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A comparison of post-operative analgesia between intrathecal nalbuphine with levobupivacaine 0.5% and intrathecal levobupivacaine 0.5% alone in intra abdominal surgeries'

ANAESTHESIOLOGY

KEYWORDS:

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1. BRIEF RESUME OF THE INTENDED WORK:

BACKGROUND AND OBJECTIVES:

Regional anaesthesia has emerged as an important technique, with rapid onset of action and good muscle relaxation and relatively simplicity of administration. Intrathecal anaesthesia is widely used regional anaesthesia technique with effective sensory and motor blockade. Racemic bupivacaine is the most frequently used local anaesthetic agent for intrathecal anaesthesia. There are also undesirable side effects associated with bupivacaine such as cardiotoxicity, CNS toxicity as well as prolonged motor blockade. Levobupivacaine , a pure S(-) enantiomer of bupivacaine , has emerged in recent years as an alternative for regional anaesthesia with desirable properties such as low cardio toxicity , less motor blockade.[1]

Because of its significantly low side effects in terms of motor blockade and lower cardiac toxicity, levobupivacaine seems to be an attractive alternative to bupivacaine. During epidural use, levobupivacaine and racemic bupivacaine have the same analgesic properties , however levobupivacaine is 13% less potent on a weight per volume basis for motor blockade. Hence, in the epidural route, levobupivacaine has greater sensory-motor dissociation in blockade than bupivacaine.[2]

Neuraxial opioids are widely used in conjunction with local anaesthetics as they permit the use of lower dose of local anaesthetics, while providing adequate anaesthesia and analgesia.3 Also neuraxial opioids allow prolonged postoperative analgesia and early recovery from spinal motor blockade.4 various opioids have been used along with bupivacaine to prolong its effect, to improve the quality of analgesia and minimize the requirement of postoperative analgesia.[5]

Adding intrathecal opioids as an adjuvant to intrathecal local anaesthetics to decrease their dose and provide a good hemodynamic stability which are the major concerns of spinal anaesthesia during intraabdominal surgeries. Combinations opioids and local anaesthetics when injected intrathecal act at two different sites, opioids act at receptor site, where as local anaesthetic acts at axons of nerve fibres, to provide adequate analgesia.[6]

Many studies evaluated the combination of bupivacaine with fentanyl for intra thecal anaesthesia. However not many studies are available on use of intrathecal levobupivacaine with nalbuphine. Hence the present study is undertaken to study the clinical efficacy in terms of sensory block, motor block and hemodynamic effects of isobaric 0.5% levobupivacaine with nalbuphine 0.8 mg in patients undergoing intraabdominal surgical procedures under intrathecal anaesthesia

1.2 REVIEW OF LITERATURE:

Spinal anaesthesia also referred as intrathecal anaesthesia or subarachnoid block. It creates an intense sensory and motor block that can be effectively achieved with small dose of local anaesthetic. Almost all local anaesthetic have been used at some point in spinal anaesthesia. First case of spinal anaesthesia in humans was performed by August Bier in 1898 using cocaine. spinal anaesthesia using levobupivacaine was introduced in1980's.[7]

Erdil et al.,(2009) in a double blinded randomized prospective study involving 80 elderly patients compared the block durations and haemodynamic effects of 0.5% bupivacaine and 0.5% levobupivacaine with fentanyl 15mcg and observed that time to reach T10, peak sensory level and to maximum motor blockade were significantly less in 2.3ml of 0.5% bupivacaine with fentanyl 15mcg group whereas hemodynamic stability were better in 2.3ml 0.5% levobupivacaine with fentanyl group in urological surgeries.[8]

Santiago et al.,(2011) in his study involving 60 patients for knee arthroscopy compared ambulation time after using 3 low dose, low concentration levobupivacaine with fentanyl solutions[3mg, 4mg, 5mg levobupivacaine plus 10 mcg fentanyl]. 3mg dosage was halted because of large number of inadequate blockade(50%). The mean ambulation time was 55±25 mins in 4mg group and 73 27mins in 5mg group. With the mentioned findings they concluded that 4mg levobupivacaine plus 10mcg fentanyl produced adequate surgical anaesthesia with shorter ambulation time.[10]

Lee et al.,(2009) in his prospective, randomized, double blind study involving 75 patients using intrathecal ropivacaine, levobupivacaine and bupivacaine for lower limb orthopaedic surgeries with duration of up to 50 minutes investigated the effective dose(ED50), found levobupivacaine and bupivacaine to be equipotent. The calculated ED50's were 5.50mgs for bupivacaine, 5.68mg for levobupivacaine and 8.41mg for ropivacaine in intrathecal anaesthesia.[9]

Gori et al., (2010) studied the influence of positioning on plain levobupivacaine in spinal anaesthesia in 46 women undergoing spinal anaesthesia. Using 12.5mg of levobupivacaine, after performing spinal blockade, one group remained seated for 2 minutes and the other group assumed supine position immediately. They found no difference in onset time, level of sensory block, Bromage score .[11]

OBJECTIVES OF THE STUDY:

1. To evaluate the onset, duration of sensory blockade, degree of motor blockade and hemodynamic effects associated with intrathecal isobaric levobupivacaine 0.5%
2. To evaluate the onset, duration of sensory blockade, degree of motor blockade and hemodynamic effects associated with intrathecal isobaric levobupivacaine 0.5% and nalbuphine0.8mg.
3. to compare the onset and duration of sensory blockade, degree of motor blockade and hemodynamic effects associated with intrathecal isobaric 0.5%levobupivacaine and levobupivacaine 0.5% with nalbuphine 0.8mg

MATERIALS AND METHODS

SOURCE OF DATA :

The study entitled " A comparison of post-operative analgesia between intrathecal nalbuphine with levobupivacaine 0.5% and intrathecal levobupivacaine 0.5% alone in intra-abdominalsurgeries" will be conducted in Father muller medical college hospital, Mangalore, from august 2016 to September 2016.

METHOD OF COLLECTION OF DATA:

Study type: Randomised double blind control study

Duration of study:2 months
Sample size: 100 patients selected using sampling technique

INCLUSION CRITERIA:
1. Patients posted for elective lower limb orthopaedic procedures
2. Age between 18 to 65 years of either sex.
3.weight between 40 to 90 kgs and height between 140 to 180 cms
4.ASA physical status between 1-2 with normal coagulation profile.
5.written informed consent.

EXCLUSION CRITERIA:
1. Emergency surgeries
2. Known hypersensitivity to amide local anaesthetics.
3. History of active neurological, cardiac, respiratory and renal diseases.
4. Blood dyscrasia, clotting disorders and platelet count <100000 mm^3.
5. Patients with Cutaneous infections or anatomical malformation of the spine.
6. Weight > 100 kgs, age > 65 years .

PLAN OF STUDY:
A detailed history and pre anaesthetic evaluation will be done on the previous day of the surgery.

Routine investigations like haemoglobin, blood grouping, blood urea, serum creatinine, blood sugar and platelet count, PT, INR will be done. ECG whenever indicated will be taken to rule out the presence of any active cardiac disease.

Written informed consent will be taken prior to surgery from the patient.

Methods :
After approval from institutional ethical committee 100 Patients of both genders ,in the age range of 18 to 65 years scheduled for intraabdominal surgery will be selected for the purpose of this study.

Patients will be kept nil oral for at least 6 hours before the surgery. All the patients will be premedicated with ranitidine 150mg on the day before surgery. Any sedatives and hypnotics are avoided during preoperative, intraoperative and postoperative period. The patients will be randomly divided into 2 groups of each consisting 50 patients by lottery method.

Group 1: inj.levobupivacaine 0.5% 3ml + inj.nalbuphine 0.8 mg(0.8ml) intrathecally

Group2: inj.levobupivacaine 0.5% 3ml + 0.8ml normal saline intrathecally

Patient will be shifted to the operation theatre and pulse oximeter, non invasive blood pressure and electrocardiography monitors will be connected. Baseline parameters like heart rate, oxygen saturation (SpO2) and non invasive blood pressure will be recorded.
A peripheral intravenous line will be secured in the hand with an intravenous cannula and preloaded with lactated ringer solution at 10ml/kg body weight. The anaesthesiologist, who performed the intrathecal injection and assessment of intrathecal block, will be blinded to the group of study solution. The study solution will be prepared by another anaesthesiologist who is not involved in the clinical care of the patient.

Thereafter under aseptic precaution 25 G Quinke Babcock spinal needle will be inserted in the lateral decubitus position at L3-L4 level with midline or paramedian approach and the respective drug will be injected intrathecally according to the group assigned. Patients will be randomly allocated by means of sealed envelope into Group A or Group B.

Group 1: inj.levobupivacaine 0.5%3ml + inj.nalbuphine 0.8 mg(0.8ml) intrathecally

Group2: inj.levobupivacaine 0.5% 3ml + 0.8ml normal saline intrathecally.

After completion of intrathecal injection, patient will be turned back immediately to supine position. Oxygen 5L/minute administered via face mask. During the procedure, patient's heart rate, blood pressure pulse oxymery, ecg monitoring will be done.

The patient will be monitored and following parameters will be noted:
Intraoperatively following observations will be made:
-T0-time of spinal anaesthesia
-T1-time of onset of sensory blockade
-T2-time of onset of motor blockade
-T3-time of first dose of rescue analgesia required

The level of the sensory blockade will be tested with pin prick method using 22 G hypodermic needle. Sensory block assessed at 1 minute interval until block reached T12 . It will be then repeated every 2 minute interval until the level stabilized for four consecutive tests. This level was as the peak sensory block level. Onset of adequate sensory block is defined as the achievement of a sensory block level of T12 dermatome or higher for initiation of surgery. If the level attained is inadequate at 10 minutes the patient will be excluded from the study and given general anaesthesia.

After the surgery, sensory block level was evaluated every 30 minutes until its regression to L5 level.

The level of motor blockade will be judged with Bromage scale.

BROMAGE SCALE

score	Degree of block	CRITERION
0	Nil(0%)	Free movement of legs and feets.
1	Partial(33%)	Just able to flex knees with free movement of feet
2	Almost complete(66%)	Unable to flex the knee but with free movement of feet
3	Complete(100%)	Unable to move legs or feet in a fully awake patient.

Intraoperative recordings included heart rate, systolic blood pressure (SBP), diastolic blood pressure(DBP) and oxygen saturation. Recordings are done every 2 minutes for the first ten minutes, every 5 minutes for next 30 minutes and every 10 minutes there after till the end of surgery. In the postoperative ward sensory and motor block are assessed every 30 minutes , time taken for sensory block to reach L5 level which will be taken as duration of analgesia and time taken for the patient to attain complete motor recovery wbich is taken as duration of motor blockade.

3. Adverse effects:
Adverse events are recorded as either spontaneously reported by the patient or observed by the investigator.

- Any episodes of nausea, vomiting, pruritis are evaluated and treated with 4mg ondansetron given slow intaravenous.
- Hypotension is defined as decrease in systolic blood pressure of more than 30% from the baseline or 100mmHg . this is treated with intravenous infusion of Ringer lactate or intravenous boluses of 6mg mephentermine.
- Bradycardia is defined as heart rate less than 50 beats per minute. And is trated with Atropine 0.01mg/kg body weight .

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STATISTICAL ANALYSIS:

Statistical analysis of the data are presented as mean and standard deviation. Qualitative data as frequency and percentage. Sensory and motor blockade are analysed with t-test. Chi-square test is used to analyse the peak sensory level attained and for adverse effects between the groups.

Power analysis from similar studies suggest that a sample size of 50 patients is required to get a power of 90% with significance.

$$n=2\,(Z_\alpha+Z_\alpha)^2\sigma^2$$
$$(X_1 X_2\ )^2$$

Z_α=1.96 at 95% C.I

Z_β=1.281 at 90% C.I

By above formula, n= 10 .

A sample size of 50 patients per group would provide 80% power to detect any difference.

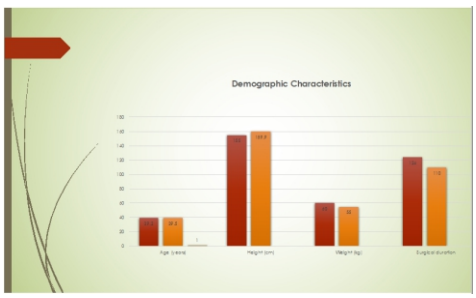
P<0.01 statistically highly significant

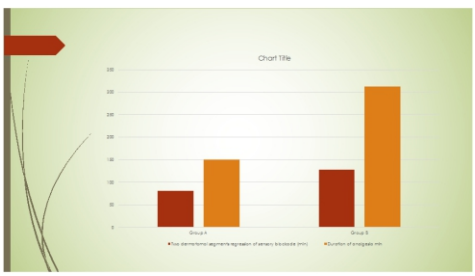
P <0.05 statistically significant

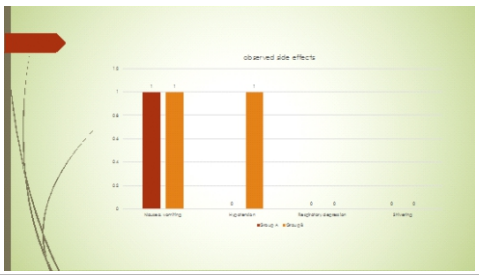
P >0.05 statistically not significant

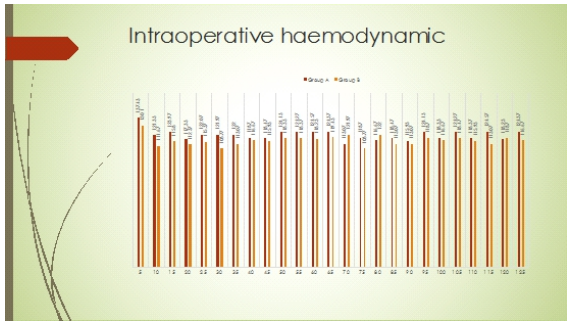
Results:

- All the demographic variables like age, weight, height, sex ratio and duration of surgery were comparable in all the four groups.
- The onset of sensory and motor blockade were found to be statistically insignificant (P>0.05) *between the two groups.*
- Maximum sensory level achieved in both groups was T6 and T10 level was achieved in all patients.
- Two-segment regression time of sensory blockade was prolonged in group B with a mean of 128.4 min.
- Group B had the longest duration of analgesia with a mean of 312.7 min compared with 150.6 min in group A.
- The patients had a highest VAS score of 3.6 at 270 min (group B).









DISCUSSION:

- We conducted this study to compare the efficacy of nalbuphine as an adjunct to intrathecal levobupivacaine in lower limb orthopedic surgeries.
- Nalbuphine, a mixed agonist-antagonist drug, binds both to mu and kappa receptors
- Number of animal studies has been under taken to prove that intrathecal nalbuphine was not neurotoxic.
- Culebras et al., studied intrathecal nalbuphine in doses of 0.2, 0.8 and 1.6 mg in 90 obstetric patients undergoing caesarean section and found 0.8 mg as the most effective dosage.
- Culebras et al., in their study concluded that intrathecal nalbuphine improves intraoperative analgesia and prolongs postoperative analgesia, without increasing the risk of side effects
- There are safety issues regarding the intrathecal use of nalbuphine and insufficient data to guarantee safe intrathecal use in human patients.
- An animal study by Rawal et al., that examined the effects of nalbuphine in a dose of 0.75 mg/kg and reported no behavioral or systematic histopathologic abnormalities.
- Neuraxial use of nalbuphine is in modern anesthesia practice for more than 10 years. We are not aware of any reports of neurotoxicity of intrathecal nalbuphine since then.
- The addition of opioids (fentanyl, morphine) improves the quality of analgesia and decrease the effective dose of levobupivacaine for post-operative analgesia.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS ORINTERVENTIONS TO BE CONDUCTED ON PATIENT OR OTHER HUMAN OR ANIMALS

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION?

Yes.

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