Peri-neural dexmedetomidine as an adjuvant to bupivacaine-induced ultrasound-guided femoral nerve block

Thesis submitted for the partial fulfilment of the Master Degree in Anesthesia, Critical Care and Pain Management

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Abstract

Rationale and background:

Peri-neural dexmedetomidine extends the duration of local anesthetic-induced peripheral nerve blocks in the experimental and the clinical settings. The effects of peri-neural dexmedetomidine on the pharmacodynamic profile of bupivacaine-induced femoral nerve block were not previously explored. We hypothesized that the addition of peri-neural dexmedetomidine will extend the duration of femoral nerve block in patients undergoing arthroscopic knee surgery.

Patients and methods:

This randomized, controlled double blinded study included 45 adult patients undergoing arthroscopic knee surgery. Ultrasound-guided femoral nerve block was initiated 30 min before induction of general anesthesia. Femoral nerve block was achieved with the use of 25 ml of bupivacaine 0.5% in all patients. Bupivacaine was combined with 0.5 ml normal saline (control group, n=15), 50 μg (0.5 ml) peri-neural dexmedetomidine (n=15), or 50 μ g(0.5 ml) intramuscular dexmedetomidine (n=15). All patients received a standard general anaesthetic after ensuring successful femoral nerve block. The onset and duration of sensory and motor blocks, the time to first request to postoperative rescue analgesic, Richmond Agitation-Sedation Score, haemodynamic data, resting and dynamic visual analogue pain scores, were reported at predetermined time assessment points. Postoperative rescue intravenous morphine consumption over 24 hours was recorded.

Results:

The onset of sensory block was significantly shorter and its duration was extended with the use of peri-neural dexmedetomidine compared to the control and systemic route of administration. The onset of motor block was comparable in the three study groups. The duration of motor block was significantly longer in the peri-neural dexmedetomidine group. The time to first request to

rescueanalgesia was prolonged and total postoperative morphine consumption was reduced in the peri-neural dexmedetomidine group. Postoperative sedation was more encountered at the 30 min and two hours assessment points in the peri-neural and intramuscular dexmedetomidine groups. Statistically significant reductions in systolic blood pressure and heart rate were observed up to 45 minutes after induction of general anesthesia in all groups compared to the baseline values. However, there were no statistically significant differences in haemodynamic variables among the three study groups.

Conclusion:

The use of peri-neural dexmedetomidine as an adjuvant to bupivacaine reduces the onset and prolongs the duration of femoral nerve block in patients undergoing arthroscopic knee surgery.

Key words

Ultrasound- femoral- bupivacaine- block- Dexmedetomidine- arthroscopy

Anatomy of the femoral nerve

The femoral nerve is the largest branch of the lumbar plexus. It arises from the second, third, and fourth lumbar nerves. [1]

Course:

The nerve descends through the fibers of the psoas muscle, emerging from the psoas at the lower part of its border, and passes down between the psoas and the iliacus. Eventually, the femoral nerve passes underneath the inguinal ligament into the thigh, where it assumes a more flattened shape. As the femoral nerve passes underneath the inguinal ligament, it is positioned immediately lateral and slightly deeper than the femoral artery (Figure. 1). At the femoral crease the nerve is covered by the fascia iliaca and is separated from the femoral artery and vein by a portion of the psoas muscle and the ligamentumileopectineum. This physical separation of the femoral nerve from the vascular fascia explains the lack of the spread of a "blind paravascular" injection of local anesthetics toward the femoral nerve. [1]

Figure 1. Anatomical relations of the femoral nerve.
FN: Femoral nerve FA: Femoral artery FV: Femoral vein [2]

Motor branches

1) Anterior division branches:
    - Sartorius,
    - Pectineus.
2) Posterior division branches:
    - Rectus femoris,
    - Vastusmedialis,
    - Vastuslateralis, and
    - Vastusintermedius.[3]

Sensory branches

1) Anterior division branches:
    - Provides sensation to antero-medial aspect of the thigh, consists of 2 branches
        a) Medial cutaneous nerve of thigh,
        b) Intermediate cutaneous nerve.
2) Posterior division:
    - Saphenous nerve provides sensation to anteromedial aspect of lower leg.
    - Infra-patellar branches to knee pierces the Sartorius and fascia lata medial to the knee, and provides cutaneous innervation to the skin anteriorly over the patella.[3]

Sono-anatomy of the femoral nerve

Distal to the inguinal ligament, the femoral nerve lies lateral to the femoral artery, deep to the fascia iliaca, on the anterior aspect of the iliopsosas muscle (Figure 2**)**. It is often found within a triangular hyperechoic region. The nerve may also appear as a

biconvex or oval hyperechoic structure. [4.5]The artery is easily located due to its pulsation and/or flow by Doppler (Figure 3).

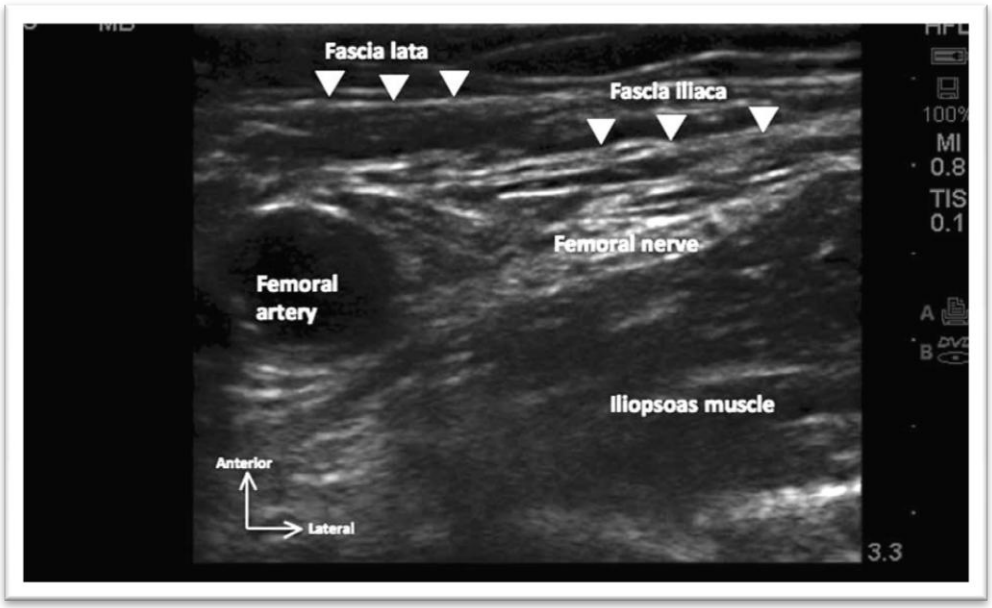

Figure 2. Scan of the left femoral nerve (short axis) at the level of inguinal crease (lateral to femoral artery, deep to fascia lata, superficial to iliopsoas muscle).

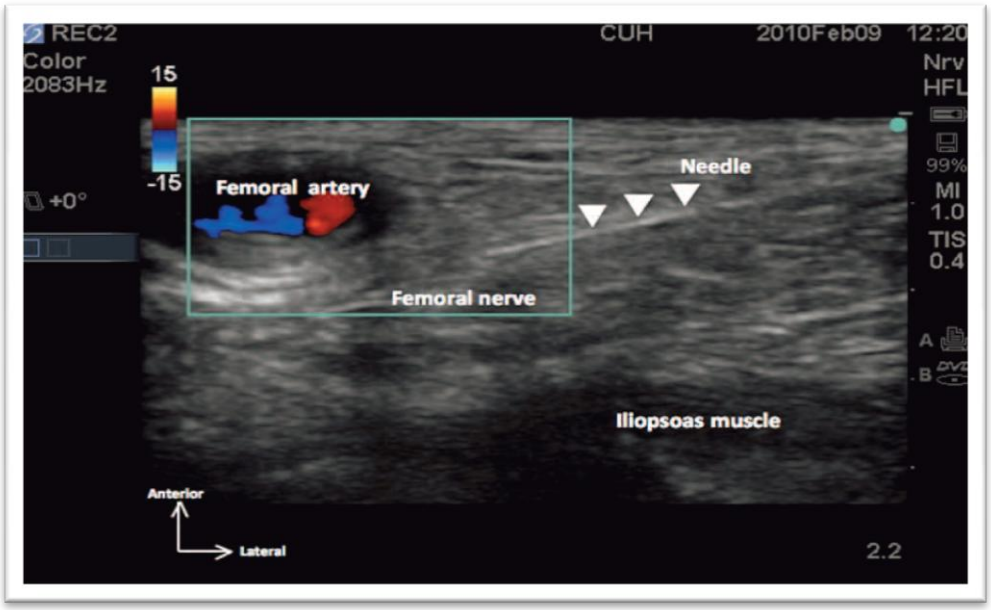

Figure3. Identification of the femoral artery by Doppler flow.

Pharmacology of dexmedetomidine

Alpha 2-adrenoceptor agonists are being increasingly used in anesthesia and critical care as they don't onlydecrease sympathetic tone and attenuate the stress responses to anesthesia and surgery; but also causesedation and analgesia. They are also used as an adjuvant during regional anesthesia. Dexmedetomidine is the most recent agent in this group approved by the FDA in 1999 for use in humans foranalgesia and sedation [(6).]

Alpha-2 receptors:

Found in the peripheral and central nervous systems, platelets, and many other organs including the liver, pancreas, kidney, and eye. Stimulation of Alpha-2 receptors in the brain and spinal cord inhibitsneuronal firing, causing hypotension, bradycardia, sedation, and analgesia. The responses from other organsinclude decreased salivation, decreased secretion, and decreased bowel motility, inhibition of renin release, increased glomerular filtration, and increased secretion of sodium and water in the kidney; decreasedintraocular pressure; and decreased insulin release from the pancreas.[(7)]

Mechanism of action:

Dexmedetomidine has selective alpha 2-adrenoceptor agonist effect especially for the 2A subtype of this receptor, which causes it to be a much moreeffective sedative and analgesic agent than Clonidine.[(7)]

Pharmacokinetics:

Dexmedetomidine undergoes almost complete hydroxylation through direct glucuronidationand cytochromeP450 metabolism in the liver. Metabolites are excreted in the urine (about 95%) and in the feces (4%). It isunknown whether they possess intrinsic activity. The elimination half-life is approximately 2 hours. It maybe necessary to decrease the dose in patients with hepatic failure, since they will have lower rates ofmetabolism of the active drug. Dexmedetomidine metabolites might accumulate in patients with renal failure with unknown consquences. [6]The average protein binding of dexmedetomidine is 94%, with negligible protein binding displacement byfentanyl, ketorolac, theophylline, and digoxin, and lidocaine.[6]

Pharmacodynamics:

The majority of patients receiving dexmedetomidine are effectively sedated yet easily arousable, aunique feature not observed with other sedatives.[6]

Dexmedetomidine does not appear to have any direct effects on the heart.[9]A biphasic cardiovascularresponse has been described after the loading dose.[6,10,11]The bolus of 1 μg/kgdexmedetomidine initially results in a transient increase of the blood pressure and a reflex fall in heart rate,especially in younger patients.[12] Stimulation of alpha B-2-adrenoceptor in vascular smooth muscleseems to be responsible for the initial rise in the blood pressure, which can be attenuated by a slow infusion.[13]However, even at slower infusion rates, the increase in mean arterial pressure over the first 10 minutes wasshown to be in the range of 7%, with a decrease in heart rate between 16% and 18%.[12]The initial responselasts for 5 to 10 minutes and is followed by a slight

decrease in blood pressure due to the inhibition of thecentral sympathetic outflow.[13] The pre-synaptic alpha 2-adrenoceptors are also stimulated decreasing thenorepinephrine release resulting in fall in blood pressure and heart rate.[11] These effects may also be observedin the postoperative period, and can be easily managed with atropine, ephedrine and fluid infusion. [13]However, these effects may be deleterious in hypovolemic patients or patients with fixed stroke volume. The respiratory depression caused by dexmedetomidine has been reported to be much less than with othersedatives.[14]

Side effects:

Dexmedetomidine crosses the placenta and its safety is not established in pregnancy and in children. Common adverse effects of dexmedetomidine include hypotension, hypertension, atrioventricular blocks, bradycardia, atrialfibrillation, nausea,hypoxia.Most of these adverse effects occur during infusion of the bolus dose. Omitting or reducing the loading dose can reduce adverse effects. [15]The use ofdexmedetomidine-based sedation in ICU is not advised in patients with intracranial pathologies until further studies prove itssafety in this group.[16]

Clinical uses:

In general anesthesia

Dexmedetomidine possesses anxiolytic, sedative, analgesic, and sympatholytic properties; it is usedfor premedication. Dexmedetomidine hasalso been found to be an effective drug for premedication before i.v regional anesthesiaas it reducespatient anxiety, sympatho-adrenal responses, and opioid analgesic requirements. [17]

For the intraoperative period, it is used in a dose 0.2 to 0.7 μg/kg/hr; it attenuates the stress-induced sympathoadrenal responses to laryngoscopy, intubation and surgery andprovides increased hemodynamic stability. It potentiates the anesthetic effects of all intraoperativeanesthetics, regardless of the method of administration (intravenous, volatile, or even regional block). It was found that dexmedetomidine has an analgesic properties and could be used alone as a single agent after minor surgery. [18]Dexmedetomidine provides intense analgesia during the postoperative period. Dexmedetomidine seems to have few respiratory side effects and it can becontinued safely in the extubated, spontaneously breathing patient. Dexmedetomidine is associated with a lower rate of shivering. [7]Overall, dexmedetomidine administration during anesthesia maintains hemodynamic stability, allows lowerdoses of anesthetics and opiates to be used, resulting in more rapid recovery from anesthesia and a reducedneed for pain medication in the PACU, thereby reducing the length of stay .[7]

In regional anesthesia and analgesia

There are only fewstudies describing the peri-neural potentiating effects of dexmedetomidine in patients receiving peripheral nerve blocks. These effects were reported with single injection infraclavicular brachial plexus block[19], posterior tibial nerve block[20], and greater palatine nerve block.[21]Administration of dexmedetomidine in subarachnoid space to ewes was found to produce dose-dependent analgesia.[22]Dexmedetomidine produces a powerful antinociceptive effect, mediated at thespinal level, while systemic redistribution of the drug leads to a hypnotic state with significant cardiorespiratory effects [23]

In critical care

Dexmedetomidine has been used in the intensive care unit for its sedative, anxiolytic, and analgesic propertiesand does not produce respiratory depression due to its non-opioid mechanism of analgesia. The doses shouldbe titrated to the desired clinical effect. For adult patients, dexmedetomidine is generally initiated with aloading infusion of 1 μg/kg over 10 minutes, followed by a maintenance infusion of between 0.2 to 0.7 μg/kg/hr. The bolus dose is not used as it cancause paradoxical increases in blood pressure.(24)

Patients who received dexmedetomidine in the intensive care unit were observed to be arousable and alertwhen stimulated from sedation and quickly return to their sleep-like state. It is not necessary to discontinue dexmedetomidine prior to extubation. Dexmedetomidine has beencontinuously infused in mechanically ventilated patients prior to extubation, during extubation, andpostextubation. (25)

Precautions:

Dexmedetomidine should be used cautiously in patients with pre-existent severe bradycardia and conductionproblems, in patients with reduced ventricular functions (ejection fraction <30%), and in patients who arehypovolemic or hypotensive. Dexmedetomidine reduces sympathetic activity resulting in lower blood pressureand reduced heart rate. These hemodynamic values return to baseline when the infusion is discontinued.(24)

Future:

If the safety of long term infusion of dexmedetomidine is established, it may be used more frequentlyfor the post- operative pain relief and for extended ICU sedation. All effects of dexmedetomidine could beantagonized easily by administering the alpha 2-