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Impact of dexamethasone added to intra-articular morphine and bupivacaine for postoperative analgesia after knee arthroscopy

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Abstract

Background: Pain relief after knee arthroscopy is very important for early recovery and rehabilitation. The study was conducted to evaluate the effects of adding dexamethasone (8 mg) to intra-articular morphine (10 mg) and bupivacaine (25 mg) combination on postoperative pain after knee arthroscopy.

Results: We enrolled 40 patients, 18–65 years-old of both sexes, ASA I and II scheduled for minor arthroscopic knee surgeries. The study group showed a lower visual analog score at rest and movement, prolonged postoperative analgesia, and decreased total analgesic consumption compared with the control group (P value < 0.05).

Conclusions: Adding dexamethasone to intra-articular combination of morphine and bupivacaine after knee arthroscopy prolongs the duration of analgesia, lowers pain scores, and decreases total analgesic consumption with no detected adverse effects.

Keywords: Dexamethasone, Bupivacaine, Morphine, Knee arthroscopy, Postoperative analgesia

Background

Postoperative pain after knee arthroscopy is usually moderate to severe and can affect the activity level and satisfaction of patients (McGrath et al., 2004).

Previous studies showed that 70% of patients had pain after knee arthroscopy. Ineffective management of pain may delay recovery, prolong hospital stay, lead to poor clinical outcomes, increase risk of thromboembolism, and increase medical care costs (Solheim et al., 2006).

Local anesthetics like bupivacaine and lidocaine, alpha 2 adrenoceptor agonists like clonidine, opioids like morphine, magnesium sulfate, and dexmedetomidine have all been tried intra-articularly to provide effective postoperative analgesia (Bhattacharjee et al., 2014).

Intra-articular bupivacaine produced effective analgesia after knee arthroscopy, but the peak blood concentration was reached within the 1st hour and the duration was only 2–4 h or even 1–2 h (Xie et al., 2015).

Prolongation of the analgesic effect can be produced in two ways: either by increasing the drug's amount or by adding drugs such as vasoconstrictor drugs (epinephrine or phenylephrine) or adding a narcotic drug (morphine). Intra-articular morphine gives later onset and peak action at 3–6 h, and pain relief was thought up to 24 h, or even 48 h (Yari et al., 2013; Xie et al., 2015).

Dexamethasone is a highly selective and potent glucocorticoid with minimal mineralocorticoid effect. It blocks the nociceptive impulse transmission along the C myelinated fibers. When combined with local anesthetics, it also increases the duration of regional blocks (Golwala et al., 2009).

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Combining local anesthetic, morphine, and dexamethasone for intra-articular injection to maximize and prolong postoperative analgesia needs more research to recommend the most effective and safest doses.

Methods

The aim of this study was to evaluate the effect of adding dexamethasone (8 mg) to intra-articular morphine (10 mg) and bupivacaine (25 mg) injection on postoperative pain after knee arthroscopy.

This randomized, double-blind, controlled clinical trial was conducted on 40 patients after approval of the Research Ethics Committee of the Faculty of Medicine and after obtaining informed consent from the patients. The study was conducted in the period from January 2020 to July 2020.

Patients with (ASA grades I and II) aged from 18 to 65 years-old of both sexes scheduled for minor arthroscopic knee surgeries (meniscectomy, chondroplasty, minor ligament repair, and diagnostic arthroscopy) were included in the study. Patients undergoing major knee surgeries and those with a history of allergy to any of the used drugs, history of diabetes mellitus, or contraindications to morphine use (addicts, COPD, and asthmatic patients) were excluded from the study.

The patients were instructed to report their pain using a visual analog score (VAS), which is a 10-cm line with 0 at one end representing “no pain,” whereas 10 cm at the other end representing “the worst imaginable pain.”

Monitoring equipment were attached to the patient including non-invasive arterial blood pressure (NIABP), oxygen saturation (SpO₂), and 3 leads electrocardiogram (ECG) were connected on arrival to the operating room and baseline vital parameters were recorded. An IV line was secured.

Patients were given general anesthesia. Preoxygenation for 3 min, induction of anesthesia was done by fentanyl (1 µg/kg), propofol (2 mg/kg), and atracurium hydrochloride (0.6 mg/kg) IV. The trachea was intubated with an appropriate size endotracheal tube after 3 min. Anesthesia was maintained using isoflurane in oxygen 60% and air 40%. Muscle relaxation was maintained with intermittent bolus atracurium as required. Patients were mechanically ventilated with volume control mode to keep EtCO₂ between 30 and 35 mmHg. Ondansetron (4 mg) was given IV for prophylaxis against nausea and vomiting.

At the end of the operation, patients were randomly allocated, using a computer-generated random lists, into two equal groups (20 patients in each group) according to the medications they will receive: group I (control, M group), 10 mg morphine in 5 ml normal saline + 10 ml of 0.25% bupivacaine (total volume 15 ml) were injected intra-articularly; group II (study, MD group), 10 mg

morphine + 8 mg dexamethasone completed to 5 ml with normal saline + 10 ml of 0.25% bupivacaine (total volume of 15 ml) were injected intra-articularly. The study drugs were prepared by one anesthesiologist and injected by another who was blind to the study drugs.

All medications were injected at the end of the operation and before releasing the tourniquet. The tourniquet was left for 10 min after the injection was administered. The drains were closed from the injection time until the release of the tourniquet. Residual neuromuscular paralysis was reversed using neostigmine and atropine IV, and then subsequent extubation was done.

Pain at rest and movement (knee flexions and extensions) was assessed by VAS at the following postoperative periods: on admission to the post anesthesia care unit when the patient is fully conscious and at 2, 4, 6, 8, 10, 12, 18, and 24 h post-operatively with an observation of hemodynamics and incidence of any complications.

Diclofenac sodium (75 mg) was administered IM as an analgesic supplement if the recorded VAS pain score was 4 or more and was reported every 8 h, if required. Pethidine 50 mg IM was used as a rescue analgesic if the patient continued to have pain after diclofenac administration. The time to the first analgesic requirement and the total diclofenac consumption during the first 24 h after the operation were also recorded.

Power of analysis

Using STATA program, setting alpha error is at 5% and power at 90%. Result from the previous study (El Bakry & Sultan, 2017) showed that the mean time for the first analgesic request was 7.83 ± 2.46 h in the M group compared to 10.88 ± 2.55 h in the MD group. Based on this, 20 cases per group (40 total) were needed, including the possible dropouts.

Results

There was no statistically significant difference between the two groups regarding demographic data and type of surgery as shown in Tables 1 and 2.

VAS was significantly lower in the MD group than the M group at rest during recovery, 2 h, 4 h, 6 h, 8 h, 10 h, 12 h, and 18 h postoperatively, while there was no statistically significant difference between the two groups regarding VAS at rest at 24 h postoperatively as shown in Fig. 1.

VAS at movement was significantly lower in the MD group than the M group during recovery, 2 h, 8 h, 10 h, 12 h, and 18 h postoperatively. The VAS values at movement during 4 h, 6 h, and 24 h postoperatively were lower in the MD group than the M group but did not reach significant levels as shown in Fig. 2.

Table 3 shows that there was a statistically significant difference between the two groups with less need for

Table 1 Demographic data

Demographic data		M group No. = 20	MD group No. = 20	Test value	P value	Sig.
Age	Mean ± SD Range	31.05 ± 9.37 18–57	36.40 ± 11.50 19–56	– 1.613•	0.115	NS
Sex	Female Male	6 (30.0%) 14 (70.0%)	5 (25.0%) 15 (75.0%)	0.125*	0.723	NS
Body weight	Mean ± SD Range	77.65±7.30 65–90	79.30±6.38 70–92	– 0.761•	0.451	NS
ASA	ASA I ASA II	13 (65.0%) 7 (35.0%)	12 (60.0%) 8 (40.0%)	0.107*	0.744	NS

Categorical variables are presented as frequencies and percentages and numerical variables are presented as means and standard deviations
P value > 0.05: non-significant (NS); P value < 0.05: significant (S); *: chi-square test; •: independent t test

analgesia, longer time for the first request of analgesia, and lower total dose of analgesia in the MD group compared with the M group with P value < 0.05

No complications or side effects to the drugs used or general anesthesia were detected among patients in our study.

Discussion

This study was done to evaluate the effect of adding dexamethasone to intra-articular morphine injection on postoperative pain after knee arthroscopy. The main finding in our study was that adding dexamethasone (8 mg) to intra-articular morphine (10 mg) bupivacaine (25 mg) combination resulted in prolonged analgesia, lower VAS for pain at rest and at movement, and decreased total analgesic consumption.

The efficacy of adding morphine to bupivacaine for intra-articular injection to augment and prolong analgesia was demonstrated in several studies.

Hosseini et al. (2012) compared the analgesic effect of intra-articular injection of 10 mg morphine + bupivacaine 0.5% (MB group), 100 mg tramadol + bupivacaine 0.5% (TB group), and control group receiving normal saline all in a total volume of 20 ml in patients undergoing arthroscopic ACL reconstruction under general anesthesia. The VAS scores at 30, 60, and 90 min and 2, 4, 12, and 24 h were significantly less in the MB and TB groups in comparison with

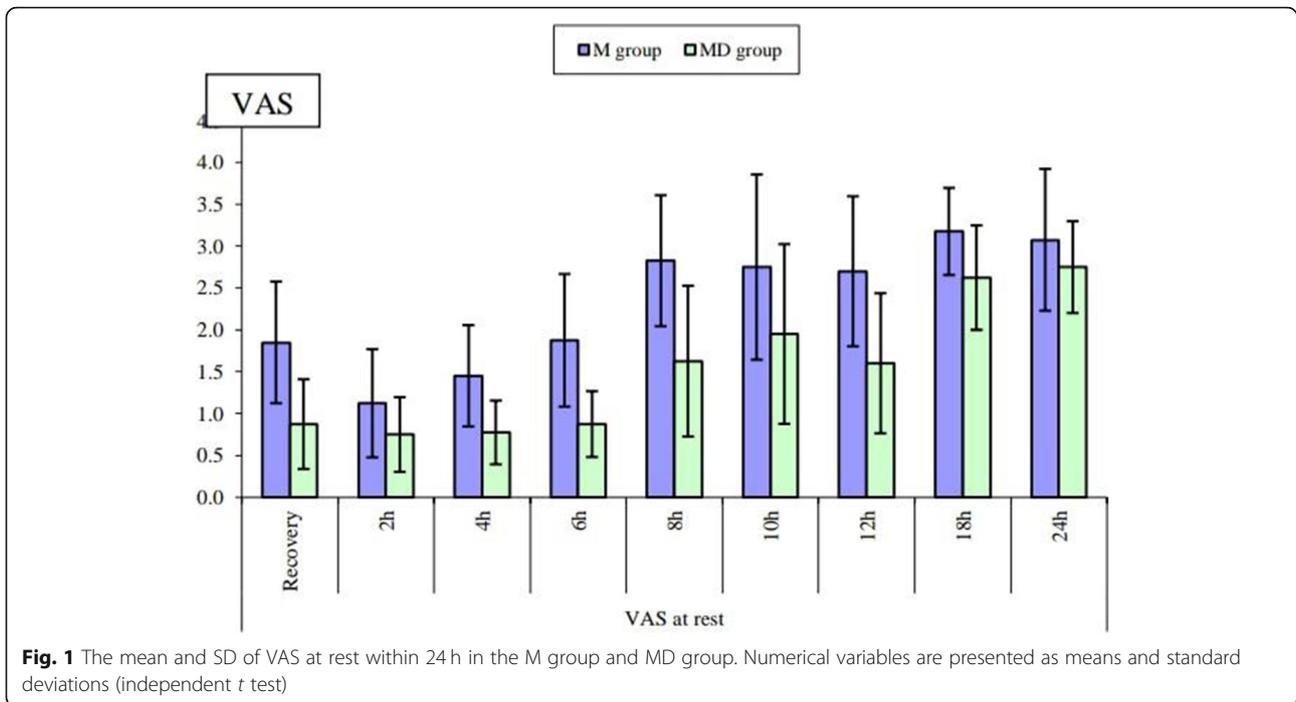
the control group. VAS scores also decreased significantly in the MB group compared to the TB group at 2, 4, and 24 h. Analgesic duration was longer and analgesic consumption was substantially less in the MB group. Moreover, unassisted ambulation and discharge times were significantly shorter in the MB group than the TB and control groups. They concluded that intra-articular morphine–bupivacaine provides effective pain relief, longer analgesic duration, less analgesic requirement, shorter unassisted ambulation, and discharge time compared with intra-articular tramadol–bupivacaine after ACL reconstruction arthroscopy (Hosseini et al., 2012).

Yari et al. (2013) studied different doses of morphine (5, 10, 15 mg) added to 20 ml of 0.5% bupivacaine and injected intra-articularly in patients scheduled for elective surgery of arthroscopic reconstruction of ACL under general anesthesia. Average time to the first analgesic request in patients receiving bupivacaine + 15 mg morphine (20.4 ± 6.2 h) was significantly higher than the other groups, and no significant differences were observed between other groups. Also, the average number of analgesic requests in patients receiving bupivacaine + 15 mg morphine (0.4 ± 0.9) was significantly less than the bupivacaine (2.6 ± 0.5) and bupivacaine + 5 mg morphine (1.8 ± 0.9) groups. They concluded that increasing the dose of intra-articular morphine provided a better analgesic effect and showed linearly

Table 2 Type of surgery

Type of surgery	M group		MD group		Test value*	P value	Sig.
	No.	%	No.	%			
Diagnostic and Debridement	7	35.0%	11	55.0%	2.317	0.509	NS
Meniscectomy	8	40.0%	6	30.0%			
Chondroplasty	4	20.0%	3	15.0%			
Backer’s cyst	1	5.0%	0	0.0%			

Categorical variables are presented as frequencies and percentages
P value > 0.05: non-significant (NS); P value < 0.05: significant (S); P value < 0.01: highly significant (HS); *: chi-square test



decreasing VAS score and less supplementary analgesics (Yari et al., 2013).

The effect of adding dexamethasone to local anesthetics for intra-articular injection following knee arthroscopy was documented in many studies.

Bhattacharjee et al. (2014) studied the postoperative analgesic effect of adding 8 mg dexamethasone to 18 ml of 0.25% levopubivacaine by intra-articular

injection in patients undergoing elective knee arthroscopy under general anesthesia. The intensity of pain was significantly less in patients receiving dexamethasone up to 9 h following surgery. However, from 10 h, the intensity of pain was comparable in both groups. The mean duration of analgesia was longer in patients receiving dexamethasone (group D) compared with patients who do not (group L) (10.24 ± 2.8 h vs. 5.48

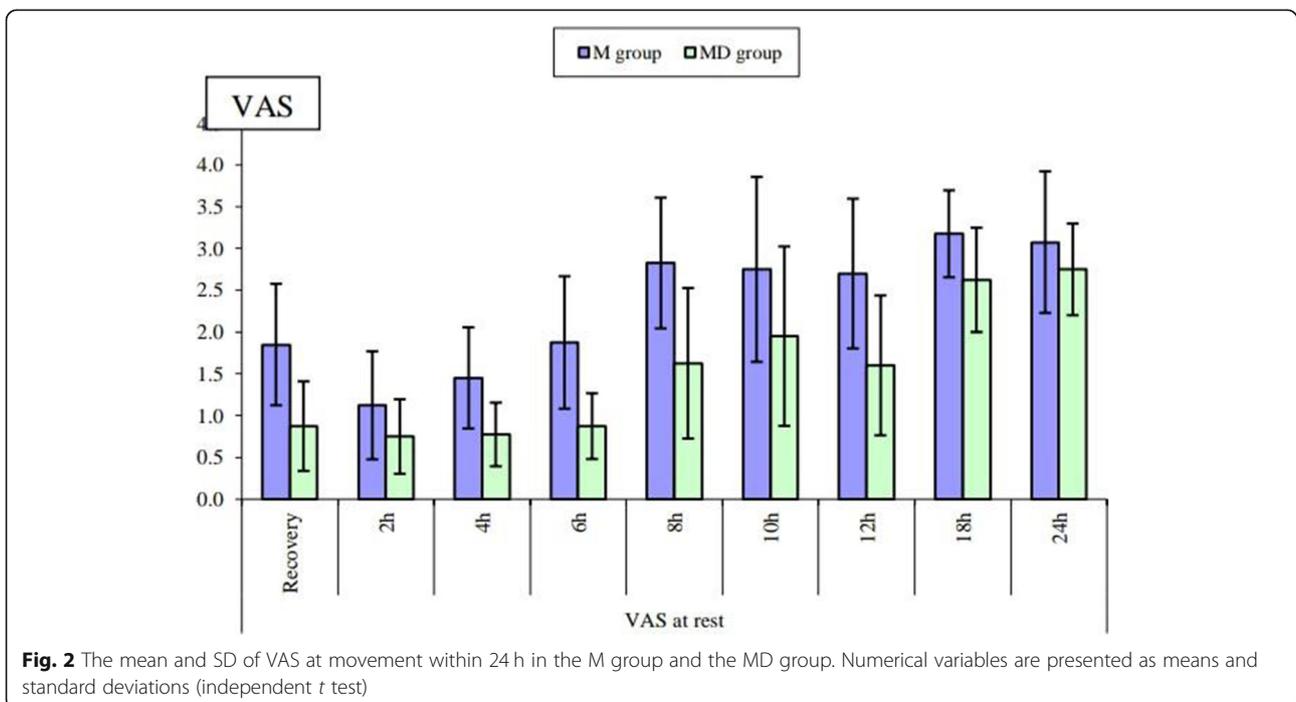


Table 3 Need for analgesia

		M group No. = 20	MD group No. = 20	Test value	P value	Sig.
Need for analgesia	No	4 (20.0%)	12 (60.0%)	6.667*	0.010	S
	Yes	16 (80.0%)	8 (40.0%)			
Time to first request of analgesia (h)	Mean \pm SD Range	9.50 \pm 1.71 6–12	12.50 \pm 3.66 8–18	-1.828•	0.081	S
Total dose of diclofenac sodium (mg)	Mean \pm SD Range	107.81 \pm 38.43 75–150	75.00 \pm 0.00 75–75	2.388•	0.026	S

Categorical variables are presented as frequencies and percentages and numerical variables are presented as means and standard deviations. *: chi-square test; •: independent t-test

\pm 1.6 h). Total supplemental analgesic consumption in the first 24 h was significantly less in group D compared with group L (88.4 \pm 38.4 mg vs 155.2 \pm 46.4 mg) (Bhattacharjee et al., 2014).

In another study by El Bakry and Sultan (2017), they studied the effect of adding 8 mg dexamethasone to 5 mg morphine and 10 ml of 0.5% bupivacaine on postoperative analgesia after their intra-articular injection in patients having minor knee arthroscopies. The time for the first analgesic request was significantly prolonged in the M group (7.83 \pm 2.46 h) and MD group (10.88 \pm 2.55 h) compared with the control group (5.77 \pm 2.88 h) and significantly prolonged in the MD group compared with the M group. The total consumption of diclofenac was significantly lower in the M group (90.56 \pm 38.56 mg) and MD group (46.41 \pm 26.41 mg) compared with the control group (160.21 \pm 40.14 mg) and significantly lower in the MD group compared with the M group. They concluded that adding dexamethasone led to a significant delay of first analgesic request and decreased total analgesic consumption (El Bakry & Sultan, 2017).

Dexamethasone interferes at several steps in the inflammatory response but the most important overall mechanism appears to be a limitation of recruitment of inflammatory cells at the local site and production of pro-inflammatory mediators like PGs, LTs, and PAF through indirect inhibition of phospholipase A2 (Tripathi, 2013).

Further studies are recommended for optimizing the adequate dose and concentration of bupivacaine and dose of dexamethasone and morphine to be injected intra-articularly by comparing different doses of the drugs to get the most effective doses.

A more comprehensive assessment of the effect of the addition of dexamethasone as an adjuvant to local anesthetics would be obtained by increasing the sample size, including other major arthroscopic procedures (e.g., ligament reconstruction arthroscopies) and evaluating their post-operative analgesic effect after spinal anesthesia as it is commonly used in arthroscopy operations.

Conclusions

In conclusion, the addition of dexamethasone to intra-articular injection of bupivacaine and morphine after knee arthroscopy potentiates their analgesic effect as manifested by lower pain scores, longer duration of analgesia (delayed first request of supplemental analgesia), and decreased total post-operative analgesic consumption which leads to early rehabilitation of patients and short hospital stay with no detected adverse effects.

Limitation of the Study

A limitation to our study was that the anti-inflammatory effect of dexamethasone was not studied on long-term recovery and rehabilitation. Further study is recommended for studying this anti-inflammatory effect.

Abbreviations

ACL: Anterior cruciate ligament; ASA: American Society of Anesthesiologists; COPD: Chronic obstructive pulmonary disease; Et CO₂: End-tidal CO₂; LTs: Leukotrienes; NIABP: Noninvasive arterial blood pressure; PAF: Platelet-activating factor; PGs: Prostaglandins; VAS: Visual analog scale

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Authors' contributions

HT: acquisition, analysis, interpretation of data, contribution in paper writing, and paper submission. RH: design of the work and work revision. AT: acquisition, analysis, interpretation of data, and contribution in paper writing. AA: acquisition, analysis, interpretation of data, and contribution in paper writing. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This randomized double-blind clinical trial was conducted after approval of the Research Ethics Committee of the Faculty of Medicine, Ain Shams University, and after obtaining informed consent from the patients. Research Ethics Committee (REC), FWA 00017585 Approval Number: FMASU MS 20/2020.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no conflicts of interest.

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