A comparative study between epidural analgesia of levobupivacaine with fentanyl versus levobupivacaine with dexmedetomidine for lower limb surgeries.

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List of abbreviations

ASA: American society of anesthesia.

ABP: Arterial blood pressure.

ACLS: Advanced cardiac life support.

ACTH: Adrenocorticotrophic hormone.

ADH: Antidiuretic hormone.

ATP: Adenosine triphosphate.

BLS: Basic life support.

CBC: Complete blood count.

CSF : Cerebrospinal fluid.

CNS: Central nervous system.

CVS: Cardiovascular system .

CYP: Cytochrome p.

CSE: Combined spinal epidural .

cAMP: Cyclic Adenosine monophosphate.

Dex: Dexmedetomidine.

ECG: Electrocardiogram.

EEG: Electroencephalogram.

FDA: Food and drug administration.

G: Gauge .

GABA: Gamma amino butyric acid.

I.v: Intravenous .

INR: International normalized ratio.

IU: International unit .

LA: Local anesthetics .

LAST: Local anesthetics systemic toxicity .

LC: Locus coeruleus.

MAP: Mean arterial blood pressure .

MEq: Mille equivalent.

Mg: milligrams .

ML: Milliliters .

Min: minute.

NMDA: N-methyl-D-aspartate.

p value: Probability value.

PACU: Post Anesthesia Care Unit.

Post-op: postoperative .

PC: Prothrombin concentration.

PDPH: Post dural puncture headache .

pH: Power of hydrogen.

PT: Prothrombin time.

PC: Prothrombin concentration .

PCEA: Patient controlled epidural analgesia.

SD: Standard deviation.

SPSS: Statistical Package for the Social Science.

SNS: Sympathetic nervous system .

USA: United states of America.

UK: United Kingdom .

VAS: visual analog score .

α: Alpha .

µg: Microgram .

µ: Mu.

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Abstract

BACKGROUND:

The use of epidural analgesia for the management of postoperative pain has evolved as a critical component of multimodal approach to achieve the goal of adequate analgesia with improved outcome. Epidural analgesia offers superior postoperative pain relief compared with systemic opioids. In addition to improved pain control, epidural analgesia can improve patient outcome by attenuating detrimental perioperative physiology.

MATERIALS AND METHODS:

60 patients ,20 to 50 years, ASA I or II scheduled for elective lower limb surgeries.were recruited for the study.Patients were randomized to receive in epidural catheter 14ml levobupivacaine 0.5% with 1ml (1mic/kg) fentanyl at induction then epidural infusion of this mixure at rate of 5ml/h till the end of the surgery "group F" or receive in epidural catheter 14ml levobupivacaine 0.5% with 1ml (1mic/kg) dexmedetomidine at inducton then epidural infusion of this mixure at rate of 5ml/h till the end of the surgery "group D". We measured intraoperative MAP ,heart rate and spo2 every 10 minutes and Ramsay sedation score every 1h. Time to reach sensory level T10, time to complete motor block, number of patients in Each group need a bolus dose, vasopressor and atropine were assessed and associated complications .We measured postoperative mean arterial blood pressure ,heart rate ,pain by VAS every one hour for the first 24h postoperative,1st time needed for rescue analgesia, return of complete motor recovery by

modified Bromage scale, sedation by ramsay score intraoperative and every one hour postoperative till 6h.

RESULTS:

Pain scores were significantly lower in dexmedetomidine group postoperatively and needed less rescue analgesic. Intraoperative and postoperative sedation was significantly higher in dexmedetomidine group.Itching occurred only in fentanyl group.

CONCLUSION:

Epidural levobupivacaine with dexmedetomidine provided better sedation, adequate surgical anesthesia with prolonged postoperative analgesia for lower limb surgeries . Both adjuvants reduced the epidural dose of levobupivacaine and potentiated its efficacy.

Keywords:

Analgesia, Analgesics.

Lower limb surgeries .

Dexmedetomidine, Fentanyl .

Levobupivacaine

Epidural .

Pain.

Sedation.

Postoperative

Aim of work

The purpose of this prospective randomized, double blind study was to investigate efficacy of epidural fentanyl and dexmetedomidine as adjuvants to epidural levobupivacaine in intraoprative hemodynamics and postoperative pain control after lower limb surgeries.

Introduction

The use of epidural analgesia for the management of postoperative pain has evolved as a critical component of multimodal approach to achieve the goal of adequate analgesia with improved outcome. Epidural analgesia offers superior postoperative pain relief compared with systemic opioids. In addition to improved pain control, epidural analgesia can improve patient outcome by attenuating detrimental perioperative physiology [(1)].

Various adjuvants are being used with local anesthetics for prolongation of intraoperative and postoperative analgesia. Dexmedetomidine, the highly selective α2 adrenergic agonist is a new neuraxial adjuvant gaining popularity [(2)] .

Dexmedetomidine is a highly selective α2-receptor agonist with sedative, analgesic and anxiolytic effects. It is chemically related to clonidine and has been an authorized drug in Europe since September 2011 [(3)].

Dexmedetomidine is as an epidural adjuvant as it provides comparable stable hemodynamics, early onset, and establishment of sensory anesthesia, prolonged post-op analgesia, lower consumption of post-op LA for epidural analgesia, and much better sedation levels [(4)] .

Opioids are often given during general anaesthesia to control autonomic reflexes. Well-known postoperative side-effects of opioids include respiratory depression, nausea, and sedation. Additionally, opioids cause acute tolerance and opioid-induced hyperalgesia. Because

of concerns about side-effects, anaesthesiologists now try to restrict perioperative opioid administration. One way to reduce the total dose is to inject the opioids in the epidural space. Bolus injections of epidural fentanyl, for example, are known to enhance analgesia in unanaesthetized subjects compared with the same dose given intravenously [(5)] .

Spinal opioid receptors that suppress nociception from lumbar dermatomes lie in the spinal cord segments below the lower thoracic epidural space. We thus asked whether these opioid receptors could be activated by administration of epidural fentanyl. If epidural fentanyl does suppress autonomic reflexes to a greater extent than i.v. fentanyl, this might be a method to reduce the total opioid dose during surgical procedures in which an epidural catheter is in place[(6)].

Based on findings that the cardiotoxicity infrequently observed with racemic bupivacaine shows enantioselectivity, i.e. it is more pronounced with the R(+)-enantiomer, the S(-)-enantiomer (levobupivacaine) has been developed for clinical use as a long acting local anesthetic. The majority of in vitro, in vivo and human pharmacodynamic studies of nerve block indicate that levobupivacaine has similar potency to bupivacaine. However, levobupivacaine had a lower risk of cardiovascular and CNS toxicity than bupivacaine in animal studies. In human volunteers, levobupivacaine had less of a negative inotropic effect and, at intravenous doses >75 mg, produced less prolongation of the QT interval than bupivacaine.Fewer changes indicative of CNS depression on EEG were evident with levobupivacaine[(7)] .

Anatomy relevant to epidural and subarachnoid blockade

Surrounding the spinal cord in the bony vertebral column are three membranes (from within to the periphery): the pia mater, arachnoid mater, and dura mater . The pia mater is a highly vascular membrane that closely invests the spinal cord and brain. The arachnoid mater is a delicate, nonvascular membrane closely attached to the outermost layer, the dura. In the subarachnoid space are the cerebrospinal fluid (CSF), spinal nerves, a trabecular network between the two membranes, and blood vessels that supply the spinal cord and lateral extensions of the pia mater and dentate ligaments, which provide lateral support from the spinal cord to the dura mater .[8] Although the spinal cord ends at the lower border of the first lumbar vertebra (L1) in adults, the subarachnoid space continues to the second sacral vertebra (S2) . The third and outermost membrane in the spinal canal is a randomly organized fibroelastic membrane, the dura mater (or theca). This layer is a direct extension of the cranial dura mater and extends as the spinal dura mater from the foramen magnum to S2, where the filum terminale blends with the periosteum on the coccyx .Surrounding the dura mater is another space that is often used by anesthesiologists, the epidural space. [9] The spinal epidural space extends from the foramen magnum to the sacral hiatus and surrounds the dura mater anteriorly, laterally, and more usefully, posteriorly. The epidural space is bounded anteriorly by the posterior longitudinal ligaments, laterally by the pedicles