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Original article

Effect of warming bupivacaine 0.5% on ultrasound-guided axillary plexus block. Randomized prospective double-blind study

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ABSTRACT

Objective: To evaluate the effect of warming bupivacaine 0.5% on ultrasound-guided axillary brachial plexus block.
Study design: Prospective, randomized, double-blind.
Patients and methods: Eighty patients undergoing elective or emergency surgery beyond the distal third of the upper limb were divided into two groups of 40 patients: the warm group received 15 mL bupivacaine 0.5% heated to 37 °C; the cold group received 15 mL 0.5% bupivacaine stored for at least 24 hours in the lower compartment of a refrigerator at 13–15 °C. Onset and duration of sensory and motor blocks were evaluated every 5 minutes for 40 minutes. Postoperative pain was evaluated at 1, 3, 6, 12 and 24 hours. Effective analgesia time was recorded as the interval between anesthetic injection and the first analgesia requirement (VAS > 30 mm).
Results: Time to onset of sensory and motor block was significantly shorter in the warm group, and mean duration of sensory and motor block and of postoperative analgesia significantly longer.
Conclusion: Warming bupivacaine 0.5% to 37 °C accelerated onset of sensory and motor block and extended action duration.

1. Introduction

Locoregional anesthesia by nerve or plexus block has undergone unprecedented development in the last two decades, tending to become the technique of choice for upper limb anesthesia, due both to the quality of intraoperative anesthesia and to postoperative comfort.

The technique, however, is not free of risk, and may lead to severe cardiotoxic events in case of accidental intravascular injection or overdose [1].

Good clinical practice rules have been progressively drawn up to reduce these risks: repeated aspiration tests, slow fractionated injection with close surveillance and, above all, smaller anesthetic volume, although this reduces block duration and analgesic quality [2].

Associating adjuvants has also been proposed, essentially to extend block duration and improve quality while limiting anesthetic volume.

Several such molecules have been reported: notably, adrenaline, opioids and clonidine [3,4]. Clonidine prolongs axillary block [4], but the associated sedative and dose-dependent hemodynamic effects led certain authors to explore alternative adjuvants.

Neostigmine [5,6] and verapamil [7] have not been sufficiently studied for their clinical interest to be established.

Bicarbonate increases anesthetic pH and thus the non-ionized fraction, accelerating onset and extending duration of action [8,9]. However, this may reduce bioavailability by inducing precipitation of the anesthetic substance [9,10].

Other authors have suggested that warming the anesthetic should have the same effect, by reducing pKa and thus increasing the non-ionized fraction underlying the pharmacological effect of the anesthetic [11].

The present study therefore sought to assess the effect of warming bupivacaine 0.5% on ultrasound-guided axillary block.

2. Material and methods

After obtaining institutional review board approval and patients' informed consent and registering the study in the Australian New Zealand Clinical Trials Registry

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Table 1
Sensory and motor test regions according to nerve.

Nerve	Motor test	Sensory test
Median	Digital flexion	Thenar eminence
Ulnar	Digital abduction	Hypothenar eminence
Radial	Wrist extension	Back of hand
Musculocutaneous	Elbow flexion	1st metacarpal base

Table 2
Modified Bromage score.

Score	Definition
4	Full muscle group strength
3	Reduced strength, but able to counter resistance
2	Able to counter gravity but not resistance
1	Very restricted motion
0	No motion

(n° ACTRN12612000923864), a prospective randomized double-blind study was run from January to October 2012.

Patients aged 18 to 75 years, classified as ASA (American Society of Anesthesiologists) I, II or III, undergoing elective or emergency surgery beyond the distal third of the upper limb (elbow, forearm, wrist or hand) were included.

Exclusion criteria comprised: pre-existing progressive demyelinizing neurologic pathology, psychiatric disorder, known allergy to the anesthetic, contraindications to axillary block (infectious or malignant axillary adenopathy, injection site infection, hemostasis disorder), inability to move the upper limb (unstable fracture, extensive scarring), and refusal, to undergo axillary block. Likewise, block failure or missing data were exclusion criteria.

On the patient's arrival in the surgery room, an 18 G or 20 G peripheral venous cannula was applied, under standard monitoring (electrocardioscopy, non-invasive blood pressure measurement, pulse oximetry) to the upper limb contralateral to the limb to be anesthetized.

Patients were randomized between two groups, using a pre-prepared urn with opaque envelopes.

The warm group received 15 mL bupivacaine 0.5% (Bupicaïne 0.5%®; UNIMED, Tunisia), warmed to 37 °C in a 37 °C *bain-marie* for 20 minutes. The empty syringes and needles, in their packaging, were held at the same temperature for at least 2 hours before initiating the block.

The cold group received 15 mL bupivacaine 0.5% held for at least 24 hours in the lower compartment of a refrigerator at 13–15 °C. The empty syringes and needles were held in the same compartment for the same time before use.

All solutions were prepared by a senior anesthesia technician, not involved in block performance, intraoperative management or data collection and analysis.

Patients were positioned supine, with the upper limb in 90° abduction and in external rotation, elbow in 90° flexion and hand in supination. A linear probe in a sterile sheath was positioned perpendicularly at the axillary fossa, which had been disinfected with antiseptic solution. A non-determined amount of sterile gel (which was never in contact with the anesthetic solution) was applied between probe and sheath at the axillary fossa. The axillary artery (the central component of the neurovascular bundle) was easily located and the surrounding neural structures were visualized and identified.

After local anesthesia by 2 mL xylocaine 2%, the short-beveled 50-mm insulated 22-G needle (Echoplex®, 50 mm, Vygon, France) was introduced in the axillary fossa under ultrasound guidance, on an "in-plane" approach: needle parallel to probe so as to be entirely visualizable, bevel included. After identifying the neural structures, 4 mL of local anesthetic was injected around each of the radial, medial and ulnar nerves and 3 mL around the musculocutaneous nerve, for a total 15 mL for all 4 nerves. Procedure time was measured as the time needed for ultrasound location and puncture up to end of injection.

Data collection was performed by an investigator not involved in either randomization or block. Sensory and motor block was checked every 5 minutes for 40 minutes. The sensory block was checked on each dermatome (Table 1) by pinprick and touch test, with identical contralateral stimulation as reference, and assessed on a 3-point scale: 0 = no block; 1 = analgesic block; 2 = anesthetic block. The motor block was assessed on the modified Bromage scale (Table 2) every 10 minutes for 40 minutes.

Block success was defined as complete sensory (score = 2) and motor block (score = 0) at 40 minutes, allowing surgery.

Time to onset of sensory block was defined as the interval between total injection and complete sensory block (score = 2).

Duration of sensory block was defined as the interval between end of injection and complete end of sensory block (score = 0).

Time to onset of motor block was defined as the interval between total injection and complete motor block (Bromage score = 2) in the muscles concerned.

Duration of motor block was defined as the interval between end of injection and recovery of normal motor function.

Postoperative pain was assessed at 1, 3, 6, 12 and 24 hours on a visual analogue scale (VAS) from 0 = no pain to 100 = worst imaginable pain.

Patients with VAS > 30 received complementary intravenous analgesia with 1 g paracetamol and 0.15 mg/kg subcutaneous morphine if pain persisted. The interval between anesthetic injection and first requirement for analgesia (VAS > 30) defined analgesia duration.

Once daily during the first 72 postoperative hours, patients were assessed for any complications such as palsy or paresthesia.

The principal assessment criterion was time to onset of sensory and motor block. Secondary assessment criteria comprised duration of sensory and motor block and of analgesia (time to first requirement for analgesia).

3. Statistical analysis

Before launching the study, a power analysis was performed to determine subgroup size. For 5% alpha risk and 80% power, 32 patients were required per group to detect a difference of 10 minutes in motor block onset time. Forty patients were therefore included in either group.

Qualitative variables were described by number and percentage, and compared on Pearson Chi^2 test. Continuous variable distributions were assessed on Kolmogorov–Smirnov test; the Student *t*-test was used for normally distributed variables and the Mann–Whitney test in case of non-normality. Continuous variables were expressed as mean (standard deviation) or median and interquartile range, according to distribution. Time to first requirement for analgesia was compared between groups by Kaplan–Meier survival analysis and log-rank test. The significance threshold was set at $P < 0.05$.

4. Results

Eighty-six patients were assessed for eligibility. Five were not included: 3 for not meeting inclusion criteria, and 2 declining to take part.

Initially, the 81 included patients were randomized between the warm and cold groups, with 41 and 40 patients, respectively; 1 warm group patient was later excluded for missing data. Thus

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