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Dexmedetomidine As an Adjuvant to Two Different Dosed of Intrathecal Hyerbaric Bupivacaine in Elective Lower Limb Orthopaedic Surgeries

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Abstract **Original Research Article**

Many adjuvants have been used to improve the duration and quality of anaesthesia and analgesiatill postoperative period. Dexmedetomidine, with its high α2 adrenoceptor agonism, has been found to be a useful adjuvant to intrathecal hyperbaric bupivacaine in prolonging sensory and motor block. Thus using Dexmedetomidine as an adjuvant can reduce local anaesthetic requirment. This study was done to compare two different doses of hyperbaric bupivacaine intrathecally with a fixed dose of dexmedetomidine in an aim to arrive at an optimum dose of hyperbaric bupivacaine with minimum adverse effects that would provide satisfactory block and hemodynamic stability for lower limb orthopedic surgeries. A prospective, non interventional, observational clinical study was carried out on 100 ASA Grade I and II patients of either sex, aged 18-70 years, undergoing various orthopaedic surgeries on the lower limb under subarachnoid block (SAB). The patients were divided into two groups of 50 patients each. Group A patients were received 2ml of 0.5% hyperbaric bupivacaine (10mg) with 5mcg of dexmedetomidine and Group B patients were received 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg) with 5mcg of dexmedetomedine. The study yields statistically significant occurrence of hypotension and delay in motor function recovery in 12.5 mg hyperbaric bupivacaine group although no statistical difference in characteristics of sensory blockade and analgesia. So the study concludes the use of dexmedetomidine could reduce the dose of intrathecal local anaesthetic requirement. A 10 mg dose of hyperbaric bupivacaine with 5 µg dexmedetomidine may be sufficient for lower limb orthopedic surgeries.

Keywords: Dexmedetomidine, Hyperbaric Bupivacaine, Subarachnoid Block, Lower LimbOrthopaedic Surgery.

I. INTRODUCTION

Regional anaesthesia is the preferred technique for most of lower abdomen and lower limb surgeries. It allows the patient to remain awake, minimises or completely avoids the problem associated with airway management. With spinal anaesthesia, the technique is simple to perform, the onset of anaesthesia is more rapid, avoids polypharmacy, allows the surgical incision to be made sooner and provides post-operative analgesia. Spinal anaesthesia with cocaine was initially produced in- advertently by Leonard J Corning in 1885 and first used deliberately by August Bier in 1898 [1].

For decades lignocaine had been the local anaesthetic of choice for spinal anaesthesia. Its advantages are rapid onset of action and good motor block manifested as good muscle relaxation. Its use was limited by its short duration of action and had been implicated in transient neurologic symptoms and cauda equina syndrome following intrathecal injection [2, 3].

Bupivacaine is three to four times more potent than ligno- caine [4] and has longer duration of action. Its disadvantages are slow onset of action and decreased motor block.

Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anaesthesia. Though the duration of action of bupivacaine is prolonged, it will not produce prolonged post- operative analgesia. Hence another adjuvant is required for producing prolonged post-operative analgesia. The discovery of opioid

receptors and endorphins in spinal and supraspinal regions soon led to the use of spinal opiates. Morphine was the first opioid administered intrathecally to augment neuraxial blocks [5]. Opioid analgesic drugs produce intense, prolonged analgesic action without gross autonomic changes, loss of motor power or impairment of sensation other than pain when injected into subarachnoid or epidural space [6].

Morphine can produce serious side effects like late and unpredictable respiratory depression, post-operative nausea and vomiting, pruritus and urinary retention [7, 8]. Recently α-2 adrenoreceptor agonists have been used as adjuvants to local anaesthetic agents because of their sedative, analgesic and haemodynamic stabilizing effect. They have been found to prolong the duration of spinal block following intrathecal administration [9].

Clonidine, an α-2 adrenergic agonist, has a variety of different actions. Oral clonidine was used to prolong lidocaine spinal anaesthesia [10], tetracaine spinal anaesthesia [11] and bupivacaine spinal anaesthesia [12]. Hypotension was more pronounced after oral than intrathecal clonidine [12]. The addi- tion of intrathecal clonidine to bupivacaine prolongs analgesia and decreases morphine consumption postoperatively more than oral clonidine. Clonidine has antihypertensive properties and the ability to potentiate the effects of local anaesthetics [13].

Clonidine has been shown to result in the prolongation of the sensory blockade and reduction in the amount or concentration of local anaesthetic required to produce post- operative analgesia [14]. Clonidine also has the ability to prolong the motor blockade produced by bupivacaine. Large doses of intrathecal clonidine (as much as 450µg) without local anaesthetics provide sedation and intense and long-lasting postoperative analgesia, are inadequate for surgical anaesthesia and for this reason, clonidine has been used as an adjuvant to local anaesthetics rather than used alone [9]. Dexmedetomidine also an α-2 adrenergic agonist, is pharmacologically related to clonidine and is the most recent agent in this group approved by FDA in 1999 for the use in humans as short term medication (<24 hrs) for analgesia and sedation in intense care unit. Its unique properties render it suitable for sedation and analgesia during the whole of perioperative period. Various studies have also found that dexmedetomidine can decrease the haemodynamic response to laryngoscopy and intubation [15].

Dexmedetomidine is a highly specific and selective α-2 adrenoceptor agonist with 8 times more affinity for α-2 adrenoceptor than clonidine. The ratio of α-1:α-2 receptor binding selectivity for dexmetomidine is 1:1620 compared to 1:220 for clonidine [15].

While clonidine has been used as an adjuvant to local anaes- thetic agents for intrathecal purposes with successful results, there are only a few studies available for dexmedetomidine for such studies.

Till recently, dexmedetomidine was not available in India though it is being used in other countries since many years. Since it has been recently introduced in India and not many studies have been done in India regarding its use as an adjuvant to local anaesthetic agents for intrathecal purpose hence there is a need to study its effectiveness for spinal anaesthesia.

Dexmedetomidine, with its high α-2 adrenoceptor agonism, has been found to be a useful adjuvant to intrathecal hyperbaric bupivacaine in prolonging sensory and motor block. Thus using Dexmedetomidine as an adjuvant can reduce local anaesthetic requirements. This study is to compare two different doses of hyperbaric bupivacaine intrathecally with a fixed dose of dexmedetomidine in the aim of arriving at an optimum dose with minimum adverse effects. This has been achieved by conducting a comparative observational and prospective study. This study has conducted in the OT Complex and postoperative ward of North 24 Parganas District Hospital, Barasat. All patients fulfilling the inclusion criteria have enrolled and observed based on predesigned and pretested proforma. Clinical Examination and necessary investigations have been done. At the end of the study, the collected data were analysed by applying appropriate statistical tests based on the results obtained, conclusions have been drawn.

II. MATERIALS AND METHODS

A. Ethical Considerations

The study protocol, informed consent form [in Bengali, Hindi, English] and case report form [CRF] were submitted to the ethical committee of R.G Kar Medical College Hospital, Kolkata, West Bengal, for approval. Written and informed con- sent has been taken from each participant of the study. Illiterate individuals have given their fingerprint [left thumb impression] instead of signature in the presence of an appropriate witness.

B. Study Area

- North 24 Paraganas District Hospital, Barasat, Kolkata, West Bengal

C. Study Period

- 2020-2021

D. Definition of Population

The study was conducted on patients of ASA (American Society of Anaesthesiology) grade 1 and 2 between the age group of 18-70yrs posted for elective lower limb orthopaedic surgeries at North 24 Parganas District Hospital. There were two groups comprising of

patients. Inform consent has been taken from all patients.

E. Sampling Techniques

- Study Type: Observational
- Study Design : Prospective Study
- Primary Purpose : To promote Adjuvant

F. Sample Size

The sample size was estimated using the mean time to reach the T10 sensory block from the study by Kanazi *et al*., using these values at 95% confidence limit, and 80% power sample size of 46 was obtained in each group. With 10% nonresponse, a sample size of 46 + 4.6 which is close 50 cases was included in each group.

G. Statistical Analysis

Statistical analysis has done after relevant data collection using available standard statistical software. Mean and Median have calculated for all qualitative variables and for measures of dispersion standard deviation, standard IQR have calculated. Student's test for the analysis of parametric data while Fishers/ chi-square test for non parametric data. P value < 0.05 has considered statistically significant. All statistical tests were two tailed.

$$n = Z1 - \alpha 2 \sqrt{2 * P(1-P)} + Z\beta \sqrt{P1(1-P1) + P2(1-P2)}2(P1-$$

Where,
$Z1 - \alpha 2 = 1.96$ (*astypeIerroris* 5%)
$Z\beta = 0.84$ (*at* 80% *power*)
$P = (P1 + P2)/2$

H. Methods

After ethical committee approval and written informed con- sent, a prospective ,non-interventional, observational clinical study was carried out on 100 ASA Grade I and II patients of either sex, aged 18-70 years, undergoing various orthopaedic surgeries on the lower limb under subarachnoid block (SAB). Each patient was visited preoperatively, and the procedure was explained. Written and informed consent was obtained. Routine investigations required for preoperative evaluation and the proposed surgery have been done. All the patients were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg night before and on the morning of surgery. Patients were kept nil per oral for solid for a period of at least eight hours and clear fluid up to two hours before surgery. The choice of anesthesia was determined solely by the clinical judgment of the treating consultant anaesthesiologist and patients have been assigned to one of the following groups accordingly:

- Group A patients were received 2ml of 0.5% hyperbaric bupivacaine (10mg) with 5mcg of dexmedetomidine.
- Group B patients were received 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg) with 5mcg of dexmedetomedine.

Patients on adrenoreceptor agonist or antagonist therapy with known hypersensitivity to local anesthetic drugs, bleeding disorders, uncontrolled diabetes mellitus, pregnant women and pre-existing peripheral neuropathy were excluded from the study.

On arrival in the operating room, intravenous line was secured with 18-G intravenous cannula and patients were co- loaded with lactated Ringer's solution at 15 ml/kg. Monitoring was done using multiparameter monitor having SPO2, electro- cardiogram and NIBP.

Patient were placed in lateral or sitting position which one more convenient to patient. Under aseptic precautions, lumbar puncture was done between L3 and L4 interspinous space with 25-G Quincke spinal needle and the drugs were injected in- trathecally by an experienced anaesthesiologist different from the one assessing the patient intra- and post-operatively. Both were blinded to the treatment groups. The patient was turned to supine posture immediately and supplemental oxygen was given.

Parameters noted were as follows:

1. Maximum sensory level
2. Time taken for maximum motor blockade
3. Time taken for two segment regression
4. Duration of surgery
5. Intraoperative sedation
6. Total duration of sensory blockade (regression to S1)
7. Time for complete motor recovery
8. Time for rescue analgesia
9. Haemodynamic monitering
10. Adverse effects.

- Sensory blockade was achieved by testing the loss of pinprick sensation to 23G hypodermic needle.
- Quality of analgesia was assessed by VAS
  - 0 – No pain
  - 1–3 – Mild pain
  - 4–6 – Moderate pain
  - 7–10 – Severe pain.

- Motor blockade was assessed using modified Bromage scale.
  - 0 – Full flexion of knee and feet
  - 1 – Inability to raise extended leg, able to move knee and feet
  - 2 – Inability to raise extended leg and move knee,

* Adverse events included hypotension, bradycar- dia, respiratory depression, nausea, pruitus,

shivering, urinary retention and dry mouth.

* Postoperatively, the pain score was recorded by using visual analogue pain scale (VAS) between 0 and 10, initially every 1 hour for first 6 hours, then every 2 hourly for the next 6 hours and then after every 4 hourly till 24 hours. Injection Diclofenac sodium (75 mg) was given intramuscularly as rescue analgesia when VAS score will 4.

III. RESULT

Total 100 patients were observed in this study and from recorded data following analysis has been done.

A. Demographic characteristics of the participants:

- Age

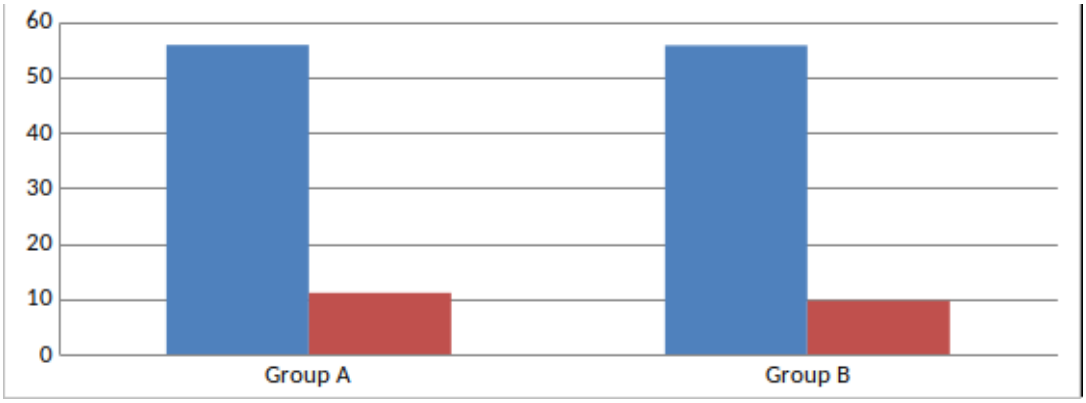

Fig 1

Mean age of the group A is (55.82±11.06) and group B is (58.74±9.62). There is no significant difference in the age of patients between two groups. Both groups were able to move feet– 3 – Complete block of lower limb.

- Sex

Similar with respect to age distribution (p≥ 0.05).

- Sedation was asssessed by Ramsay sedation scale
  - ➢ Patient anxious, agitated, or restless
  - ➢ Patient-cooperative, oriented, and tranquil alert
  - ➢ Patient responds to commands
  - ➢ Asleep but with brisk response to light glabellar tap or loud auditory stimulus
  - ➢ Asleep, sluggish response to light glabellar tap or loud auditory stimulus
  - ➢ Asleep, no response to light glabellar tap or loud auditory stimulus.

* Vitals included HR, mean arterial pressure (MAP), SPO2 and respiratory rate (RR) recorded at 0, 3, 6, 9,12, 15, 20, 25, 30, 35,40, 45 then every 10mins till end of surgery and at recovery area.
* Any decrease in SBP < 100 mmHg or a drop > 20% of baseline value was considered as hypotension and SBP< 90 mm Hg or a drop> 25% of baseline value was treated with 6 mg slow i.v.

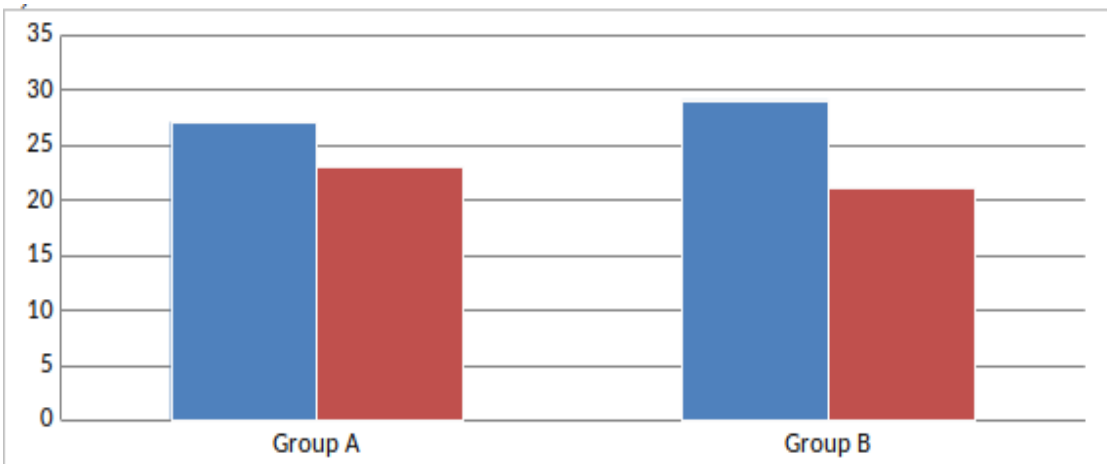

Fig 2

Total male and female ratio in group A and B is (27:23) and (29:21) respectively. Both groups were similar with respect to male and female distribution (p≥ 0.05).

- Height

Mean height of group A is (161.54±8.05) and group B is (162.26±8.49). There is no significant difference in the height of patients between two groups.

Both groups were similar with respect to height distribution (p≥ 0.05). Injection mephenteramine which may be repeated.

- Weight

After 5 min if SBP not corrected. Tachycardia was defined as HR>100 and bradycardia when HR<60. When HR falls <50 beats/min inj atropine 0.5mg i.v. was administered.

Mean weight of group A is (69.42±5.57) and group B is (70.64±5.38). There is no significant difference in the weight of patients between two groups. Both groups were similar with respect to weight distribution (p≥ 0.05).

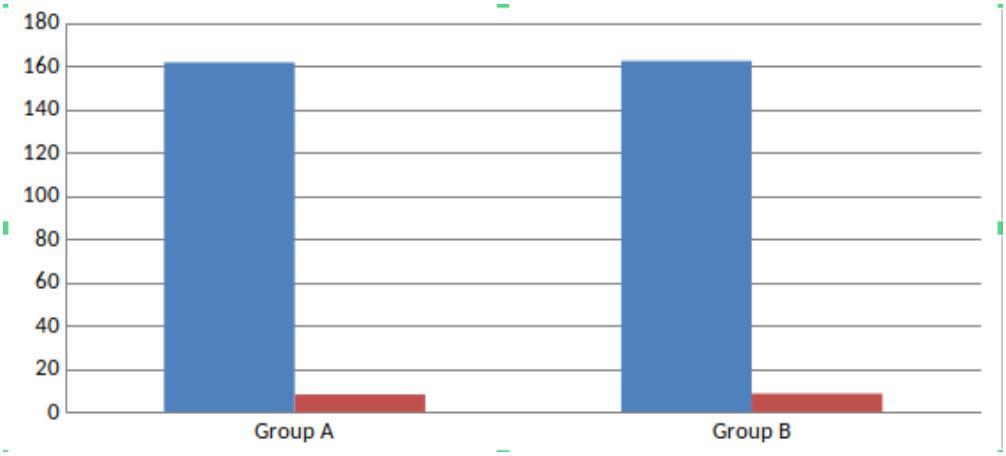

Fig 3

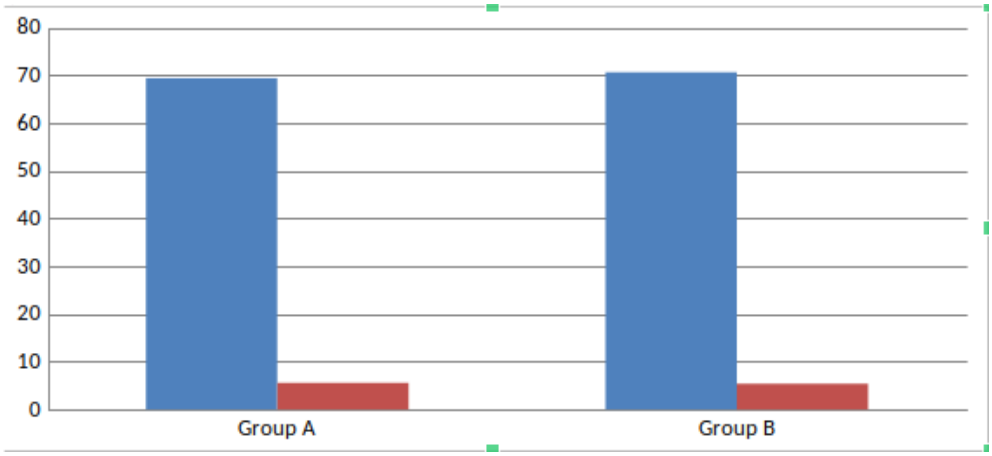

Fig 4

- Type of Surgery

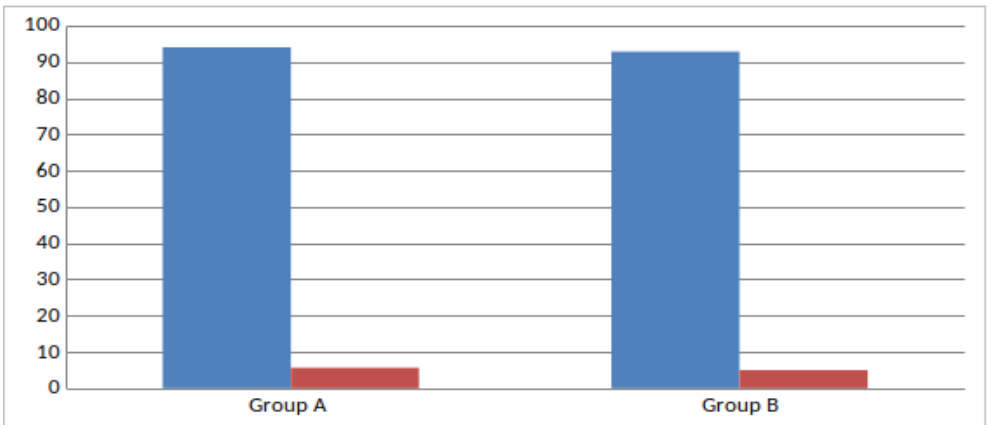

Fig 5

Mean time taken to attain maximum grade of motor blockade in group A is (8.88±0.77) minutes and in group B is (8.60±0.86) minutes). There is no significant difference in attaining maximum grade of motor blockade of patients between two groups. Both groups were similar in respect to this parameter (p>0.05).

TIME TAKEN FOR TWO SEGMENT REGRES-SION:

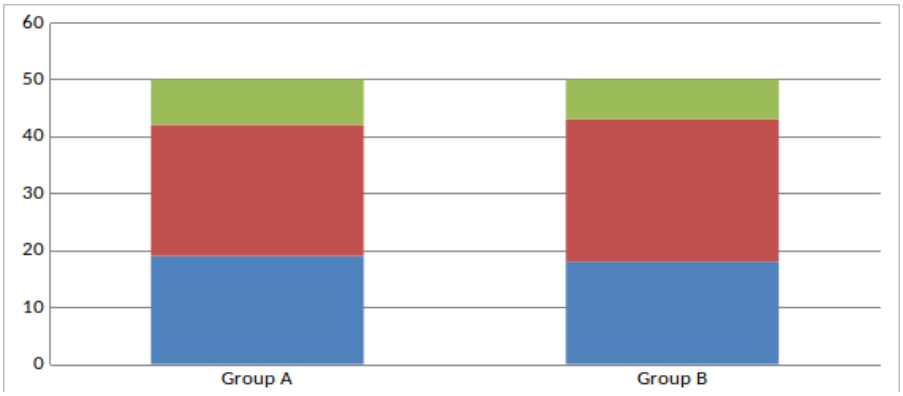

Fig 6

- Duration of Surgery

Mean duration of surgery in group A is (94±5.62) minutes and in group B is (92.80±4.97) minutes. Both groups are comparable according to time duration for surgery (p≥ 0.05).

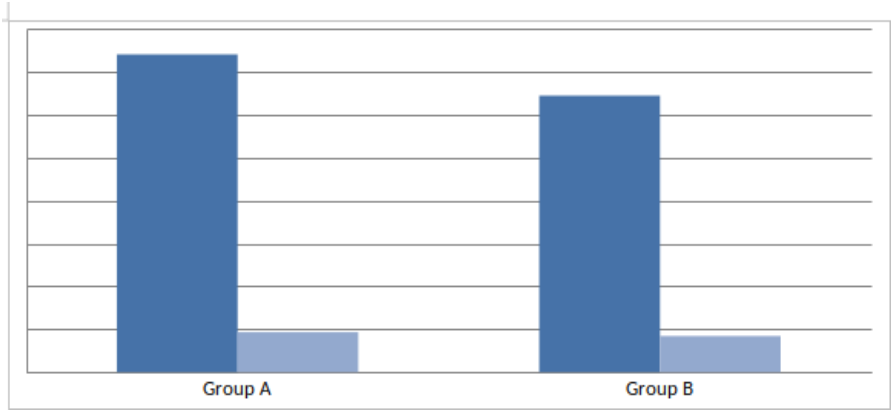

Fig 7

Mean maximum sensory level in group A is (7.4±0.93) and in group B is (6.44±0.84). There is no significant difference in the achieving maximum sensory level as per thoracic dermatome of patients between two groups. Both groups were similar in respect to this parameter (p>0.05).

TIME TAKEN TO ATTAIN MAXIMUM GRADE OF MOTOR BLOCKADE:

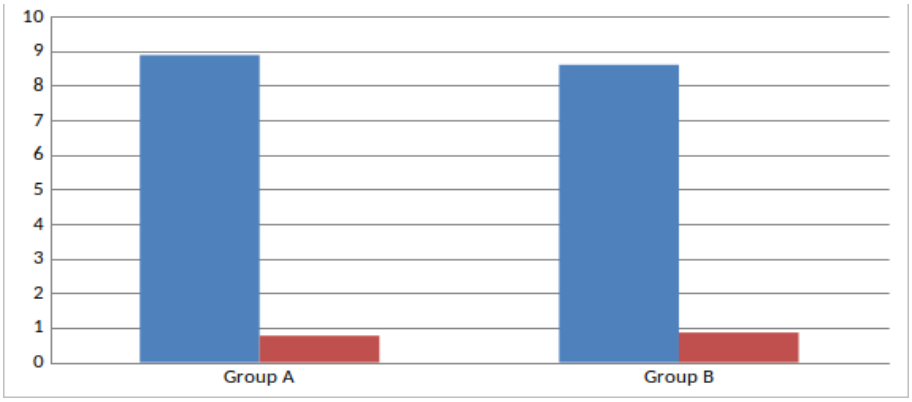

Fig 8

Out of 50 cases 0f each group, 19 dynamic hip screw(DHS), 23 proximal femur nailing (PFN) and 8 fixation of shaft of femur fracture (SOF) in group A and 18 dynamic hip screw (DHS), 25 proximal femur nailing (PFN) and 7 fixation of shaft of femur. Fracture (SOF) in group B. Type of surgeries in each group were comparable ($p \geq 0.05$).

B. Characteristics of blockade

MAXIMUM SENSORY LEVEL ACHEIVED

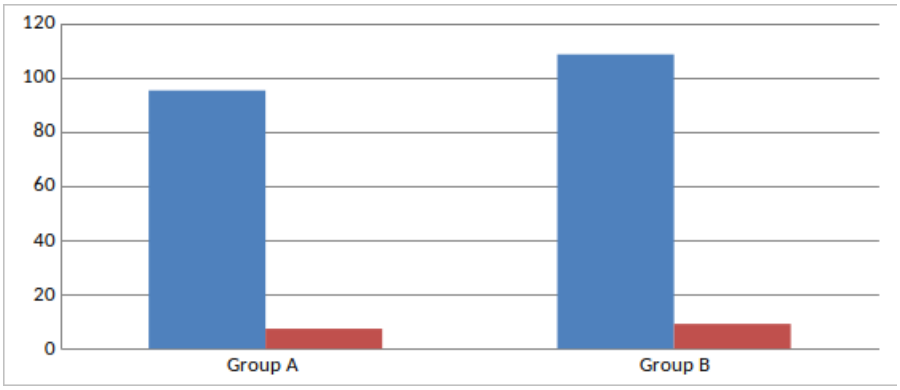

Fig 9

Mean time has taken to regress the block by two segment is (95.10±7.32) minutes in group A and (108.40±9.12) minutes in group B. There is no significant difference in terms of time taken to regress by two segment of dermatomes between two groups. Both groups were similar in respect to this parameter ($p>0.05$).

COMPLETE MOTOR RECOVERY

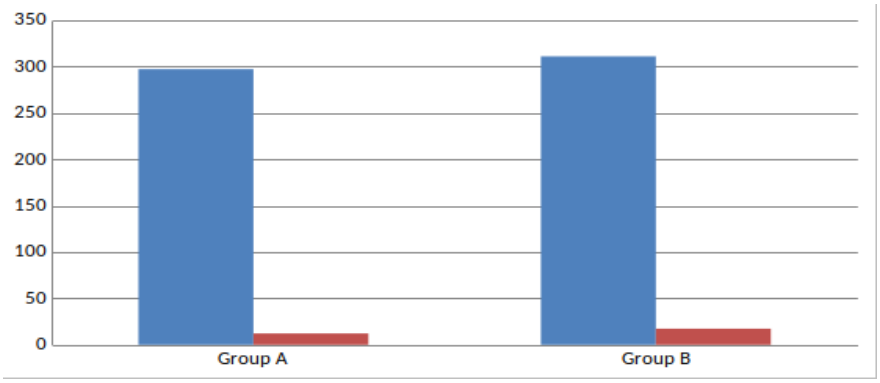

Fig 10

Mean time taken to completely recover from motor blockade is (297.20±12.13) minutes in group A and (331±17.29) minutes in group B. Group B has taken significant more time to recover from motor blockade than group A ($p <0.05$).

DURATION OF SENSORY BLOCKADE:

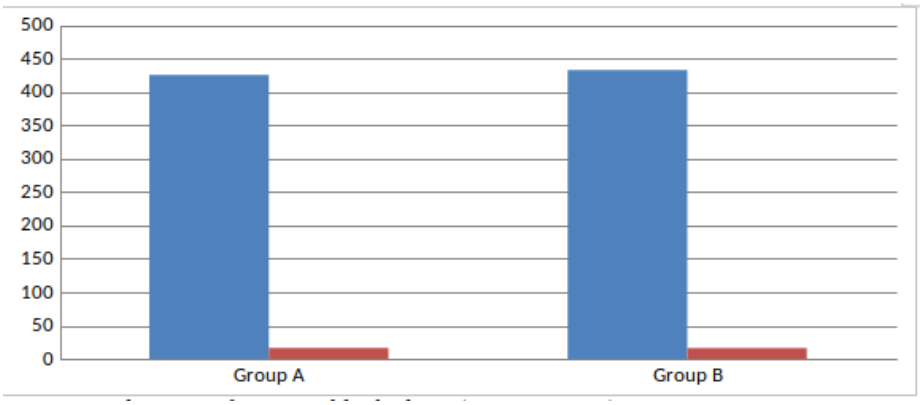

Fig 11

Mean duration of sensory blockade is (425.60±16.64) minutes in group A and (432.80±16.29) minutes in group B. There is no significant difference in the duration of sensory blockade of patients between two groups. Both groups were similar in respect to duration of sensory blockade (p>0.05).

TIME OF RESCUE ANALGESIA:

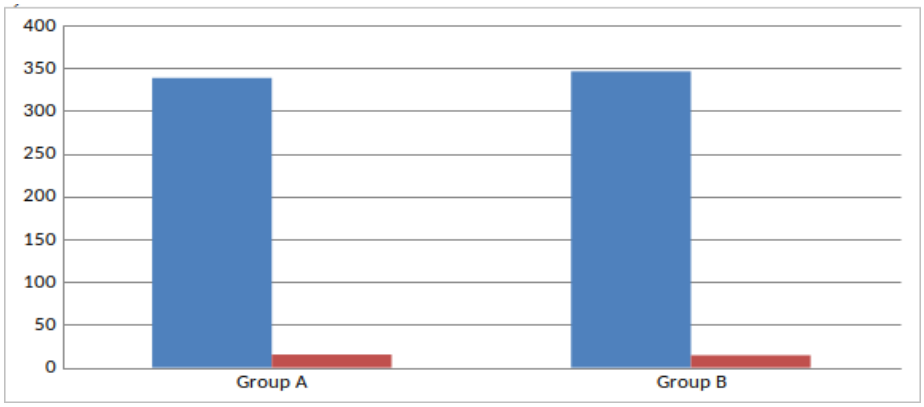

Fig 12

Mean time of rescue analgesia in group A is (338.60±15.12) minutes and in group B is (346.20±14.41) minutes. There is no significant difference in the time of rescue analgesia of patients between two groups. Both groups were similar (p>0.05).

C. Haemodynamics

HYPOTENSION

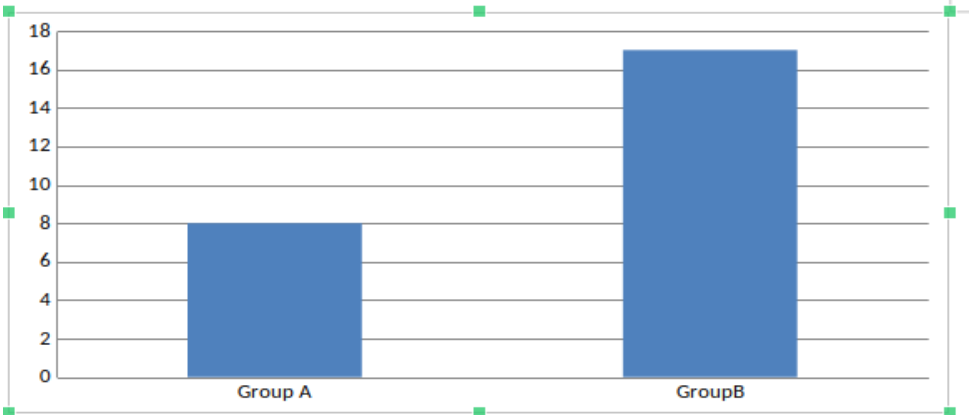

Fig 13

Hypotension occurred in 8 patients of group A where as in 17 patients of group B. Occurrence of hypotension is significantly high in group B than group B ($p < 0.05$). These patients are treated with intravenous fluid and vasopressor accordingly.

BRADYCARDIA

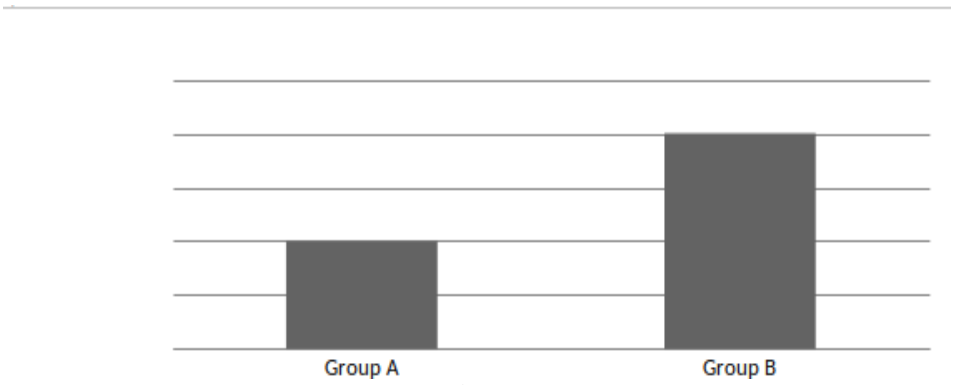

Fig 14

Bradycardia happened in 1 patient of group A where as in 2 patients of group B. Occurrence of bradycar- dia is not significant between the both groups (p > 0.05).Patients are treated with injection Atropine.

HEART RATE

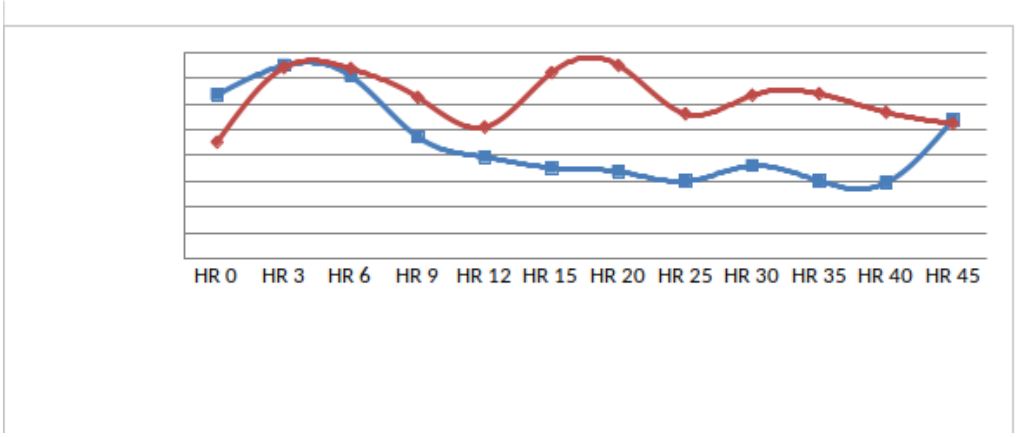

Fig 15

Mean heart rates were comparable in both groups (p > 0.05).

SYSTOLIC AND DIASTOLIC BLOOD PRES- SURE:

All mean systolic blood pressures are comparable (p > 0.05) in both group. Diastolic blood pressure at baseline and at 3,9,12 20,25 and 30 minutes are not significant between two groups (p > 0.05) but diastolic blood pressure at 6,15,35,40 and 45 minutes are significantly lower in group B than group A (p < 0.05).

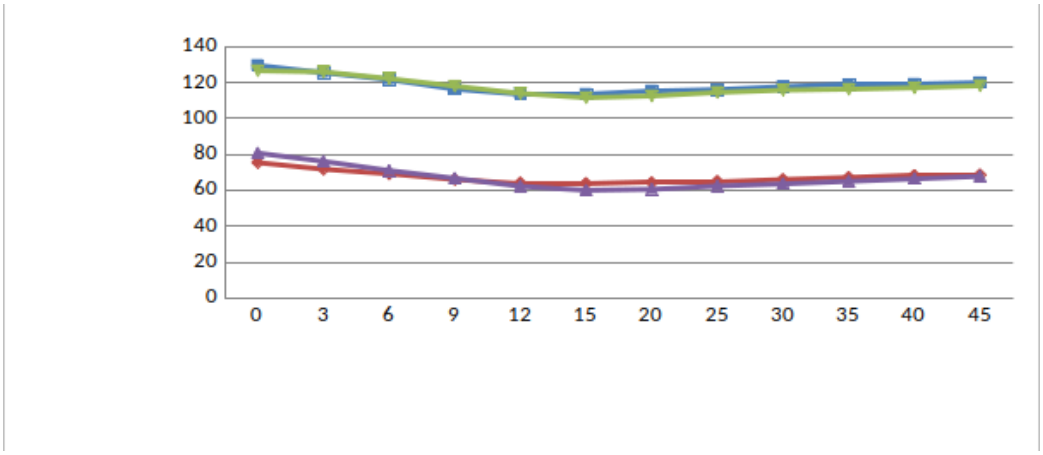

Fig 16

DISCUSSION

Subarachnoid block is the most commonly used regional anaesthetic technique for lower limb surgery. Intrathecal use of hyperbaric 0.5% bupivacaine is appropriate for most of lower limb surgeries but may lead to early analgesic in- tervention in the postoperative period [1]. In search for ad- juvants that prolong the duration of analgesia with lesser side effects various drugs as opioids, alpha agonists and midazolam have been tried with local anesthetics [2]. For intrathecal alpha agonist, many literature is for clonidine and dexmedetomidine [3]. Dexmedetomidine is a potent α2 agonist and is approximately eight-times more selective towards the α2 adrenergic receptor than clonidine. Dexmedetomidine is now emerging as an adjuvant to regional anesthesia and analgesia, where evolving studies can build the evidence for its safe use in central neuraxial blocks [4]. Intrathecal high dose of hyperbaric bupivacaine can cause many adverse effects including haemodynamic instability mainly hypotension. Low- dose bupivacaine can limit the spinal block level with minimal hemodynamic effects and yield a rapid recovery, but some- times it may not provide adequate anesthesia for surgery. A few studies have attempted to compare the effects of adjuvants with varying doses of bupivacaine for spinal anesthesia in an attempt to arrive at an optimum dose with minimum adverse effects. We want to find out whether alterations in the dose of bupivacaine would produce changes in spinal block characteristics and hemodynamic effects and if we could arrive at an optimum lower dose of bupivacaine, which in combination with

dexmedetomidine would provide satisfactory block without hemodynamic instability. This would be beneficial in the orthopedic population who are mostly elderly with various comorbidities. We have planned a double blind randomized control study to compare the efficacy of dexmedetomidine adjuvant to two different doses of intrathecal hyperbaric bupivacaine with regards to on set and duration of sensory and motor blockadge, haemodynamic changes as well as postoperative analgesia and adverse effects in patients scheduled for elective lower limb orthopaedic surgery.

Demographic data: Demographic data comparing age, sex, height, weight, type of surgery and duration of surgery were showed no statistical difference between both groups.

Hypothesis done before the study: It was hypothe-sised that dexmedetomidine will produce an effective surgical anaestheia as well as postoperative analgesia in both groups. There will be difference regarding the duration of analgesia and haemodynamic parameters between two groups as different doses of bupivacaine heavy are used.

Dosages of drugs selected: Dexmedetomidine: Various authors have used different doses of dexmedeto- midine for intrathecal blockade starting from 3 µg to 15µg along with local anesthetics.

Authors	Year	Dose of Dexmedetomidine used	Onset of sensory block in Dexmedetomidine group	Max sensory level attained in Dexmedetomidine group	Duration of analgesia in Dexmedetomidine group	Quality of motor block attained in Dexmedetomidine group	Duration of motor blockade in Dexmedetomidine group	Side effects
Kanazi GEet al.[53]	2006	3µg	8.6±3.7 mins	T6	303±75min	Bromage grade 3	250±76 min	Hypotension 1/16 patients
Al-Ghanem SM et al.[68]	2009	5µg	7.5±7.4mins	T6	274±73min	Bromage grade 3	240±60 min	Mild-moderate Hypotension 4/38 patients
Al-Mustafa MM et al.[69]	2009	5µg 10µg	6.3±2.7 mins 4.7±2 mins	-----	277.1±23min 338.9±44.8 mins	Bromage grade 3	246.4±25.7 min 302.9±36.7 min	Bradycardia 1/21 patients Hypotension 1/21 patients
Gupta R et al.[73]	2011	5µg	4.8±1.2 mins	T5	478.4±20.9 min	Bromage grade 3	------	Bradycardia 2/16 patients Hypotension 2/16 patients
Gupta R et al.[74]	2011	5µg	11.6±1.8 mins	T5	251.77±30.69 min	Bromage grade 3	421±21 min	No deleterious side effects
Eid HEA et al.[69]	2011	10µg 15µg	---	T5 T7	320±65.8min 336±58 mins	Bromage grade 3	280±46 min 336±58 min	Hypotension 3/15 patients Hypotension 2/16 patients
Shukla D et al.[66]	2011	10µg	2.27±1.09 mins	----	352±45 mins	Bromage grade 3	331±35 min	No deleterious side effects

Fig 17

IV. CONCLUSION

Five-microgram dexmedetomidine added to doses of 10 and 12.5 mg bupivacaine heavy produced satisfactory anesthesia and analgesia for lower limb orthopedic surgeries. There was no difference between the groups with respect to duration of anaesthesia and analgesia though duration of motor block was prolonged in the 12.5 mg bupivacaine heavy group. Moreover, the use of 12.5 mg dose was associated with more incidence of hypotension. Hence, higher doses of bupivacaine may be associated with delayed ambulation and more requirement of intravenous fluid and vasopressor agents. Hence, a 10 mg dose of bupivacaine heavy with 5 µg dexmedetomidine may be sufficient for lower limb orthopedic surgeries.

Limitations

A control without adjuvant was not used. However, many studies and meta-analysis have shown that adjuvants prolong the blocks and provide longer duration of postoperative analgesia.

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