Morphine as an adjuvant to local anesthetics in axillary brachial plexus block in forearm and hand surgery

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Background
The axillary brachial plexus block is a popular nerve block for forearm, wrist, and hand surgery. The use of local anesthetic peripheral nerve blocks for surgical anesthesia and postoperative pain management has increased significantly with the advent of ultrasound-guided techniques. The discovery of peripheral opioid receptors led to the clinical application of adding opioids to local anesthetics for peripheral nerve blocks. This study is done to evaluate effect of morphine on onset, duration, and quality of analgesia when added to local anesthetics in axillary brachial plexus block and to detect any complications that occurred with this technique.

Patients and methods
In this prospective controlled clinical trial, 60 adult patients aged 18–60 years scheduled for orthopedic surgery of the forearm and hand with axillary brachial plexus block were selected and randomly allocated to two groups. Placebo group received 24 ml bupivacaine 0.5%, and morphine group received 24 ml bupivacaine 0.5%+5 mg morphine. The onset and duration of sensory and motor blocks, duration of analgesia, and adverse events (such as nausea and pruritus) during perioperative period were recorded.

Results
Onset of touch and pain block was faster in morphine group, with *P* values of 0.016 and 0.025, respectively. Onset of motor block was similar in the two groups. Duration of touch block was longer in morphine group, with *P* value of 0.022. Duration of motor block showed no change between the two groups. Duration of analgesia was longer in the morphine group, with *P* value of 0.001, with lower consumption of analgesia. No complications were recorded perioperatively.

Conclusion
We concluded that morphine provide better postoperative analgesia when injected with local anesthetics in ultrasound-guided axillary brachial plexus block without an increase in the frequency of complications.

Keywords:
axillary block, morphine, opioids, local anesthetics

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Introduction

The axillary brachial plexus block is a popular nerve block for forearm, wrist, and hand surgery. It can be used to provide regional anesthesia or as an analgesic technique to be used in combination with general anesthesia. It has the advantage of being performed away from the pleura and neuraxial structures. The block was first described in New York in 1884 by Halstead, being performed using cocaine under direct vision of the plexus [1]. The first percutaneous block was described in 1911 by Hirschel [2]. Since then, it has become the most used peripheral nerve block for forearm and hand surgery, especially owing the low incidence of complications compared with the more proximal approaches to the brachial plexus.

In 1981, Abramowitz and Cohen[3] described the first use of Doppler ultrasound to identify the axillary artery, thereby aiding the performance of axillary plexus block for upper limb surgery. However, it was the use of B-mode ultrasound in 1989 for axillary block performance that heralded the era of ultrasound-guided peripheral nerve block [4]. With the refinement of ultrasound technology and ultrasound-guided block techniques, it is gradually replacing nerve stimulator-based techniques. Ultrasonographic visualization of target nerve, needle, and local anesthetic injectate spread has been associated with improved block success rates, decreased block onset times, and a decrease in the local anesthetic dose needed for successful nerve block [5–7].

In 2012, the American Society of Anesthesiologists (ASA) released an update to its Practice Guidelines for Acute Pain Management in the Perioperative Setting [8]. In this report, the ASA strongly recommends use of a multimodal approach to pain management whenever possible. This includes the administration of two or more drugs that act by a different mechanism to provide analgesia. Additionally, the ASA strongly recommends that regional blockade with local anesthetics be considered as part of the multimodal approach for pain management. Peripheral nerve blocks using local anesthetics are commonly administered to control postoperative pain in patients undergoing surgery. They are simple and effective in providing postoperative analgesia and have fewer adverse effects than do conventional systemic opioid analgesics [9]. Unfortunately, their duration may not be adequate to provide analgesia sufficient to ensure a seamless transition to oral analgesics [10]. Anesthesia providers have addressed this limitation by adding adjunctive drugs to local anesthetics to prolong duration and enhance quality of regional blocks.

First given to human in the neuroaxial spaces in the late 1970s, opioids are one of the most frequently used classes of adjuvant [11]. Opioid antinociceptive properties is well documented, so consequently their addition to a local anesthetic solution as a means of extending the duration of pain relief and as a way of decreasing the dosage of local anesthetic required for pain treatment is apparent. The mechanism by which opioids affect local anesthetic action is through a G-protein-coupled-receptor system. Opioids competitively bind to specific receptors to induce pain relief by hyperpolarizing the afferent sensory neurons in which the receptors are imbedded. Hyperpolarization of the cell membrane by an opiate decreases the propagation of neuronal action potentials thereby inhibiting afferent pain signals. Eventually this produces a decrease in the perception of pain [12]. Besides being located in the central nervous system, opioid receptors have been identified on a number of cells in the periphery of the body [13,14].

Recent reports have suggested that morphine injected perineurally in patients with chronic pain may also have a clinically significant effect and that its duration of action may be longer than that of systemically administered morphine [15]. The neuroaxonal transport of morphine to the spinal cord is an explanation for this effect [16]. Other mechanisms that have been put forward are a local anesthetic-like action or a direct effect of morphine on stereospecific opioid receptors on the cell membrane of peripheral nerve axons [17,18]. Other investigators [19,20], however, have failed to demonstrate any significant analgesic effect of morphine administered perineurally.

Aim of study

The primary outcome is evaluating the effect of morphine on onset, duration, and quality of analgesia when added to local anesthetics in axillary brachial plexus block during the first 24 h (8, 12, 18, 24 h).

The secondary outcome is detecting any complications that occurred with this technique.

Patients and methods

It was a prospective controlled double-blind (patients and data collectors) clinical trial study that was carried out in Assuit University Hospital, Orthopedic Trauma Unit, and Postoperative Care Unit from May 2017 to July 2018. It was performed after approval of ethical committee.

Inclusion criteria included patients who planned for forearm and hand surgery aged from 18 to 60 years and ASA grades I–III. Exclusion criteria included patient refusal, patients with any contraindication to regional anesthesia block (coagulopathy, infection at the needle insertion site, contralateral pneumothorax, or diaphragmatic paralysis), or patients with allergy to amide local anesthetics or morphine.

Patients were randomized using computer-generated random number tables into two groups. Placebo group included 30 patients injected with 24-ml bupivacaine 0.5% and morphine group included 30 patients who received 24-ml bupivacaine 0.5%+5-mg morphine.

The selected patients were prepared preoperatively by the standard anesthetic techniques, and venous access was obtained in the contralateral upper limb with a 20 G catheter. Overall, 500 ml of intravenous Ringer's solution was started. Intraoperative monitoring was done by 5-lead ECG, pulse oximetry, noninvasive blood pressure, and capnography.

With the patient in the proper position, the skin is disinfected and the transducer is positioned in the short-axis orientation to identify the axillary artery about 1–3 cm from the skin surface. Once the artery is identified, an attempt is made to identify the hyperechoic median, ulnar, and radial nerves. However, these may not be always well seen on an ultrasound image. Prescanning should also reveal the position of the musculocutaneous nerve, in the plane between the coracobrachialis and biceps muscles.

The needle is inserted in-plane from the cephalad aspect and directed toward the posterior aspect of the axillary artery. Local anesthetic should be deposited posterior to the artery first, to avoid displacing the structures of interest deeper and obscuring the nerves, which is often the case if the median or ulnar nerves are injected first. Once 5–10 ml is administered, the needle is withdrawn almost to the level of the skin, redirected toward the median and ulnar nerves, and a further 10–15 ml is injected in these areas to complete the circle around the artery. Finally, the needle is once again withdrawn to the biceps and redirected toward the musculocutaneous nerve. Once adjacent to the nerve (stimulation will result in elbow flexion), 5–7 ml of local anesthetic is deposited.

Hemodynamics such as heart rate, noninvasive blood pressure, and arterial oxygen saturation were recorded.

Motor block was evaluated by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion at the elbow (musculocutaneous nerve) on a three-point scale for motor function (0 = normal motor function, 1 = reduced motor strength but able to move fingers, and 2 = complete motor block). Sensory block was assessed by ice packs using a three-point scale: 0 = normal sensation, 1 = loss of sensation of cold (analgesia), and 2 = loss of sensation of touch (anesthesia). Pain block was assessed by pinprick using two-point scale: 0 = pain and 1 = no pain.

Onset time of sensory and motor block is recorded which is defined as the time interval between the end of total local anesthetic administration and complete sensory and motor block correspondingly.

Duration of sensory and motor block is recorded. Duration of sensory block was defined as the time interval between the end of local anesthetic administration and the complete resolution of anesthesia on all nerves.

Duration of motor block was defined as the time interval between the end of local anesthetic administration and the recovery of complete motor function of the hand and forearm.

Duration of analgesia is the interval between onsets of the block to the time of the first analgesic consumption. Quality of analgesia was recorded in PACU by nurse. The pain score was recorded using the visual analog scale (VAS) 8 (T8 h), 12 (T12 h), 18 (T18 h), and 24 h (T24 h) after the surgery. Significant pain is defined as one that has a score of more than or equal to 3 or above and as a consequence required a supplementary dose of analgesia. When the patient is first asked for analgesia was assessed in the two groups. Patients with a pain score of 3 or above in the recovery room is an indication for analgesia. Overall, 30 mg of ketorolac tromethamine is administered to them and recorded. If the pain is not relieved or the patient is not satisfied second dose is added and if not relieved other analgesics may be administered and recorded.

Statistical analysis

To detect 20% decrease in pain intensity 24 h after operation, we need to include 27 patients in each group; additional three cases were added to compensate for dropouts.

The data were tested for normality using the Anderson–Darling test and for homogeneity variances before further statistical analysis. Categorical variables were described by number and percent, where continuous variables described by mean and SD. χ^2 test was used to compare between categorical variables whereas comparison between continuous variables was done by unpaired *t* test. A two-tailed *P* value less than 0.05 was considered statistically significant. All analyses were performed with the IBM SPSS 20.0 software (IBM CORP. released 2011. IBM SPSS statistics for windows version 20.0 Ar monk, NY: IBM CORP).

Results

Patient characteristics

There was no significant difference between the two groups regarding age, weight, height, BMI, and sex (Table 1).

Onset of sensory and motor block

Touch onset was significantly shorter in morphine group (11.1 ± 5.7 min) in comparison with placebo group (19.2 ± 3.7 min), with *P* value of 0.016 (Table 2).

Pain onset is significantly shorter in morphine group (13.7 ± 5.2 min) in comparison with placebo group (23.4 ± 3.5 min), with *P* value of 0.025.

Motor onset shows no significant change between morphine group (17.4 ± 5.7 min) and placebo group (25.8 ± 6.2 min), with *P* value of 0.879.

Duration of sensory and motor block

Sensory duration is significantly longer in morphine group (11.3 ± 2.9 min) than placebo group (7.2 ± 1.7 min), with *P* value of 0.022 (Table 3).

Table 1 Demographic data

Parameters	Placebo group	Morphine group	*P*
Sex (male/female)	25/5	27/3	0.706
Age (years)	33.2±11.2	33.2±10.2	0.949
Weight (kg)	77.6±10.9	74.5±8.5	0.161
Height (cm)	170±9.1	171±7.8	0.34
BMI	26.7±2.9	25.4±2.6	0.768

Data are presented as mean±SD.

Table 2 Onset of sensory and motor block

Parameters	Placebo group	Morphine group	*P*
Onset of touch block (min)	19.2±3.7	11.1±5.7	0.016
Onset of pain block (min)	23.4±3.5	13.7±5.2	0.025
Onset of motor block (min)	25.8±6.2	17.4±5.7	0.879

Data are presented as mean±SD.

Table 3 Duration of sensory and motor block

Parameters	Placebo group	Morphine group	*P*
Duration of touch block (h)	7.2±1.7	11.3±2.9	0.022
Duration of pain block (h)	7.8±2.2	12±3.6	0.116
Duration of motor block (h)	6.4±1.8	10.3±2.5	0.148

Data are presented as mean±SD.

Pain duration shows no significant change between morphine group (12 ± 3.9 min) and placebo group (7.8 ± 2.2 min), with *P* value of 0.116.

Motor duration shows no significant change between morphine group (10.3 ± 2.5 min) and placebo group (6.4 ± 1.8 min), with *P* value of 0.0148.

Postoperative analgesia

VAS at 8 h shows no significant change between two groups, with *P* value of 0.091 (Tables 4 and 5).

VAS at 12 h was significantly lower in morphine group (1 ± 1) than placebo group (2 ± 2), with *P* value of 0.001.

VAS at 18 h was significantly lower in morphine group (1 ± 3) than placebo group (3 ± 2), with *P* value of 0.001.

VAS at 24 h was significantly lower in morphine group (1 ± 3) than placebo group (3 ± 2), with *P* value of 0.001.

First analgesic request is significantly longer duration in morphine group (23.3 ± 8 min) than in placebo group (12.8 ± 4.1 min), with *P* value of 0.001.

Total analgesic consumption is significantly lower in morphine group (10.3 ± 17.7) than placebo group (30 ± 12.2), with *P* value of 0.001.

Discussion

The primary end point of our study is that there is significant difference in postoperative analgesic duration which is longer duration in morphine group (23.3 ± 8 min) than in placebo group (12.8 ± 4.1 min), with *P* value of 0.001. Moreover, total analgesic consumption was lower in morphine group (10.3 ± 17.7) than placebo group (30 ± 12.2), with *P* value of 0.001. Moreover, VAS (12, 18, and 24) was lower in morphine group, with *P* value of 0. The study also shows that touch onset was significantly shorter in morphine group (11.1 ± 5.7 min) in comparison with placebo group (19.2 ± 3.7 min), with *P* value of 0.016. Pain onset was significantly shorter in morphine group (13.7 ± 5.2 min) in comparison with placebo group (23.4 ± 3.5 min), with *P* value of 0.025. Motor onset shows no significant change between morphine group (17.4 ± 5.7) and placebo group (25.8 ± 6.2), with *P* value of 0.879. Moreover, sensory duration was significantly longer in morphine group (11.3 ± 2.9 min) than placebo group (7.2 ± 1.7 min), with *P* value of 0.022. Pain duration shows no significant change between morphine group (12 ± 3.9 min) and placebo group (7.8 ± 2.2 min), with *P* value of 0.116. Motor duration shows no significant change between morphine group (10.3 ± 2.5 min) and placebo group 6.4 ± 1.8 min), with *P* value of 0.0148.

The secondary end point is that no complication occurred with technique owing to morphine or local anesthetic injection.

Limitations of our study was small sample size and dependence on an objective measure (VAS score) to compare primary end point.

Similar to our results, a study done by Bazin *et al.*[21] concluded that the addition of morphine to a local anesthetic mixture lengthens the duration of analgesia. The study compared the duration of analgesia produced by a mixture of lignocaine and bupivacaine, either alone or combined with morphine (75 μg/kg), buprenorphine (3 μg/kg) or sufentanil (0.2 μg/kg). The study showed ~ 21 h as duration of analgesia with morphine, which is similar to our study. Another prospective, randomized, double-blind clinical trial done by Bourke and Furman[22] concluded that addition of morphine 0.1 mg/kg to the local anesthetic axillary block solution provided improved postoperative analgesia without an increased frequency of adverse effects or major complications. The study shows that morphine group required approximately half of analgesic dose than the other group. Another study by Saryazdi *et al.*[23] showed comparative evaluation of adding different opiates (morphine,

Table 4 Visual analog scale score

Parameters	Placebo group	Morphine group	*P*
VAS 8	1 (1)	1 (0)	0.091
VAS 12	2 (2)	1 (1)	0
VAS 18	3 (2)	1 (3)	0
VAS 24	3 (2)	1 (3)	0

VAS, visual analog scale.

Table 5 First analgesic request and total analgesia

Parameters	Placebo group	Morphine group	*P*
First analgesic request (h)	12.8±4.1	23.3±8	0.001
Total analgesia requirements (mg)	30±12.2	10.3±17.7	0.001

Data are presented as mean±SD.

meperidine, buprenorphine, or fentanyl) to lidocaine in duration and quality of axillary brachial plexus block. Similar to our result, onset of sensory block was 11.76 ± 3.43 min. Different to our result , onset of motor block was slower than our results 23.4 ± 9.08, duration of sensory block was lower than our result 1.85 ± 0.43 hours , also duration of motor block was lower than our result 1.41 ± 0.46 hours and (VAS 24) was 2.5 ± 2.46 which is also different. Another study by Viel *et al.*[24] evaluated the effectiveness of buprenorphine and morphine, administered into the brachial plexus sheath. The duration of analgesia was 18.25 ± 1.15 h in morphine group, which is nearly similar to our study. In another prospective, randomized, double-blind study by Flory *et al.* [25], it was concluded that addition of morphine 5 mg to interscalene brachial plexus block does not improve quality of intraoperative analgesia, prolong effect of block, nor decrease requirement of analgesia in the first 48 h after operation. Analgesic duration of morphine group in this study was 12.8 ± 7 h which is about half the duration in our study. Another randomized, double-blind study by Racz *et al.*[26] was performed on 50 patients scheduled for elective hand and forearm surgery under axillary plexus block to evaluate the effect of perineuronal morphine on the quality of postoperative analgesia. The time at which analgesia was first required was 646 ± 58 min. These results were widely different to our study in which duration of analgesia was more than double.

Conclusion

We concluded that morphine provides better postoperative analgesia when injected with local anesthetics in ultrasound-guided axillary brachial plexus block without an increase in frequency of complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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