



OPEN ACCESS

EDITED BY

Tobias Piegeler,
University Hospital Leipzig, Germany

REVIEWED BY

Dmytro Dmytriiev,
National Pirogov Memorial Medical University,
Ukraine
Arsen Uvelin,
Clinical Center of Vojvodina, Serbia

*CORRESPONDENCE

Svetlana Sreckovic
✉ svetlanasreckovic@yahoo.com

RECEIVED 04 February 2025

ACCEPTED 10 April 2025

PUBLISHED 29 April 2025

CITATION

Sreckovic S, Milovanovic D, Vukman P,
Djukanovic M, Simic M, Vesic J, Milenkovic M,
Aleksic M and Ladjecic N (2025) The effect of
adding dexamethasone to adductor block
and IPACK block on acute postoperative,
rebound, and chronic pain following knee
arthroplasty—1-year follow-up.
Front. Med. 12:1570795.
doi: 10.3389/fmed.2025.1570795

COPYRIGHT

© 2025 Sreckovic, Milovanovic, Vukman,
Djukanovic, Simic, Vesic, Milenkovic, Aleksic
and Ladjecic. This is an open-access article
distributed under the terms of the [Creative
Commons Attribution License \(CC BY\)](#). The
use, distribution or reproduction in other
forums is permitted, provided the original
author(s) and the copyright owner(s) are
credited and that the original publication in
this journal is cited, in accordance with
accepted academic practice. No use,
distribution or reproduction is permitted
which does not comply with these terms.

The effect of adding dexamethasone to adductor block and IPACK block on acute postoperative, rebound, and chronic pain following knee arthroplasty—1-year follow-up

Svetlana Sreckovic^{1,2,3*}, Darko Milovanovic^{2,3}, Petar Vukman²,
Marija Djukanovic^{1,3}, Marko Simic^{2,3}, Jovan Vesic²,
Marija Milenkovic^{1,3}, Milica Aleksic² and Nebojsa Ladjecic^{1,3}

¹Centre of Anesthesia and Resuscitation, University Clinical Center of Serbia, Belgrade, Serbia, ²Clinic for Orthopedics Surgery and Traumatology, University Clinical Center of Serbia, Belgrade, Serbia,

³Medical School, University of Belgrade, Belgrade, Serbia

The analgesic efficacy of nerve blocks depends on the duration of local anesthetics, whose effects can be extended with adjuvant drugs. This prospective interventional study aimed to assess the impact of adding dexamethasone to levobupivacaine on the postoperative analgesic efficacy of the adductor canal block (ACB) and IPACK block after knee arthroplasty (TKA), as well as the incidence of rebound and chronic postsurgical pain. One year after TKA, 80 patients were analyzed (dexamethasone vs. control group). Opioid analgesics were administered to 10% of patients in the dexamethasone group and 50% of patients in the control group ($\chi^2 = 13.393$, $p < 0.001$), with no difference in opioid dosage ($p = 0.368$) during the first 24 h postoperatively. Rebound pain was observed in 5% of patients in the dexamethasone group and 30% in the control group ($\chi^2 = 7.013$, $p = 0.008$). Chronic postsurgical pain 1 year after TKA was found in 5% of patients in the control group, without significant differences between the groups. Adding dexamethasone to the local anesthetic for ACB and IPACK blocks, along with a non-opioid scheduling strategy, enhances postoperative pain management, reduces opioid consumption, and helps decrease the occurrence of rebound pain and chronic postsurgical pain 1 year after TKA.

KEYWORDS

dexamethasone, adductor block, knee arthroplasty, IPACK block, rebound pain, chronic-postsurgical pain

Introduction

Total knee arthroplasty (TKA) that is followed by inadequately treated postoperative pain can reduce the benefits of early rehabilitation (1). Different types of nerve blocks have been used as part of a multimodal regime for postoperative analgesia after this type of surgery (2–4). The adductor canal block (ACB) and infiltration in the space between the popliteal artery and the capsule of the posterior knee (IPACK block) were confirmed to be an efficient combination in postoperative pain control, reducing the incidence of chronic post-surgical pain after TKA (5–9). However, the analgesic efficacy of nerve blocks, among others, depends on the duration of action of local anesthetics. Adjuvant drugs such as adrenaline, bicarbonates, dexmedetomidine, and

dexamethasone are all used to prolong the effects of local anesthetics (10–12). The intravenous dosage of dexamethasone administered as an adjuvant is higher than that given perineurally as an adjunct to local anesthetics in peripheral nerve blocks. Currently, no recommendations exist regarding the dosage of dexamethasone or the type of nerve block (13–16). Approximately 50% of patients may experience rebound pain after the resolution of a nerve block. Rebound pain is characterized by a transient acute increase in postoperative pain once a peripheral nerve block wears off. It typically manifests within 24 h after the nerve block and can result in sleep disturbances, hinder further rehabilitation, and increase opioid consumption (17). This phenomenon is more prevalent in young individuals, those undergoing bone surgery, and in situations where perioperative dexamethasone is not administered (18). Various strategies, including early identification of at-risk patients, educating patients about multimodal analgesia, administering adjuvant medications, or prescribing opioids, can help address rebound pain, although their effectiveness may vary (17, 18).

The study aims to assess the effect of adding dexamethasone to ACB and IPACK blocks on acute postsurgical pain scores, the occurrence of rebound pain, and chronic pain in these patients after 1 year of TKA.

Materials and methods

Patients and study design

This prospective interventional study included patients who underwent elective TKA after receiving approval from the Ethics

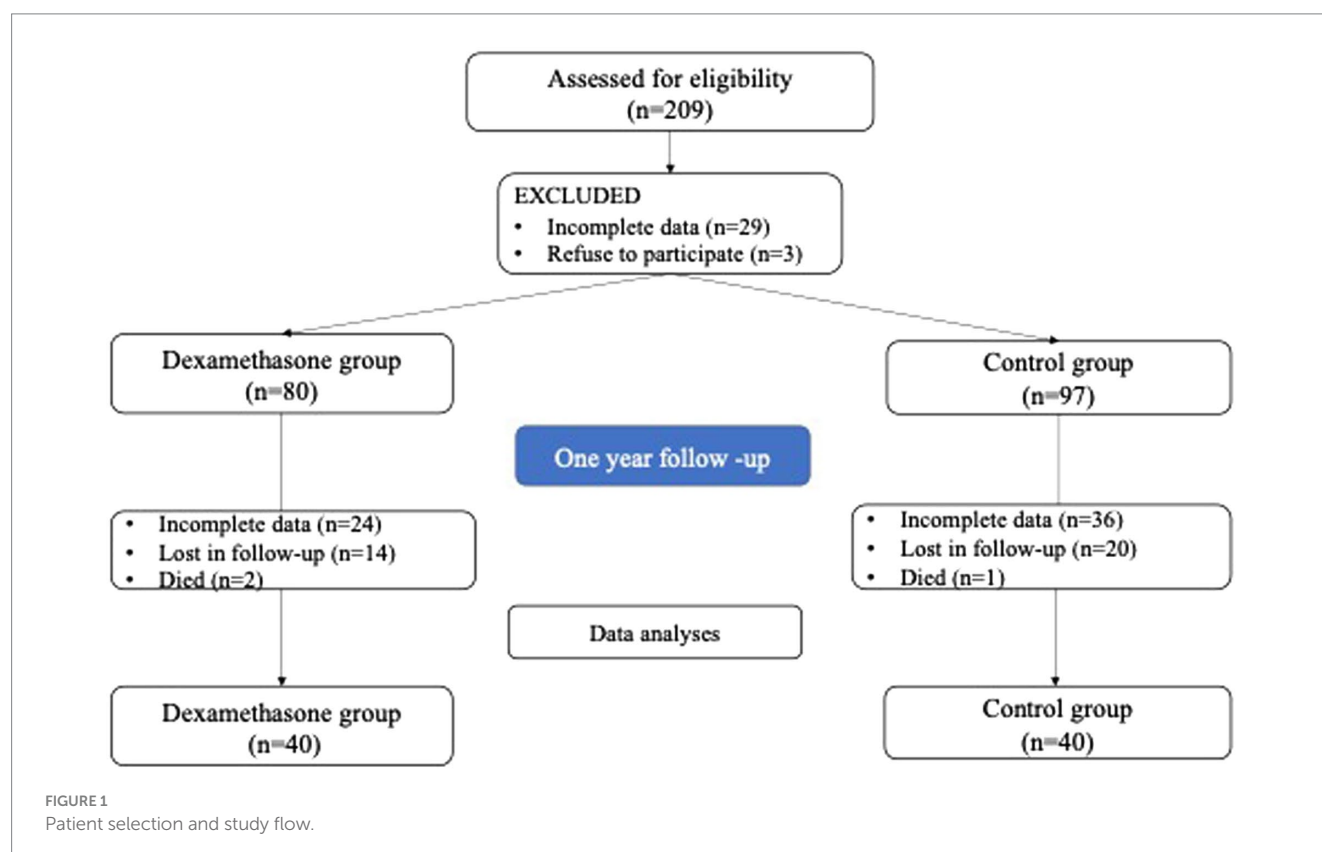
Committee (No 622/5 24, January 2022). The study was conducted from February 2022 to July 2023 at the Clinic for Orthopedic Surgery and Traumatology, University Clinical Centre of Serbia, by the principles of the Helsinki Declaration. Written informed consent was obtained from all study participants (Figure 1).

Inclusion criteria included patients aged 40–90 years, with an ASA physical status of I–III, receiving the same type of implant, and experiencing pain solely in the knee for surgery (without pain in any other body part). Exclusion criteria comprised individuals with incomplete medical records, refusal of spinal anesthesia or regional block, contraindications to a nerve block, allergies to local anesthesia, opioid use within 30 days prior to surgery, and conditions (such as drug or alcohol abuse, and mental illness) that could compromise rehabilitation.

Intervention

ACB and IPACK blocks were administered by an experienced anesthesiologist familiar with this technique at the end of surgery. During the block procedure, vital parameters such as electrocardiography, non-invasive blood pressure, and oxygen saturation were monitored, and non-opioids were initiated. In one group of patients, dexamethasone (4 mg for ACB and 4 mg for IPACK blocks) was added to the local anesthetic.

TKA was completed in a bloodless field using a tourniquet inflated to 300 mmHg, without resurfacing the patella, and under spinal anesthesia. Spinal anesthesia was performed with the patients seated. At the L3–L4 level, 3 mL of local anesthetic (0.5% levobupivacaine) was injected.



ACB was performed at the adductor canal's midpoint after identifying the sartorius muscle using the linear probe (10–12 MHz). Approximately 15 mL of 0.33% levobupivacaine was injected laterally into the femoral artery.

The IPACK block was performed using a curved (2–5 MHz) transducer positioned 2–3 cm above the patella on the medial thigh, flexed at the knee. The needle was inserted into the space between the popliteal artery and the femur, and 15 mL of 0.33% levobupivacaine was injected.

Paracetamol 1 g IV and 30 mg of ketorolac IV were used as non-opioid medications. They were administered alternately, starting with one and introducing the other in the third hour (ketorolac/paracetamol every 6 h).

In the first 48 h following surgery, pain intensity was assessed using the Numerical Rating Scale (NRS, where 0 indicates *no pain* and 10 signifies *the worst pain possible*) at several intervals: 1, 2, 3, 4, 6, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 h.

If the pain score was four or higher on the NRS scale, morphine was administered intravenously at a dose of 1 mg every 10 min until the pain intensity decreased. A standardized morphine milligram equivalent (MME) was used to express opioid consumption.

Patients reported postoperative complications, including nausea and drowsiness. Rebound pain, wound drainage, and urinary tract infections were also noted. Rebound pain was defined as a pain intensity NRS score exceeding seven following the resolution of the nerve block.

The same patients were assessed 1 year after surgery by pain specialists for chronic post-surgical pain (CPSP), defined as the persistence of pain in the surgical knee according to the International Classification of Diseases, Eleventh Revision (ICD-11) (19).

Statistical analysis

The primary outcome measure was the Numerical Rating Scale (NRS) score. Based on preliminary experiments involving 10 patients, the mean 24-h NRS scores for the two groups were 2.2 and 1.4, with standard deviations of 0.91 and 0.87, respectively. Following the requirements of a bilateral test, with α set at 0.05 and a power of 90% ($1-\beta$), along with a projected dropout rate of 30%, the required sample size was calculated to be $n = 38$ patients per group. Therefore, this study included 40 patients per group.

Data analysis was conducted in the statistical program R [version 4.3.1 (2023-06-16 ucrt)—“Beagle Scouts”; Copyright (C) 2023 The R Foundation for Statistical Computing; Platform: x86_64-w64-mingw32/x64 (64-bit)] (available at: www.r-project.org; retrieved: 21 August 2023). Numeric data were tested for normal distribution using a normal K–K plot and histogram, as well as Kolmogorov–Smirnov and Shapiro–Wilk. Data were expressed as mean $\pm$ standard deviation (SD). All statistical tests were two-sided, and the p -value of <0.05 was statistically significant. To test the difference between the examined groups, and depending on the nature of the examined parameters, the Pearson χ^2 test, Fisher's exact test, and Wilcoxon rank sum test were used.

Results

The groups did not differ in patient characteristics such as age, gender, BMI, and ASA status. The average age in the dexamethasone

group was 67 years, while in the control group, it was 70 years. Seventy percent of the dexamethasone group were male, compared to 55% in the control group; however, this difference was not statistically significant ($\chi^2 = 1.92$, $p = 0.166$) (Table 1). Normal body weight (BMI = 18.5–24.9 kg/m²) was observed in 17.5% of the dexamethasone group and 10% of the control group. Additionally, 47.5% of the dexamethasone group and 65% of the control group were classified as overweight (BMI = 25–29.9 kg/m²) ($p = 0.46$). Most patients in both groups had an ASA status of II (55% vs. 52.5%), with no significant difference between them ($\chi^2 = 0.028$, $p = 0.986$) (Table 1).

In the first 24 h, 97.5% of patients in both groups experienced mild pain intensity (NRS < 3), which was statistically significantly higher in the control group (1.08 ± 0.27 vs. 1.62 ± 0.63) ($p < 0.001$). There was also a statistically significant difference between groups regarding the number of patients at various time points during the first 24 h postoperatively (Table 2). While performing activities, 85% of patients in the dexamethasone group had an average pain intensity of 1.41 ± 0.61 . In comparison, 67.5% of patients in the control group experienced pain but with a significantly higher average intensity of 1.74 ± 0.53 ($p = 0.016$) (Table 2).

In the dexamethasone group, 92.5% of patients experienced pain 24–48 h after surgery, with an average intensity of 1.38 ± 0.55 . This was not significantly different from the control group, where 87.5% reported pain at an intensity of 1.31 ± 0.53 (Table 3). At 48-h post-surgery, the incidence and intensity of pain were comparable between the groups (Table 4).

On the first postoperative day, there was no statistically significant difference between the groups in the number of doses of non-opioid analgesics ($\chi^2 = 3.392$, $p = 0.64$) (Figure 2). Most of the patients in the dexamethasone group were administered two doses, with 13 (32.5%) patients needing this amount, while 12 (30%) patients received three doses of non-opioid analgesics. In the control group, most patients

TABLE 1 Patient characteristics.

Characteristics	Dexamethasone group ($n = 40$)	Control group ($n = 40$)	P
Age (y), mean (SD)	66.85 (9.1)	70.5 (6.46)	0.109
TV (m), mean (SD)	1.69 (0.09)	1.7 (0.09)	0.396
TT (kg), mean (SD)	81.2 (12.67)	83.98 (9.75)	0.194
BMI (kg/m ²)	28.22 (3.36)	28.62 (2.97)	0.4009
Normal weight, n (%)	7 (17.5)	4 (10)	0.46
Overweight, n (%)	19 (47.5)	26 (65)	
Obese, n (%)	14 (35)	10 (25)	
Sex, n (%)			0.166
Male	28 (70)	22 (55)	
Female	12 (30)	18 (45)	
ASA physical status, n (%)			0.986
ASA I	0 (0)	1 (2.5)	
ASA II	22 (55)	21 (52.5)	
ASA III	18 (45)	18 (45)	

BMI, body mass index; ASA, American Society of Anesthesiologists.

TABLE 2 Pain score in the first 24 h postoperatively.

Pain after surgery, at rest	In pain— <i>n</i> (%)		<i>p</i>	Pain (NRS)—mean (SD)		<i>p</i>
	Dexamethasone (<i>n</i> = 40)	Control group (<i>n</i> = 40)		Dexamethasone (<i>n</i> = 40)	Control group (<i>n</i> = 40)	
1 h	8 (20)	1 (2.5)	0.03*	1 (0)	1 (0)	–
2 h	12 (30)	26 (65)	0.002*	1.08 (0.29)	1.54 (0.71)	0.04*
3 h	17 (42.5)	34 (85)	<0.001	1.53 (0.8)	1.65 (0.92)	0.706
4 h	30 (75)	39 (97.5)	0.003*	1.2 (0.48)	1.92 (1.48)	0.007*
6 h	35 (87.5)	40 (100)	0.06	1.4 (0.69)	2.42 (1.8)	0.0013*
8 h	36 (90)	38 (95)	0.67	1.42 (0.6)	2.58 (2)	0.0017*
12 h	34 (85)	37 (92.5)	0.48	1.85 (1.05)	2.22 (1.25)	0.129
16 h	37 (92.5)	37 (92.5)	0.67	2 (1.47)	2.65 (1.81)	0.031*
20 h	37 (92.5)	35 (87.5)	0.71	1.65 (0.72)	2.11 (1.13)	0.045*
24 h	37 (92.5)	36 (90)	0.69	1.68 (0.63)	1.89 (0.85)	0.367
Within 24 h	39 (97.5)	39 (97.5)	0.47	1.08 (0.27)	1.62 (0.63)	<0.001
Pain during activity	34 (85)	27 (67.5)	0.07	1.41 (0.61)	1.74 (0.53)	0.016*

**p* < 0.05.

were administered two doses, 12 (30%), one dose, 11 (27.5%), and three doses, 7 (17.5%) of non-opioids (Figure 2).

In the first 24 h after surgery, more patients in the control group requested rescue opioid administration compared to the dexamethasone group ($\chi^2 = 13.393$, $p < 0.001$). However, no statistically significant difference was found in the average dose of opioid analgesics between the two groups. On the first postoperative day, only two patients in the control group received 5 mg of opioids (Table 3).

Rebound pain ($\chi^2 = 7.013$, $p = 0.008$), nausea ($\chi^2 = 4.505$, $p = 0.034$), and drowsiness ($\chi^2 = 12.655$, $p < 0.001$) were statistically more frequent in the control group (Table 5). Two patients had urinary tract infections in each group (Table 5). One year after TKA, CPSP was present in 5% of patients in the group without dexamethasone (Table 5).

Discussion

Our study's findings indicated that adding dexamethasone to the local anesthetic for ACB and IPACK blocks, along with a non-opioid scheduling strategy, improves postoperative pain management during the first 24 h following TKA. Patients reported mild pain intensity in both groups, with differences observed in the number of patients experiencing pain and in pain intensity. Furthermore, fewer patients in the dexamethasone group required opioids and reported a lower incidence of nausea and drowsiness. Dexamethasone also reduced the occurrence of rebound pain and chronic postsurgical pain 1 year after TKA.

The implantation of a total knee prosthesis aims to reduce pain, minimize disability, and improve quality of life (20). The choice of anesthesia for TKA, whether general or neuraxial, should be customized based on the individual patient's preferences, considering comorbidities and their level of optimization (21, 22). Neuraxial anesthesia is frequently preferred for these patients, as it

reduces the risk of acute renal and respiratory failure, thromboembolic complications, the need for blood transfusions, and infections. This type of anesthesia has also been associated with decreased admission rates to the intensive care unit, reduced re-admission rates, and shorter hospital stays (3, 23). In our study, all patients received spinal anesthesia, and 54% were classified as ASA status II.

TKA is associated with high-intensity pain, not only in the first 24 h postoperatively. Additionally, early rehabilitation, which is crucial for these patients, complicates the selection of an appropriate analgesic modality. The optimal approach to postoperative pain management should be as selective as possible, focusing on the area near the surgical site to provide adequate analgesia without inducing muscle weakness, thereby facilitating early rehabilitation (24, 25). Combining the ACB and IPACK blocks may provide a potential therapeutic solution after TKA (26). Guo et al. included 14 studies in their meta-analysis, demonstrating that adding the IPACK block to the ACB is an effective method for pain management. This combination reduces postoperative VAS scores, decreases cumulative morphine use, shortens hospital stays, and enhances patients' activity levels after TKA without causing additional side effects (26). These findings were supported by Wang et al. in a meta-analysis comparing the addition of the IPACK block to the ACB within a multimodal pain management protocol, showing that this combination reduces opioid consumption in the early postoperative period (27). However, despite the numerous advantages and technical improvements using ultrasound, nerve blocks are limited by the duration of LA (28). An effective alternative is to place a nerve catheter to provide a continuous block; however, the costs, complexity of placement, and potential morbidity from catheter infections and accidental dislodgement outweigh its benefits (3, 28). Therefore, administering a single dose of an adjuvant to extend the duration of LA is preferable (13, 15, 28). Dexamethasone can be added to local anesthesia to prolong its effects; however, the method of administration—whether perineural or systemic—remains a topic of debate (11, 29). Baeriswyl et al. conducted a meta-analysis comparing the analgesic efficacy of both methods, which included 11 randomized

TABLE 3 Postoperative opioid consumption.

Opioids consumption	Patients who needed opioids—N (%)			Dose of opioids (mg)—mean (SD)		
	Dexamethasone (n = 40)	Control group (n = 40)	p	Dexamethasone (n = 40)	Control group (n = 40)	p
Within 24 h	4 (10)	20 (50)	<0.001	5 (0)	6 (2.05)	0.368
24–48 h	0 (0)	2 (5)	0.47	0 (0)	5 (0)	–
Total	40 (100)	40 (100)		40 (100)	40 (100)	

p < 0.001.

TABLE 4 Pain intensity 28–48 h postoperatively.

Time	In pain—n (%)			Pain (NRS)—mean (SD)		
	Dexamethasone (n = 40)	Control group (n = 40)	p	Dexamethasone (n = 40)	Control group (n = 40)	p
28 h	35 (87.5)	34 (85)	0.75	1.63 (0.65)	1.62 (0.78)	0.72
32 h	36 (90)	32 (80)	0.35	1.61 (0.8)	1.69 (1.12)	0.89
36 h	35 (87.5)	31 (77.5)	0.24	1.69 (0.83)	1.45 (0.68)	0.25
40 h	34 (85)	29 (72.5)	0.172	1.35 (0.54)	1.45 (0.57)	0.476
44 h	32 (80)	28 (70)	0.302	1.38 (0.55)	1.21 (0.42)	0.252
48 h	28 (70)	29 (72.5)	0.8	1.21 (0.42)	1.1 (0.31)	0.26
24–48 h	37 (92.5)	35 (87.5)	0.71	1.38 (0.55)	1.31 (0.53)	0.574

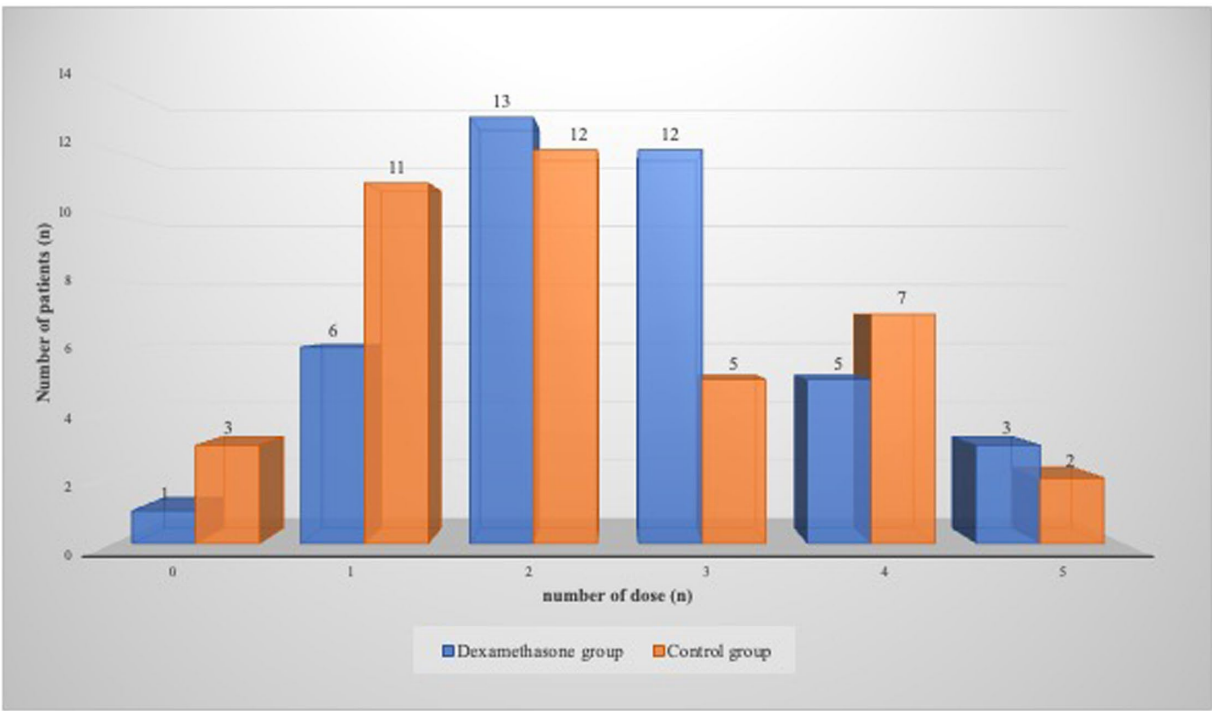


FIGURE 2 Consumption of non-opioid analgesics 24–48 hours postoperatively.

studies with 914 patients. The duration of analgesia was significantly longer with perineurally administered dexamethasone compared to systemic administration, showing an average difference of 3 h. The perineural administration of dexamethasone, in combination with bupivacaine but not with ropivacaine, slightly extended the duration of analgesia without affecting other pain-related outcomes when compared to systemic dexamethasone (30). Another systematic review indicated that both perineural and intravenous administration of dexamethasone

TABLE 5 Postoperative complications.

Characteristics	Dexamethasone group (n = 40)	Control group (n = 40)	p-value
Postoperative complications			
Rebound pain, n (%)	2 (5%)	12 (30%)	0.008*
Nausea, n (%)	0 (0%)	6 (15%)	0.034*
Drowsiness, n (%)	3 (7.5%)	18 (45%)	<0.001
Wound drainage, n (%)	0 (0%)	0 (0%)	–
Urinary tract infection, n (%)	2 (5%)	2 (5%)	0.61
Characteristics, 1 year after surgery			
Chronic post-surgical pain, n (%)	0 (0%)	2 (5%)	0.47

*p < 0.05.

effectively prolongs sensory block duration and reduces postoperative pain intensity and opioid consumption compared to placebo. When comparing intravenous and perineural dexamethasone, perineural administration was found to be more effective than intravenous. The sensory block lasted over 3 h, and postoperative pain intensity was significantly lower in the perineural dexamethasone group (13). However, an optimal dose of perineurally administered dexamethasone has not been defined. Kirkham et al., in the meta-analysis, showed that the dose of 4 mg dexamethasone in combination with short/intermediate and long-acting local anesthetics prolonged analgesia after brachial plexus blockade in patients undergoing upper extremity surgery (31). Moreover, the potential neurotoxic effects of dexamethasone, including bioenergetic disruption, mitochondrial dysfunction, oxidative stress, and apoptosis, should be considered (32).

Dexametomidine, another adjuvant, is combined with dexamethasone to prolong the duration of the blockade. Maagaard et al. demonstrated in their meta-analysis that this combination increased the duration of analgesia compared to placebo and dexmedetomidine alone. This combination likely provided an analgesia duration comparable to dexamethasone concluding that using dexamethasone as the sole adjunct is reasonable if the goal is to enhance analgesia duration (16). Dexamethasone significantly lowered the need for opioids by prolonging the analgesic effect of LA and reducing rebound pain (33, 34). Singh et al. have shown in a meta-analysis that dexamethasone administered either intravenously or perineurally decreases the incidence of rebound pain after a peripheral nerve block in postoperative analgesia (17). In our study, 10% of patients in the dexamethasone group received an opioid analgesic at a dose of 5 mg, whereas 50% of patients in the control group received a dose of 6 mg.

Up to 44% of patients experienced chronic pain after TKA, with 15% suffering from severe pain. This condition affects quality of life, leads to dissatisfaction, and increases the likelihood of revision surgery (35). Dexamethasone, administered in one or two intravenous doses of 24 mg, did not influence the development of chronic pain or physical function 3 years after TKA (36). However, the combination of ACB and IPACK blocks reduces the incidence of chronic pain and enhances functional tests 2 years after TKA (9).

Conclusion

Adding dexamethasone to the local anesthetic for ACB and IPACK blocks, along with a non-opioid scheduling strategy, improves

postoperative pain management after TKA. It also decreases opioid consumption, nausea, and drowsiness. Furthermore, dexamethasone contributes to reducing the occurrence of rebound pain and chronic postsurgical pain 1 year following TKA.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethics Committee of Clinical Centre of Serbia. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

SS: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. DM: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. PV: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Writing – original draft, Writing – review & editing. MD: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. MS: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. JV: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. MM: Conceptualization, Data curation, Investigation, Methodology, Project administration, Validation, Writing – original draft, Writing – review & editing. MA: Data curation, Formal analysis, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. NL: Conceptualization, Data curation, Formal analysis, Investigation,

Methodology, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Rasmussen S, et al. Total knee replacement and non-surgical treatment of knee osteoarthritis: 2-year outcome from two parallel randomized controlled trials. *Osteoarthritis Cartil.* (2018) 26:1170–80. doi: 10.1016/j.joca.2018.04.014
- Dong P, Tang X, Cheng R, Wang J. Comparison of the efficacy of different analgesia treatments for Total knee arthroplasty: a network meta-analysis. *Clin J Pain.* (2018) 34:1047–60. doi: 10.1097/AJP.0000000000000631
- Memtsoudis SG, Cozowicz C, Bekker J, Bekere D, Liu J, Soffin EM, et al. Peripheral nerve block anesthesia/analgesia for patients undergoing primary hip and knee arthroplasty: recommendations from the international consensus on anesthesia-related outcomes after surgery (ICAROS) group based on a systematic review and meta-analysis of current literature. *Reg Anesth Pain Med.* (2021) 46:971–85. doi: 10.1136/rapm-2021-102750
- Hasabo EA, Assar A, Mahmoud MM, Abdalrahman HA, Ibrahim EA, Hasanin MA, et al. Adductor canal block versus femoral nerve block for pain control after total knee arthroplasty: a systematic review and meta-analysis. *Medicine (Baltimore).* (2022) 101:e30110. doi: 10.1097/MD.00000000000030110
- Sankineani SR, Reddy ARC, Eachempati KK, Jangale A, Gurava Reddy AV. Comparison of adductor canal block and IPACK block (interspace between the popliteal artery and the capsule of the posterior knee) with adductor canal block alone after total knee arthroplasty: a prospective control trial on pain and knee function in immediate postoperative period. *Eur J Orthop Surg Traumatol.* (2018) 28:1391–5. doi: 10.1007/s00590-018-2218-7
- Hussain N, Brull R, Sheehy B, Dasu M, Weaver T, Abdallah FW. Does the addition of IPACK to adductor canal block in the presence or absence of periarticular local anesthetic infiltration improve analgesic and functional outcomes following total knee arthroplasty? A systematic review and meta-analysis. *Reg Anesth Pain Med.* (2021) 46:713–21. doi: 10.1136/rapm-2021-102705
- Zheng FY, Liu YB, Huang H, Xu S, Ma XJ, Liu YZ, et al. The impact of IPACK combined with adductor canal block under ultrasound guidance on early motor function after total knee arthroplasty. *Braz J Anesthesiol Engl Ed.* (2022) 72:110–4. doi: 10.1016/j.bjane.2021.04.012
- Et T, Korkusuz M, Basaran B, Yarımoğlu R, Toprak H, Bilge A, et al. Comparison of iPACK and periarticular block with adductor block alone after total knee arthroplasty: a randomized clinical trial. *J Anesth.* (2022) 36:276–86. doi: 10.1007/s00540-022-03047-6
- Sreckovic S, Ladjevic N, Milicic B, Tulic G, Milovanovic D, Djukanovic M, et al. Chronic post-surgical pain after knee arthroplasty: a role of peripheral nerve blocks. *Front Med.* (2024) 10:1335405. doi: 10.3389/fmed.2023.1335405
- Schotanus MGM, Bemelmans YFL, Van Der Kuy PHM, Jansen J, Kort NP. No advantage of adrenaline in the local infiltration analgesia mixture during total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc.* (2017) 25:2778–83. doi: 10.1007/s00167-015-3723-4
- Muñoz-Leyva F, Jack JM, Bhatia A, Chin KJ, Gandhi R, Perlas A, et al. No benefits of adding dexmedetomidine, ketamine, dexamethasone, and nerve blocks to an established multimodal analgesic regimen after total knee arthroplasty. *Anesthesiology.* (2022) 137:459–70. doi: 10.1097/ALN.00000000000004326
- Bjørn S, Linde F, Nielsen KK, Børglum J, Hauritz RW, Bendtsen TF. Effect of Perineural dexamethasone on the duration of single injection saphenous nerve block for analgesia after major ankle surgery: a randomized, controlled study. *Reg Anesth Pain Med.* (2017) 42:210–6. doi: 10.1097/AAP.0000000000000538
- Pehora C, Pearson AM, Kaushal A, Crawford MW, Johnston B. Dexamethasone as an adjuvant to peripheral nerve block. *Cochrane Database Syst Rev.* (2017) 11:CD011770. doi: 10.1002/14651858.CD011770.pub2

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

- Yadav S, Yadav K, Bogra J, Kohli M, Gupta R. A comparison between dexamethasone and clonidine as adjuvants to levobupivacaine in the supraclavicular approach to the brachial plexus block: a double-blind study. *Cureus [Internet].* (2023); Available online at: <https://www.cureus.com/articles/100407-a-comparison-between-dexamethasone-and-clonidine-as-adjuvants-to-levobupivacaine-in-the-supraclavicular-approach-to-the-brachial-plexus-block-a-double-blind-study>
- Gasbjerg KS, Hägi-Pedersen D, Lunn TH, Laursen CC, Holmqvist M, Vinstrup LO, et al. Effect of dexamethasone as an analgesic adjuvant to multimodal pain treatment after total knee arthroplasty: randomised clinical trial. *BMJ.* (2022) 376:e067325. doi: 10.1136/bmj-2021-067325
- Maagaard M, Andersen JH, Jaeger P, Mathiesen O. Effects of combined dexamethasone and dexmedetomidine as adjuncts to peripheral nerve blocks: a systematic review with meta-analysis and trial sequential analysis. *Reg Anesth Pain Med.* (2024) 50:311–20. doi: 10.1136/rapm-2023-105098
- Singh NP, Makkar JK, Chawla JK, Sondekoppam RV, Singh PM. Prophylactic dexamethasone for rebound pain after peripheral nerve block in adult surgical patients: systematic review, meta-analysis, and trial sequential analysis of randomised controlled trials. *Br J Anaesth.* (2024) 132:1112–21. doi: 10.1016/j.bja.2023.09.022
- Barry GS, Bailey JG, Sardinha J, Brousseau P, Uppal V. Factors associated with rebound pain after peripheral nerve block for ambulatory surgery. *Br J Anaesth.* (2021) 126:862–71. doi: 10.1016/j.bja.2020.10.035
- Schug SA, Lavand'homme P, Barke A, Korwisi B, Rief W, Treede RD, et al. The IASP classification of chronic pain for ICD-11: chronic postsurgical or posttraumatic pain. *Pain.* (2019) 160:45–52. doi: 10.1097/j.pain.0000000000001413
- Brophy RH, Fillingham YA. AAOS clinical practice guideline summary: Management of Osteoarthritis of the knee (nonarthroplasty), third edition. *J Am Acad Orthop Surg [Internet].* (2022) 30:e721–9. doi: 10.5435/JAAOS-D-21-01233
- Golaz R, Tangel VE, Lui B, Albrecht E, Pryor KO, White RS. Post-operative outcomes and anesthesia type in total hip arthroplasty in patients with obstructive sleep apnea: a retrospective analysis of the state inpatient databases. *J Clin Anesth.* (2021) 69:110159. doi: 10.1016/j.jclinane.2020.110159
- Osinski T, Bekka S, Regnaud JP, Fletcher D, Martinez V. Functional recovery after knee arthroplasty with regional analgesia: a systematic review and meta-analysis of randomised controlled trials. *Eur J Anaesthesiol.* (2019) 36:418–26. doi: 10.1097/EJA.0000000000000983
- Soffin EM, Memtsoudis SG. Anesthesia and analgesia for total knee arthroplasty. *Minerva Anesthesiol [Internet].* (2018); 84. Available online at: <https://www.minervamedica.it/index2.php?show=R02Y2018N12A1406>
- Berninger MT, Friederichs J, Leidinger W, Augat P, Bühren V, Fulghum C, et al. Effect of local infiltration analgesia, peripheral nerve blocks, general and spinal anesthesia on early functional recovery and pain control in total knee arthroplasty. *BMC Musculoskelet Disord.* (2018) 19:232. doi: 10.1186/s12891-018-2154-z
- Lavand'homme PM, Kehlet H, Rawal N, Joshi GPO on behalf of the PROSPECT Working Group of the European Society of Regional Anaesthesia and Pain Therapy (ESRA). Pain management after total knee arthroplasty: PROCEDURE SPECIFIC postoperative pain Management T recommendations. *Eur J Anaesthesiol.* (2022) 39:743–57. doi: 10.1097/EJA.00000000000001691
- Guo J, Hou M, Shi G, Bai N, Huo M. IPACK block (local anesthetic infiltration of the interspace between the popliteal artery and the posterior knee capsule) added to the adductor canal blocks versus the adductor canal blocks in the pain management after total knee arthroplasty: a systematic review and meta-analysis. *J Orthop Surg.* (2022) 17:387. doi: 10.1186/s13018-022-03272-5

27. Wang JH, Ma HH, Chou TFA, Tsai SW, Chen CF, Wu PK, et al. Does the addition of IPACK block to Adductor Canal block provide improved analgesic effect in Total knee arthroplasty? A systematic review and Meta-analysis. *J Knee Surg.* (2023) 36:345–53. doi: 10.1055/s-0041-1733882
28. Edinoff AN, Fitz-Gerald JS, Holland KAA, Reed JG, Murnane SE, Minter SG, et al. Adjuvant drugs for peripheral nerve blocks: the role of NMDA antagonists, neostigmine, epinephrine, and sodium bicarbonate. *Anesthesiol Pain Med* [Internet] (2021); 11. Available online at: <https://brieflands.com/articles/aapm-117146.html>
29. Krishna Prasad G, Khanna S, Jaishree S. Review of adjuvants to local anesthetics in peripheral nerve blocks: current and future trends. *Saudi J Anaesth.* (2020) 14:77–84. doi: 10.4103/sja.SJA_423_19
30. Baeriswyl M, Kirkham KR, Jacot-Guillarmod A, Albrecht E. Efficacy of perineural vs systemic dexamethasone to prolong analgesia after peripheral nerve block: a systematic review and meta-analysis. *Br J Anaesth.* (2017) 119:183–91. doi: 10.1093/bja/aex191
31. Kirkham KR, Jacot-Guillarmod A, Albrecht E. Optimal dose of Perineural dexamethasone to prolong analgesia after brachial plexus blockade: a systematic review and Meta-analysis. *Anesth Analg.* (2018) 126:270–9. doi: 10.1213/ANE.0000000000002488
32. Elmorsy EM, Al-Ghafari AB, Al Doghaither HA, Fawzy MS, Shehata SA. Neurotoxic mechanisms of dexamethasone in SH-SY5Y neuroblastoma cells: insights into bioenergetics, oxidative stress, and apoptosis. *Steroids.* (2024) 212:109514. doi: 10.1016/j.steroids.2024.109514
33. Fang J, Shi Y, Du F, Xue Z, Cang J, Miao C, et al. The effect of perineural dexamethasone on rebound pain after ropivacaine single-injection nerve block: a randomized controlled trial. *BMC Anesthesiol.* (2021) 21:47. doi: 10.1186/s12871-021-01267-z
34. Woo JH, Lee HJ, Oh HW, Lee JW, Baik HJ, Kim YJ. Perineural dexamethasone reduces rebound pain after ropivacaine single injection interscalene block for arthroscopic shoulder surgery: a randomized controlled trial. *Reg Anesth Pain Med.* (2021) 46:965–70. doi: 10.1136/rapm-2021-102795
35. Rosenberger DC, Pogatzki-Zahn EM. Chronic post-surgical pain – update on incidence, risk factors and preventive treatment options. *BJA Educ.* (2022) 22:190–6. doi: 10.1016/j.bjae.2021.11.008
36. Mølgaard AK, Gasbjerg KS, Skou ST, Mathiesen O, Hägi-Pedersen D. Chronic pain and functional outcome 3 years after total knee arthroplasty and perioperative dexamethasone: a follow-up of the randomized, clinical DEX-2-TKA Trial. *J Arthroplasty.* (2023) 38:2592–2598.e2. doi: 10.1016/j.arth.2023.05.060