Randomized Controlled Trial

Combined Intrathecal Dexmedetomidine and Adductor Canal Block for Analgesia in Total Knee Arthroplasty: A Randomized Controlled Trial

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Background: Pain management following total knee arthroplasty (TKA) is critical for enhancing outcomes such as minimizing opioid consumption and hospital stay, overall function, and rehabilitation.

Objectives: To evaluate the effectiveness of combined intrathecal dexmedetomidine (ITD) and adductor canal block (ACB) in relieving post TKA pain.

Study Design: Double-blind, randomized controlled trial.

Setting: KafrElsheikh University, Kafrelsheikh, Arab Republic of Egypt.

Methods: A total of 75 patients, aged 18 to 75, who underwent TKA under spinal anesthesia participated in this double-blind, randomized controlled trial.. Three equal sets of patients were formed. Group ITD patients received 15 mg of hyperbaric bupivacaine in 3 mL via intrathecal injection, with 5 µg of dexmedetomidine (DEX) in 0.5 mL (total volume 3.5 mL) and an ACB with 20 mL of 0.9% saline. Group ACB patients received an intrathecal injection containing 15 mg of hyperbaric bupivacaine along with 0.5 mL of saline and an ACB with 20 mL of 0.25% bupivacaine. Group ITD+ACB patients received 15 mg of hyperbaric bupivacaine in 3 mL via intrathecal injection, with 5 µg in 0.5 mL of DEX and an ACB using 20 mL of 0.25% bupivacaine. The amount of morphine taken in the first postoperative 48 hours was the primary outcome.

Results: Compared to Group ITD and Group ACB, the total amount of morphine needed in the first postoperative 24 and 48 hours was significantly lower in Group ITD+ACB, and in group ACB compared to group ITD ($P < 0.05$). Visual Analog Scale pain scores were markedly reduced in Group ITD+ACB and in Group ACB than in Group ITD at postoperative 4 hours ($P = 0.018$ and $P = 0.041$, respectively); in Group ITD+ACB than in Group ITD and Group ACB at postoperative 8 hours ($P = 0.005$ and $P = 0.011$, respectively); and in Group ITD+ACB compared to Group ITD at postoperative 12 hours ($P = 0.005$). The time to the first rescue analgesic was notably longer in Group ITD+ACB compared to Group ITD and Group ACB (P value < 0.05)and in Group ACB compared to Group ITD ($P < 0.001$). Side effects were similar in all 3 groups.

Limitations: Our trial had a relatively limited sample size and was conducted at a single center.
Conclusions: Combined ITD and ACB were superior in TKA postoperative pain management and required decreased postoperative analgesia without significant side effects compared to ACB alone or ITD alone.

Key words: Intrathecal dexmedetomidine, adductor canal block, pain, analgesia, total knee arthroplasty

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Total knee arthroplasty (TKA) is used to treat end-stage knee osteoarthritis (1). Nevertheless, the early postoperative period may be characterized by moderate to severe pain following TKA (2).

An optimal TKA analgesia regimen should preserve the knee's mobilization ability; facilitate early physical therapy; expedite recovery; reduce the risk of postoperative complications and hospital stays; and boost patient satisfaction (3). Traditional opioid-based analgesia is effective but is often associated with adverse symptoms, such as respiratory depression, nausea, and vomiting (4). Hence, multimodal analgesia is preferred to effectively treat postoperative pain (5).

Peripheral nerve blocks have recently been performed to minimize postoperative pain and improve functional status (6). The adductor canal block (ACB) blocks the saphenous and vastus medialis nerves. The anterior branch of the obturator nerve, the terminal end of its posterior branch, and additional sensory nerves—including the femoral and medial cutaneous nerves—are partially covered by the ACB when it reaches the distal section of the canal (7,8).

Numerous techniques have been put forth to extend the duration of anesthesia, including the intravenous delivery of medicines or the use of local anesthetic adjuvants (9). Many anesthesiologists have clinically studied local anesthetic adjuvants for their ability to lower local anesthetic concentrations and offer efficient perioperative pain relief. Both opioid and nonopioid local anesthetic medication adjuvants have been the subject of an increasing number of clinical trials (10,11).

An extremely selective α_2 adrenergic agonist, dexmedetomidine (DEX) has sedative, anxiolytic, analgesic, sympatholytic, and antihypertensive effects (12). According to many meta-analyses, intrathecal DEX (ITD) prolongs sensory-motor blockage and shortens its onset time while causing few hemodynamic alterations (13,14). Consequently, DEX has a greater potential utility than other adjuvants used with local anesthetics (15,16).

No previous studies have compared the effectiveness of ITD with and without ACB. Our study's objective was to assess the efficacy of ACB and ITD together for post TKA analgesia.

Methods

Our randomized, controlled, and double-blinded study involved 75 patients of both genders aged 18 to 75. All study patients had an American Society of Anesthesiology Physical Status of either I or II and underwent TKA under spinal anesthesia. The study was conducted from February 2025 through July 2025 following the KafrElsheikh University Hospitals Ethical Committee's approval (approval code: MKSU 50-1-7) and registration at clinicaltrials.gov (ID: NCT06837844). All patients provided written informed consent.

Exclusion criteria were neurological or intellectual disability; an injection site infection; an allergy to local anesthetics or DEX; long-term use of sedatives or analgesics; coagulation abnormalities; pregnancy; and obesity (body mass index [BMI, kg/m^2] > 30).

Randomization and Blinding

We used an online randomization application to generate a random list (http://www.randomizer.org); opaque, sealed envelopes contained the credentials for each patient. Three equal groups of patients were created utilizing a 1:1:1 allocation ratio. The patients and outcome assessors were unaware of the group assignments.

The groups and their injectates were as follows: Group ITD patients received 15 mg of hyperbaric bupivacaine in 3 mL via intrathecal injection, with 5 µg of dexmedetomidine (DEX) in 0.5 mL (total volume 3.5 mL) and an ACB with 20 mL of 0.9% saline. Group ITD served as the active comparator group, as all three groups received pharmacologically active intrathecal agents; the saline ACB in Group ITD was used to maintain blinding rather than to represent a true placebo. Group ACB patients received an intrathecal injection containing 15 mg of hyperbaric bupivacaine along with 0.5 mL of saline and an ACB with 20 mL of 0.25% bupivacaine. Group ITD+ACB patients received 15 mg of hyperbaric bupivacaine in 3 mL via intrathecal injection, with 5 µg in 0.5 mL of DEX and an ACB using 20 mL of 0.25% bupivacaine at the end of the surgery. The interventional drugs were produced by a pharmacist who was not engaged with the study.

The patients' medical and surgical histories were documented, along with their clinical examinations and laboratory tests, such as complete blood counts and coagulation studies. Postoperative pain assessment using the Visual Analog Scale (VAS) was taught to every patient. On the VAS scale, 0 represents no pain, and 10 cm represents the most excruciating agony a person might experience (17).

Patient monitoring included a temperature probe, electrocardiogram, pulse oximetry, and noninvasive

blood pressure monitoring. Lactated Ringer solution was given to each patient at a 7 mL/kg/h rate. A 25G needle and the midline technique were used to provide spinal anesthetic at the L2-L3 or L3-L4 interspace while the patient was positioned laterally with the surgical side superior. After the free passage of cerebrospinal fluid, in Groups ITD and ITD+ACB, 15 mg of hyperbaric bupivacaine was administered intrathecally in 3 mL with either 5 µg in 0.5 mL DEX or 0.5 mL saline 0.9%. Group ACB received 0.5 mL of saline 0.9%. Postsurgery, a linear probe was conducted on the block under complete aseptic conditions and with ultrasound guidance.

Adductor Canal Block Technique

The patient was placed supine on the table. The inner thigh, which is situated almost halfway between the superior border of the patella and the anterior superior iliac spine, was reached by moving the probe from the mid-thigh level. The sartorius muscle, saphenous nerve, superficial femoral artery, and anterolateral hyperechoic structure were then identified. Using an in-plane technique, a 22G needle was inserted from the lateral orientation. The needle's tip was gradually advanced until it touched the superficial femoral artery's lateral border and the area beneath the sartorius muscle. The needle tip's position was verified using a hydrodissection technique. Then, following negative blood aspiration, 20 mL of bupivacaine 0.25% was administered to Group ACB patients and Group ITD+ACB patients;, Group ITD patients received 20 mL of saline 0.9%.

Every 5 minutes during the procedure the patient's heart rate and mean arterial pressure were noted until transfer to the postanesthesia care unit.

The pinprick test was used to determine the extent of sensory obstruction, and until sensory level regression (S1) occurred, the maximal sensory level was measured every 10 minutes during the procedure and every 30 minutes afterward. The modified Bromage scale was used to assess motor block (18) after the subarachnoid block; the time was recorded every minute until Bromage 3 was achieved (0 denotes no motor nerve block, one denotes inability to lift the leg, 2 denotes inability to bend the knee, and 3 denotes inability to flex the ankle).

Each patient was prescribed a consistent pain medication regimen following the surgery. One gram of of intravenous acetaminophen was given every 6 hours for all patients. If the patient's VAS pain score exceeded 3 cm, a 3 mg intravenous dose of morphine was administered as rescue analgesia. If the VAS score remained ≥ 4 cm after 30 minutes, an additional 3 mg morphine dose was given; this was repeated at 30-minute intervals to a ceiling dose of 12 mg per 4-hour period. No patient reached the ceiling dose during the study period. VAS scores were recorded immediately upon arrival to the PACU (time 0, reflecting immediate post procedure status), and at post procedure hours 4, 8, 12, 18, 24, 36, and 48. The initial analgesic request time and the cumulative analgesic consumption at postprocedure 24 hours and 48 hours were documented.

Sedation was evaluated intraoperatively and in the postanesthesia care unit using the Ramsay Sedation Scale (19). The patient is described on a scale of one to 6, as follows: Awake: one, restless or anxious, or both; 2, cooperative, oriented, and tranquil; 3, responding to commands; 4, slumber; 5,rapid response to stimulus; 6, nonexistent response to stimulus.

Postoperative Pain Control

Adverse effects were evaluated and managed as follows: hypotension (a 20% decrease in basal mean arterial pressure) treated by intravenous ephedrine 5 mg–10 mg; bradycardia (a 20% decrease in basal heart rate) treated by intravenous atropine 0.02 mg/kg; respiratory depression (SpO_2 < 95%) treated by oxygen supplementation; and postoperative nausea and vomiting treated by intravenous ondansetron 0.1 mg/kg.

Utilizing a 5-point Likert scale, patients' satisfaction levels were assessed: 1, extremely dissatisfied; 2, unsatisfied; 3, neutral; 4, satisfied; 5, extremely satisfied (20).

The amount of morphine taken in the first 48 hours was the primary outcome. The secondary outcomes were hemodynamics, patient satisfaction, adverse events, pain severity, and time to first rescue analgesia.

Sample Size Calculation

The sample size was calculated using G*Power 3.1.9.2 (Heinrich Heine University). Our pilot investigation, which had 5 patients per group, indicated that the mean (SD) total morphine consumption during the first 48 hours was 7.2 (1.6) mg in Group ITD, 6.6 (2.5) mg in Group ACB, and 5.4 (1.34) mg in Group ITD+ACB. To reduce dropout, five patients were included in each group; 25 patients were thus distributed to each group based on a 95% CI, 80% power, a 1:1:1 allocation ratio, and an effect size of 0.415.

Statistical Analysis

The statistical analysis was performed using IBM SPSS Statistics 27.0 (IBM Corporation). The normality of

the data distribution was measured using histograms and the Shapiro-Wilks test. Quantitative parametric data, displayed as mean (SD), were assessed using the Analysis of Variance F-test and Tukey post hoc test. The median and interquartile range of quantitative nonparametric data were used to compare each group using the Kruskal-Wallis test and the Mann-Whitney test. The χ^2 test assessed the qualitative variables, which were conveyed as frequency and percentage. If the 2-tailed *P* value was ≤ 0.05, it was considered statistically significant.

Results

Figure 1 shows the CONSORT (Consolidated Standards of Reporting Trials) patient flow chart. We assessed 93 patients for eligibility; 7 chose not to participate and 11 did not meet the eligibility requirements. The remaining 75 patients were randomly assigned to one of the 3 study groups—25 to each group. Statistical analyses were conducted on all patients who were allocated.

There was no appreciable difference in the 3 groups' demographic information and procedure length (Table 1).

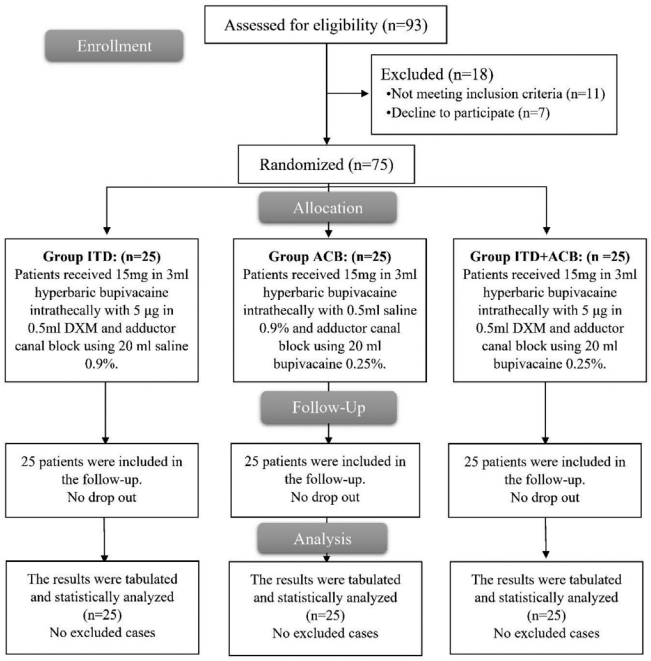


Fig. 1. *CONSORT (Consolidated Standards of Reporting Trials) flowchart of the enrolled patients.*
DEX = dexmedetomidine

The amount of morphine taken in the first post-procedure 48 hours was the primary outcome. The total amount of morphine used in the first postoperative 24 hours and by postoperative hour 48 was considerably reduced in Group ITD+ACB compared to Group ITD and Group ACB ($P < 0.05$). It was decreased markedly in Group ACB compared to Group ITD ($P < 0.05$) (Table 2).

Heart rate and mean arterial pressure measurements at baseline, and during the procedure at 5, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, and 110 minutes, and in the postanesthesia care unit were not appreciably different across the 3 groups. Heart rate and mean postprocedure arterial pressure measurements were markedly reduced in Group ITD+ACB and Group ITD compared to Group ACB at 10, 15, 20, 25, and 30 minutes ($P < 0.05$) and showed no important differentiation between Group ITD+ACB and Group ITD (Fig. 2).

Table 3 shows that the 3 groups' VAS scores at postprocedure hours 0 18, 24, 36, and 48 did not differ substantially. VAS score measurements were notably lower in Group ITD+ACB and Group ACB than in Group ITD ($P = 0.018$ and $P = 0.041$, respectively) and were not notably different Between Group ACB and Group ITD+ACB at postprocedure hour 4. VAS score measurements showed negligible differentiation between Group ITD and Group ACB and were substantially reduced in Group ITD+ACB than in Group ITD and Group ACB ($P = 0.005$ and $P = 0.011$, respectively) at postprocedure hour 8. VAS score measurements were minimally different between Group ITD and Group ACB and between Group ACB and Group ITD+ACB, and were markedly reduced in Group ITD+ACB compared to Group ITD ($P = 0.005$) at postprocedure hour 12.

The 3 groups' intraoperative and postanesthesia care unit Ramsay Sedation Scale scores did not differ significantly.

The time of first rescue analgesia was notably delayed in Group ITD+ACB compared to Group ITD and Group ACB ($P < 0.001$) and was notably delayed in Group ACB compared to Group ITD ($P < 0.001$) (Table 2).

The bradycardia, hypotension, and PONV incidences were not substantially different among the 3 groups. Local anesthetic systemic toxicity and respiratory depression did not occur in any patient in the 3 groups. The 3 groups did not exhibit a significant difference in patient satisfaction (Table 4).

Discussion

Recently, regional anesthetic techniques have become more accepted as useful strategies for enhancing postoperative analgesia while reducing the adverse effects associated with opioids. Of them, intrathecal anesthesia using local anesthetics and adjuvants has demonstrated potential for improving the duration and quality of spinal blocks. A variety of compounds have been employed in extending the duration of spinal anesthesia (21).

During spinal anesthesia for knee arthroscopies, ITD has proved to be a safe adjuvant to bupivacaine. The intrathecal route supplies better postoperative analgesia; more augmentation to sensory and motor block; more stable hemodynamics, and fewer overall side effects (22).

Our results show that heart rate and mean arterial pressure measurements after 10, 15, 20, 25, and 30 minutes were markedly reduced in Group ITD+ACB and Group ITD than in Group ACB; there was a negligible difference between Group ITD+ACB and Group ITD.

DEX is administered intrathecally. It acts directly on the spinal cord, particularly at the dorsal horn neurons and pre- and postsynaptic α_2 adrenergic receptors (23). Presynaptic α_2 receptor activation reduces norepinephrine release. The result is a decrease in sympathetic outflow from the spinal cord to the periphery, which results in vasodilation and a reduction in systemic vascular resistance, thereby lowering blood pressure (24).

Our results align with the findings made by Ismail, et al (25), who reported that heart rate was significantly reduced by ITD compared to a control group, which received an intrathecal block and intra-articular saline following arthroscopic knee surgery.

Our study showed that VAS score measurements were markedly reduced in Group ITD+ACB and Group ACB compared to Group ITD at postprocedure hour 4 and were decreased notably in Group ITD+ACB compared to Group ITD and Group ACB at postprocedure hour 8; at postprocedure hour 12, Group ITD+ACB's VAS score was considerably lower than Group ITD's score. The time to first rescue was notably prolonged in Group ITD+ACB compared to Group ITD and Group ACB, and was notably extended in Group ACB compared to Group ITD. The total consumption of morphine during the first postprocedure 24 and 48 hours was markedly reduced in Group ITD+ACB compared to Group ITD and Group ACB, and was much reduced in Group ACB compared to Group ITD.

Table 1. *Demographic data and duration of surgery of the studied groups.*

		Group ITD (n=25)	Group ACB (n=25)	Group ITD+ACB (n=25)	*P* Value
Age (years)		43.6 (13.44)	46.3 (13.38)	44.9 (12)	0.754
Gender	Men	11 (44%)	13 (52%)	10 (40%)	0.686
	Women	14 (56%)	12 (48%)	15 (60%)	
Weight (kg)		76.4 (8.07)	72.8 (7.45)	74.9 (7.29)	0.235
Height (m)		1.68 (0.07)	1.67 (0.07)	1.68 (0.06)	0.774
BMI (kg/m^2)		27.1 (1.52)	26.3 (2.71)	26.7 (2.8)	0.480
ASA Physical Status	I	15 (60%)	18 (72%)	16 (64%)	0.662
	II	10 (40%)	7 (28%)	9 (36%)	
Duration of surgery (min)		75.2 (19.28)	76.4 (24.22)	79.6 (21.55)	0.762

Data are presented as mean (SD)or frequency (%). BMI: Body mass index, ASA: American Society of Anesthesiologists.

Table 2. *Ramsay Sedation Scale, time of first rescue analgesia and total pethidine{pethidine is not the same drug as morphine} consumption in the first postoperative 24 and 48 hour periods of the studied groups.*

	Group ITD (n=25)	Group ACB (n=25)	Group ITD+ACB (n=25)	*P* Value	Post hoc
Intraoperative Ramsay Sedation Scale	3 (3-4)	3 (2-4)	3 (3-4)	0.672	
Ramsay Sedation Scale in PACU	2 (1-2)	2 (1-2)	2 (1-3)	0.798	
Time of first rescue analgesia (h)	5.5 (1.19)	7.8 (1.57)	11.4 (1.98)	< 0.001	P1 < 0.001 P2 < 0.001 P3 < 0.001
Total morphine consumption in first postoperative 24 hours in mg	8.4 (2.12)	7 (2.24)	5.6 (1.32)	< 0.001	P1 = 0.028 P2 < 0.001 P3 = 0.048
Total morphine consumption in the first postoperative 48 hours in mg	11.5 (2.4)	9.7 (2.78)	7.8 (1.5)	< 0.001	P1 = 0.019 P2 < 0.001 P3 = 0.011

Data are presented as mean (SD). The Ramsay scores represent Median (IQR). PACU: postanesthesia care unit. P1: *P* value between group ITD and group ACB, P2: *P* value between group ITD and group ITD+ACB, P3: *P* value between group ACB and group ITD+ACB. *P* value < 0.05.

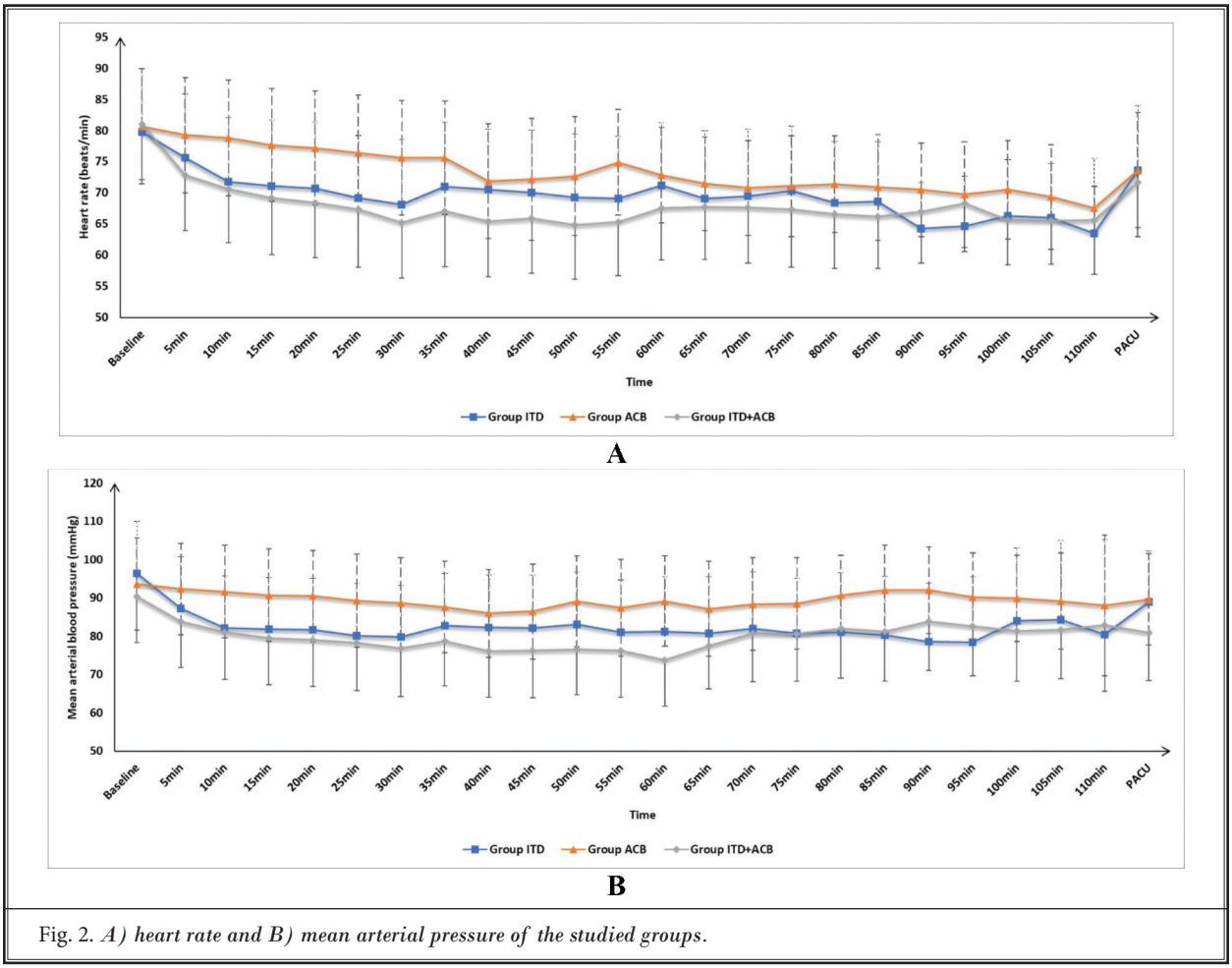


Fig. 2. *A) heart rate and B) mean arterial pressure of the studied groups.*

Table 3. *Postprocedure Visual Analog Scale (VAS) pain scores of the studied groups.*

	Group ITD (n = 25)	Group ACB (n = 25)	Group ITD+ACB (n = 25)	*P* Value	Post hoc
0h	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	---	
4h	1 (0 - 1)	2 (1 - 2)	2 (1 - 3)	0.038	P1 = 0.018 P2 = 0.041 P3 = 0.755
8h	3 (2 - 4)	2 (1 - 4)	2 (1 - 2)	0.009	P1 = 0.803 P2 = 0.005 P3 = 0.011
12h	3 (2 - 3)	2 (2 - 4)	2 (1 - 4)	0.019	P1 = 0.168 P2 = 0.005 P3 = 0.153
18h	4 (3 - 5)	3 (2 - 4)	2 (2 - 4)	0.521	
24h	4 (2 - 4)	4 (2 - 5)	3 (2 - 4)	0.340	
36h	4 (3 - 5)	3 (2 - 5)	3 (2 - 4)	0.341	
48h	4 (2 - 5)	3 (2 - 4)	3 (2 - 4)	0.306	

Data are presented as median (IQR). P1: *P* value between group ITD and group ACB, P2: *P* value between group ITD and group ITD+ACB, P3: *P* value between group ACB and group ITD+ACB. *P* value < 0.05.

The difference noted between the groups in terms of time of first rescue analgesia may indeed be clinically significant; so too the difference in rescue analgesic medication use (and to a small extent, the VAS scoring as well) between Group ITD group and Group ACB. In alignment with our results, Taha, et al (26) reported that ACB is an effective postoperative analgesic for knee arthroscopy performed under spinal anesthesia. They combined DEX (8 mg) with bupivacaine (0.25%) in ACB. This resulted in superior postoperative analgesia and less analgesic usage compared with bupivacaine alone. Concurring with our finding, Gupta, et al (27) re-

ported that the intrathecal administration of DEX with ropivacaine reduces pain scores and prolongs the duration of anesthesia in patients undergoing lower limb surgeries. Moreover, Panse, et al (28) reported that postoperative analgesia duration is considerably extended by using DEX as an adjuvant to ropivacaine in ACB after arthroscopic knee surgeries, thereby lowering the overall need for rescue analgesia and lessening any negative side effects.

Table 4. *Complications and patient satisfaction of the studied groups.*

		Group ITD (n = 25)	Group ACB (n = 25)	Group ITD+ACB (n = 25)	*P* Value
Complications	Bradycardia	3 (12%)	1 (4%)	4 (16%)	0.376
	Hypotension	5 (20%)	2 (8%)	7 (28%)	0.189
	PONV	6 (24%)	4 (16%)	2 (8%)	0.304
	Local anesthetic systemic toxicity	0 (0%)	0 (0%)	0 (0%)	---
	Respiratory depression	0 (0%)	0 (0%)	0 (0%)	---
Patient satisfaction	Extremely satisfied	7 (28%)	11 (44%)	15 (60%)	0.302
	Satisfied	9 (36%)	10 (40%)	8 (32%)	
	Neutral	6 (24%)	3 (12%)	2 (8%)	
	Unsatisfied	2 (8%)	1 (4%)	0 (0%)	
	Extremely unsatisfied	1 (4%)	0 (0%)	0 (0%)	

Data are presented as a frequency (%). PONV: Postoperative nausea and vomiting. *P* value > 0.05

In our trial, the bradycardia, hypotension, and PONV incidences were not notably different among the 3 groups. Aligned with our results, Taha, et al (26) reported a nonsignificant variation between their DEX+ACB group and their bupivacaine + ACB group regarding adverse effects including postoperative nausea and vomiting, hypotension, and bradycardia.

Our trial has limitations. It had a relatively limited sample size and was conducted at a single center. Further studies are required using a larger sample size, being conducted at multiple locations, and using various additives, different concentrations, and volumes of DEX either in ACB or intrathecally.

Conclusion

Combined DEX and ACB using bupivacaine 0.25% was superior in postoperative pain management. This combination reduced postoperative analgesia without severe adverse effects compared to ACB alone or DEX with ACB using saline 0.9%.

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