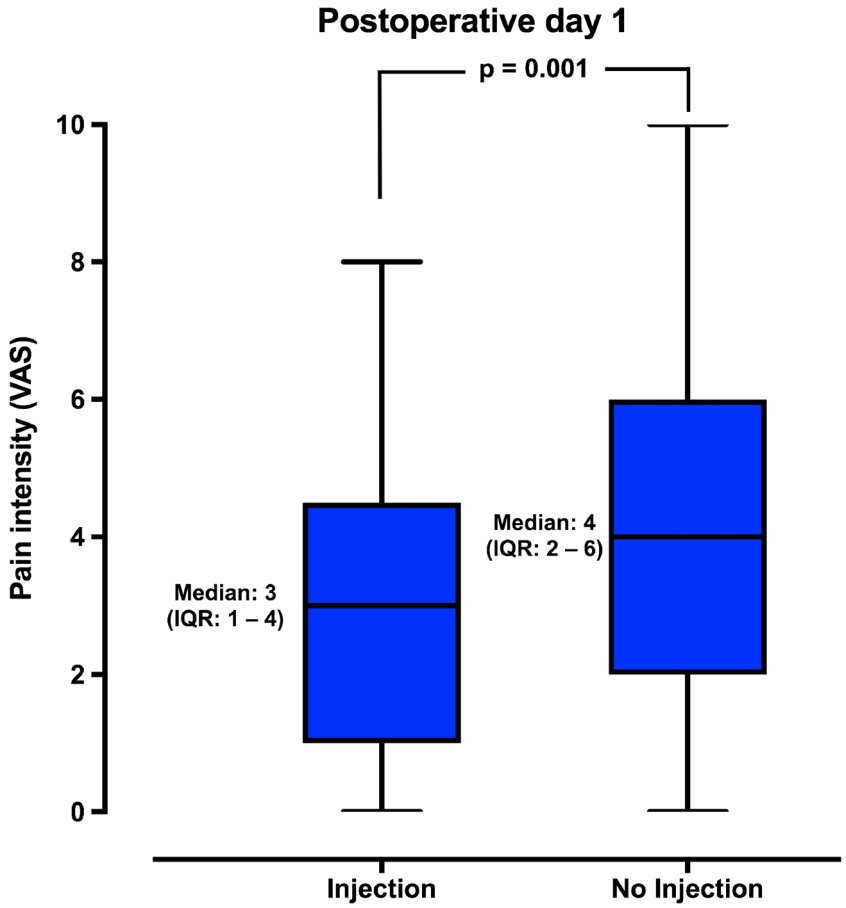


**Fig. 5** Box plot of the median and interquartile range (IQR) of pain intensity according to the verbal analogue scale assessed during the first post-operative day for patients who received the injection and those who did not, and the *p* value calculated for this difference

In addition, given that both statistically significant and clinically evident differences were found, the sample size and power might not be worth of discussion.

The rationale for the use of a mixture containing a local anesthetic agent (Bupivacaine) in order to control pain immediately and a non-steroidal anti-inflammatory (Ketorolac) seeking for a more prolonged effect was that the use of local anaesthetics alone does not produce large difference in pain outcomes [11, 26, 27]. The superior results presented in this study might be explained by the possible synergistic effect between local anaesthetics and non-steroidal anti-inflammatory drugs, an effect that has been previously described [12, 22, 26, 28]. This analgesic effect could be enhanced by the incorporation of epinephrine into the mixture [10, 11, 13]; however, we did not include the use of this pharmaceutical agent.

Although the amount of the clinical benefit shown in this study seems small, we consider it relevant. Since post-operative pain is a multifactorial symptom and pain management is multimodal, we do not seek for a single intervention that produces an enormous improvement, but the sum of multiple

**Table 2** Summary of outcomes: median and interquartile range of pain intensity and opioid consumption by group, assessed in the PACU and first postoperative day, and the *p* value calculated for each difference

| Variable | Injection (*N* = 129) | No injection (*N* = 71) | *p** |
|---|---|---|---|
| Pain intensity (VAS) | Median (interquartile range) | | |
| PACU | 4 (2–7) | 7 (4–8) | 0.001 |
| Post-operative day 1 | 3 (1–4) | 4 (2–6) | 0.001 |
| Opioid consumption (mg morphine eq) | Median (interquartile range) | | |
| PACU | 0 (0–2.68) | 2.6 (2.6–5.6) | 0.002 |
| Post-operative day 1 | 2.68 (0.5–9) | 4 (0–1.7) | 0.350 |

**p* value (Mann-Whitney *U* test)

interventions with small effects which at the end result in a significant improvement.

In conclusion, despite the limitations of this study, soft tissue injection of an analgesic mixture allows adequate pain control and reduces opioid consumption during the immediate post-operative period. Therefore, we recommend the implementation of this safe and effective strategy in pain management protocols after total hip arthroplasty.

## Compliance with ethical standards

**Conflict of interest** Maria Bautista MD MSc has received royalties for research support from a company or supplier as a Principal researcher for Grunenthal and has received financial support for attending symposia from De Puy Synthes (Orthopedics), outside this work. Meilyn Muskus MD declares that she has no conflict of interest. Adolfo Llinás MD has received royalties from Innomed, Novamed, and 3M; has participated as paid speaker for Zimmer, Shire, Novonordisk, Novartis, Johnson & Johnson, Medtronic and Procaps; has participated as paid consultant for Zimmer and Medtronic, outside this work. Guillermo Bonilla MD has participated as paid speaker for Boehringer-Ingelheim, Pfizer, Sanofi, and DePuy Synthes (Orthopedics); has received other financial support from DePuy Synthes (Orthopedics); and has received research support from a company or supplier as a Principal researcher for Grunenthal and Johnson & Johnson, outside this work. Carlos Guerrero MD has participated as paid speaker for Grunenthal, outside this work. Jairo Moyano MD MSc declares that he has no conflict of interest.

**Ethical approval** Internal Review Board approval was granted to this protocol before it was initiated. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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