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Comparative study of intrathecal bupivacaine and bupivacaine with clonidine to assess degree of sensory and motor effect and postoperative analgesia in lower limb orthopedic surgeries

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***Abstract*---**Background: Subarachnoid blockade amongst regional anesthesia has been most commonly used for performing abdominal and umbilical surgeries. There is persistent search for finding an adjuvant to local anesthetics to prolong its action along with hemodynamic stability. In this study we have used clonidine as an adjuvant to local anaesthetic agent and have assessed its ability to prolong motor and sensory blockade and hemodynamic stability. Methods: This observational study was conducted on 56 patients of ASA grade I/II, undergoing lower limb orthopedic surgeries who were divided into 2 groups: Group B : Injection 3.0 ml hyperbaric Bupivacaine 0.5% + 0.12 ml normal saline was given intrathecally and Group C : Injection 3.0 ml Bupivacaine (0.5%

hyperbaric) + 0.12 ml injection clonidine (20 mcg) was given intrathecally. We compared duration of sensory and motor blockade, hemodynamic changes, duration of analgesia and complications in both groups. Result: The onset of sensory and motor blockage was comparable in both groups. Duration of sensory and motor blockade was significantly longer in Group C than group B (P < 0.0001, P < 0.0001, respectively). Duration of post-operative analgesia was longer in Group C (314 min) than Group B (238 min).Hemodynamic parameters were comparable in both the groups. Conclusion: Intrathecal clonidine (20µg) added to 0.5% hyperbaric bupivacaine provides longer duration of motor, sensory and postoperative analgesia as compared to 0.5% hyperbaric bupivacaine in patients undergoing lower limb orthopedic surgeries without causing any hemodynamic instability.

***Keywords*---**Clonidine, Bupivacaine, spinal anesthesia, analgesia.

Introduction

Spinal anesthesia gained its popularity due to its simplicity, comparatively easier to learn, provide optimal operative condition, lowered risk of aspiration, low intra-operative blood loss, continued analgesia in the post-operative period and minimal postoperative morbidity[1] .It is widely practiced for providing sensory and motor block for lower limb and abdominal surgeries.

Local anesthetics are the commonest agents used for spinal anesthesia, but they have a short duration of action and can cause undesirable effects such as hemodynamic disturbance and short duration of blockade.[2] The use of local anesthetic adjuvants attempt to prolong intra-operative anesthesia and postoperative analgesia but they are limited by their various early & late side effects.

Clonidine with its alpha-2 adrenergic agonist and selective alpha -1 agonist property blocking properties has been found to be an effective analgesic with fewer adverse effects as compared to opioids. Clonidine, an imidazoline compound, is a selective agonist for α2- adrenoceptors with an α2:α1 selectivity ratio of approximately 220:1.[3] It has been used as an adjuvant in spinal anesthesia as it increases the duration of anesthesia by local vasoconstriction, enhancement of C fiber blockade by increasing potassium conductance or action on spinal cord through retrograde axonal transport or diffusion along the nerve and also has anti nociceptive properties[4,5,6]

It increases duration of postoperative pain relief and thus decreases requirement of rescue analgesia. Various doses of clonidine have been used like 20 mcg,30 mcg and 50 mcg to increase the duration and efficacy of anesthesia, but hemodynamic instability were seen with higher doses .[7,8]

Here we have conducted the study using optimal dose of clonidine 20 mcg as an adjuvant to bupivacaine and bupivacaine alone spinal anesthesia in lower limb

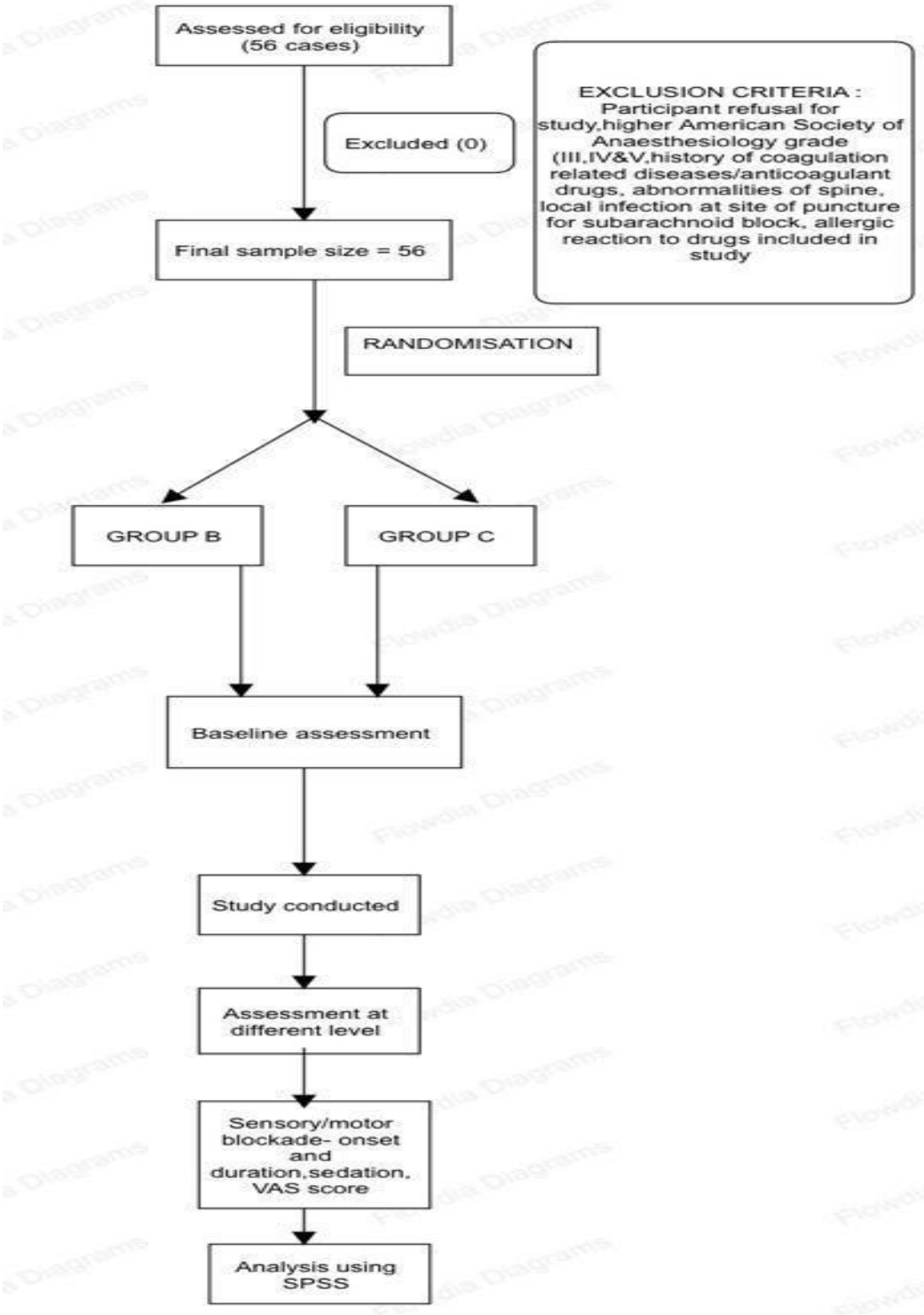
surgeries with the aim to evaluate the efficacy ,duration, hemodynamic stability, characteristic of sensory and motor blockage during spinal anesthesia.

Material and Methodology

Prospective observational, randomized double blinded study was done for period of 18 months on 56 patients of American Society of Anesthesiologists (ASA) physical status I and II in age group of 18 to 65 of either sex in Dhiraj general hospital, Vadodara, Gujarat. After obtaining permission from Institutional ethical committee and written and informed consent from patients scheduled for elective lower limb orthopedic surgeries under spinal anesthesia.

Patient who refused from taking part in the study, who had contraindication for subarachnoid block, ASA Grades ≥ III patients, allergy to local anesthesia and clonidine, hemodynamic instabilities, significant cardiovascular, renal, hepatic dysfunction or morbidly obese patients were excluded from study.

All patients underwent preanesthetic checkup and vitals were examined .After written and informed consent, 56 patients were randomly allocated in two groups by computer generated randomization.
Group **B** (n=28)**-** patients received intrathecal injection 0.5 % hyperbaric bupivacaine 3 ml with 0.12 ml normal saline. (By 1 ml BD syringe)
Group **C** (n=28)**-** patients received intrathecal injection 0.5 % hyperbaric bupivacaine 3 ml with 20 mcg clonidine (loaded in 1 ml in BD syringe and took0.12 ml / one and half marks).


Assessed for eligibility (56 cases)
Excluded (0)
EXCLUSION CRITERIA : Participant refusal for study,higher American Society of Anaesthesiology grade (III,IV&V,history of coagulation related diseases/anticoagulant drugs, abnormalities of spine, local infection at site of puncture for subarachnoid block, allergic reaction to drugs included in study
Final sample size = 56
RANDOMISATION
GROUP B
GROUP C
Baseline assessment
Study conducted
Assessment at different level
Sensory/motor blockade- onset and duration,sedation, VAS score
Analysis using SPSS

On arrival in operating room, iv line was secured with 18 G iv cannula and patients were preloaded with ringer lactate solution @ 15 ml/kg. Basic vitals like electrocardiogram, heart rate, blood pressure (SBP and DBP) and O2 saturation were recorded in multipara monitor. All the patients were premedicated with Inj. Glycopyrrolate 0.004 mg/kg iv and Inj. ondansetron 0.1 mg/kg iv.

Under all aseptic precaution lumbar puncture was performed at L3- L4 /L4-L5 space with 23 G / 25 G spinal needle in sitting position midline or paramedian approach. After free flow of cerebrospinal fluid, study drug was injected over 10 to 20 seconds according to group allocation. Supine position was given to patient immediately after injection. Heart rate, NIBP, spo2 and respiratory rate were recorded after every 5 min initially and every 15 min thereafter up to 75 minutes. Time of onset of sensory and motor blockage were noted.

Motor :

- Time of onset -Time from intrathecal injection to grade 3 motor block and
- Motor block assessment was done by using modified Bromage scale. [9]
- Duration of motor block -Time from intrathecal injection to grade 0 motor block .

Bromage 0	Subject is able to move the hip, knee and ankle and is able to lift his leg against gravity
Bromage 1	Subject is unable to lift his leg against gravity but is able to flex his knee and ankle
Bromage 2	Subject is unable to flex his hip and knee, but is able to flex his ankle
Bromage 3	Subject is unable to flex his hip, knee and ankle, but is able to move his toes
Bromage 4	Complete paralysis

Figure I: Modified Bromage scale

Sensory:

- Onset of sensory block -inability to feel pain using pinprick method at T12.
- Duration of sensory block - Time taken from onset of sensory to return of sensation be felt at T_{12} .

Sedation: Sedation was assessed by Ramsay Sedation Scale:
Time of onset of sedation was noted when the score was 3 and Duration of sedation was considered till score returned back to 2.

Sedation score	Response
1	Anxious and agitated or restless or both
2	Co-operative, oriented and tranquil
3	Responding to commands only
4	Brisk response to light glabellar tap or loud auditory stimulus
5	Sluggish response to light glabellar tap or loud auditory stimulus
6	No response to stimulus

Figure II : Ramsey sedation score

Two segment regression was noted and side effects like hypotension, bradycardia were noted which was treated with iv mephenteramine 6mg and iv atropine 0.6 mg respectively. Degree of postoperative analgesia was assessed by using the 10-point visual analog scale(VAS) (where 0 denotes no pain and 10 denotes worst imaginable pain) at 1,2, 4, 6, 12, 18, and 24h. Postoperative pain was managed by rescue analgesia like iv paracetamol 1 gm ,iv diclofenac 75 mg and iv tramadol 50 mg sos and total requirement dose was calculated

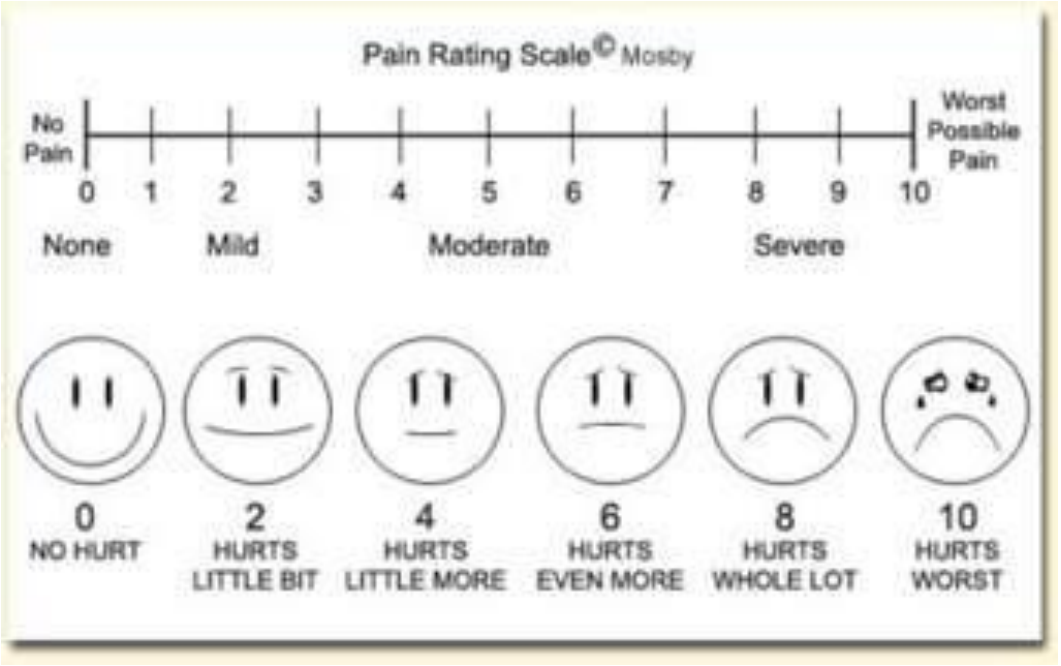


Figure III :Visual Analogue Scale[2]

In case of failure of effect of spinal anesthesia in form of severe pain and inadequate motor block ,patients were given either re spinal /general anesthesia and were excluded from study.

Observation and Results

Statistical analysis

Data was collected and entered in excel sheet and analyzed using SPSS software. Descriptive data like ASA grade, type of surgery, gender requirement of additional analgesia, postoperative complications were compared using chi square test or fischers exact test.
The demographic profile include age, weight and ASA grading were comparable and not significant difference between two groups (p >0.05).

Table I
Demographic Data and Asa Grading

Parameter	Group B	Group C	P value
Age (years)	40.61	36.93	0.1823
Weight (kg)	60.36	64.04	0.1358
ASA grade	42.86 (grade I) 57.14 (grade II)	35.71(grade I) 64.29(grade II)	0.7840

Hemodynamic parameter namely HR, SBP, DBP and SPO_2 were comparable in both groups.
Onset of sensory and motor block was comparable in both groups.Group C had early onset of sensory blockage at T12 level (mean 2.82 ± 0.72 minutes) than group B (mean 3.21 ± 0.88 minutes) but it was statistically insignificant (p >0.05) Mean onset of motor blockage (grade 3 bromage) was earlier in group C (mean 3.96 ± 0.84 minutes) than group B (mean 4.32 ± 0.90 minutes) but was statistically insignificant. (p value >0.05)
Two segment regression mean time was significantly faster in group B (102.86 ± 13.29 minutes) than group C (145.18 ± 15 minutes) which was statistically highly significant. (p <0.0001).

Table II
Onset of blockage and two segment regression

Parameter	Group B	Group C	P value
ONSET OF SENSORY BLOCK AT T12 (IN MINS)	3.21 ± 0.88	3.96 ± 0.84	0.2576
ONSET OF MOTOR BLOCK (GRADE 3 BROMAGE)(IN MINS)	4.32 ± 0.90	3.96 ± 0.84	0.1246
TWO SEGMENT REGRESSION (IN MINS)	102.86 ± 13.29	145.18 ± 15	P < 0.0001

The mean duration of sensory block was significantly prolonged in group C (261.61 ± 19.39 minutes) than in group B (218.39 ± 19.10 minutes) which was

statistically highly significant. (p <0.0001) and motor block was significantly longer in group C (213.54 ± 19.08 minutes) as compared to group B (160.86 ± 13.65 minutes) which was statistically highly significant.(p <0.0001)
The time of first rescue analgesia was significantly prolonged in group C (314.39 ± 19.07 minutes) as compared to group B (238 .04 ± 19.80 minutes) which was statistically highly significant (p <0.0001)

Table III
Duration Of Blockage And Analgesia

Parameter	Group B	Group C	P value
DURATION OF SENSORY BLOCK (MIN)	218.39 ± 19.10	261.61 ± 19.39	p <0.0001
DURATION OF MOTOR BLOCK (MIN)	160.86 ± 13.65	213.54 ± 19.08	p <0.0001
DURATION OF ANALGESIA (MIN)	(238 .04 ± 19.80	314.39 ± 19.07	P < 0.0001

In group C sedation was frequent as compared to group B which was statistically insignificant (p>0.05)

Discussion

Neuraxial anesthesia is greatly use now a days and also provides alternatives to general anesthesia, mostly in the lower abdominal and lower limb surgeries. Clonidine, an alpha-2 adrenergic agonist, potentiates the effects of local anesthetics.[3] In lower limb surgery, it is beneficial to use a drug which provides good anesthesia and prolonged analgesia in postoperative field at same time caused minimum disturbance in hemodynamic parameter. This study was carried out to assess the analgesic and hemodynamic effects of clonidine as an adjuvant to bupivacaine intrathecally in lower limb orthopedic surgeries under spinal anesthesia.

Demographic data
To make study unbiased and valid demographic parameters like age, weight, gender, ASA grading were comparable in both groups.

Onset of sensory block
The mean onset of sensory block signifies the time taken for effect of anesthesia to manifest which can be assess by pin prick method. In our study we found that mean time to onset of sensory blockage was comparable in both the groups. Group C (mean 2.82 ± 0.72 minutes) had early onset of sensory blockage at T12 level than group B (mean 3.21 ± 0.88 minutes) but was statistically insignificant.(p>0.05)

Arora R et al (2018)[10] in their study discovered that the mean time to onset of sensory block was shorter in Group III (12.5 mg bupivacaine with 30 mcg clonidine) than in Group II (bupivacaine 12.5 mg with clonidine 15 mcg) and in Group I(bupivacaine alone intrathecally). The difference in mean time of the onset

of the sensory block between Group II and Group III was not significant. Sheema shande et al (2014) [11] concluded that mean time in onset of sensory blockage in control group was 181 ± 37.35 seconds and in clonidine group 172 ± 37.17 seconds which was shorter in clonidine group but was statistically insignificant.

Onset of motor block

Onset of motor block was assess by bromage score.
In this study the mean onset of motor blockage was compared between two groups and it show that group C (mean 3.96 ± 0.84 minutes) had early onset of motor block (grade 3 bromage) than group B (mean 4.32 ± 0.90 minutes) but was statistically insignificant.

Similarly Arora et al 2018[10] found mean time of onset of motor block was faster in groups with clonidine and bupivacaine as compared with groups with bupivacaine alone, this difference was however not significant. According to Saxena H et (2009)[12] al, the onset of motor block in clonidine groups with different doses was faster but statistically insignificant. Hence, Adjuvance of clonidine with bupivacaine had almost similar onset of motor blockage as with bupivacaine alone.

Two segment regression

In our study, we found that the two segment regression mean time was faster in group B (102.86 ± 13.29 mins) than group C (145.18 ± 15 mins) which was statistically highly significant. In accordance to our observation Singh RB et al (2014)[13] ($p < 0.05$) and Nikita Devara et al (2018)[14] also observed two segment regression was longer in 75 mcg clonidine Group than in 50 mcg clonidine group

Duration of sensory block

On comparing duration of sensory block between both the groups, significant prolongation was observed in group C (261.61 ± 19.39 mins) than in group B (218.39 ± 19.10 mins) which was statistically highly significant. H Saxena et al (2009)[12] et al also emphasized that mean time of duration of sensory block was significantly longer in clonidine groups in a dose dependent manner compared to control. In accordance to our findings, Arora R et al (2018)[**10**] also agreed from their study that the mean duration of sensory block was significantly longer in Group II (bupivacaine 12.5 mg with 15 mcg) and Group III (bupivacaine 12.5 mg with clonidine 30 mcg intrathecally) than in Group I (12.5 mg bupivacaine).

Duration of motor block

Similarly, on comparing the mean duration of motor block between both the groups, significant longer motor blockade was seen in group C (213.54 ± 19.08 mins) as compared to group B (160.86 ± 13.65 mins) ($p < 0.0001$)

Arora R et al (2018)[10] concluded that the duration of motor block was longer in Group III (bupivacaine 12.5 mg with clonidine 30 mcg intrathecally) and group

II(bupivacaine 12.5 mg with 15 mcg) in comparison to Group I (12.5 mg bupivacaine), but statistically significant.

Singh RB et (2014)[13] al also found that mean duration of motor block in Group B (bupivacaine 0.5 percent, 3 ml with clonidine 50 mcg) was substantially longer (280.80 66.88 min) than in Group A (bupivacaine 0.5 percent, 3 ml with placebo) (183.60 77.06 min).

DURATION OF ANALGESIA:
In terms of mean duration of analgesia in our study it was significantly prolonged in group C (314.39 ± 19.07 mins) as compared to group B (238 .04 ± 19.80 mins) which was statistically highly significant (p <0.0001) which helped in reducing post operative need of analgesics.

Arora R et al 2018 [10] and Sethi BS et al 2007[7] also had convincing results as per ours regarding duration of analgesia suggesting longer time to request for rescue analgesic in clonidine group than the control group.
Sedation was higher in clonidine with bupivacaine group than plain bupivacaine but was insignificant which can be because of slow intravenous absorption.
Shende S et al[11] and Bhat RR et al (2020)[15] found more sedation in patients in clonidine group compared to control group.

Conclusion

Clonidine an alpha 2 agonist is a very good adjuvant when given along with bupivacaine to improve quality of anesthesia. The onset of sensory and motor block is not much effected but duration of anesthesia and analgesia gets prolonged. Not much variation was seen in hemodynamic parameters (heart rate, blood pressure, Oxygen saturation, respiratory rate) intraoperatively as well as postoperatively. No significant side effects were seen with clonidine or bupivacaine. Sedation was mild and did not hamper early mobility in patients. Clonidine with bupivacaine was well tolerated by patients. Hence, It can be concluded that Clonidine as an adjuvant to intrathecal Bupivacaine can be preferred as drug of choice for spinal anesthesia with minimal adverse effects.

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