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Original Research Article

Comparative Study to Assess the Synergistic Effect and Safety Profile of Adding Adjuvants Dexmedetomidine and Clonidine with 0.5% Bupivacaine Intrathecally in Elective Lower Abdominal Surgeries

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Abstract

Background: In this study we wanted to assess the synergistic effect and safety of adding Dexmedetomidine to 0.5% hyperbaric Bupivacaine compared with Clonidine to 0.5% hyperbaric Bupivacaine in patients undergoing elective lower abdominal surgeries under spinal anaesthesia.

Methods: This was a randomized comparative study carried out in the Department of Anesthesiology and Critical care, Kempegowda Institute of Medical Sciences, Bangalore among two groups of 30 patients each, from August 2020 to September 2021.

Results: The difference in onset of the sensory blockade was significant as indicated by the p-value of < 0.001. The difference in onset of the motor blockade was insignificant as indicated by the p-value of 0.883. Clinically the mean SBP was lower in Group D as compared to group C. Clinically the mean DBP was lower in Group D as compared to group C.

Conclusion: 10µg of Dexmedetomidine as adjuvant to intrathecal 0.5% bupivacaine provides better postoperative analgesia, longer duration of motor and sensory blockade, optimal sedation and is safe with regard to the haemodynamic variables and adverse effects when compared to 50µg of clonidine as an adjuvant to intrathecal 0.5% bupivacaine.

Keywords: Synergistic Effect, Safety, Dexmedetomidine, Clonidine, Bupivacaine, Subarachnoid Block, Elective Lower Abdominal Surgeries

Introduction

Dexmedetomidine, a new, highly specific, potent and selective α2-adrenoceptor agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. [1] Based on earlier human studies, it is hypothesized that intrathecal 5-10 μg dexmedetomidine would produce more postoperative analgesic effect in spinal anesthesia with minimal side effects. [1]

While clonidine has been in use as an adjuvant to bupivacaine in subarachnoid block, there are only a few studies available on human upon intrathecal uses of dexmedetomidine. Therefore, we designed this study to compare the effect and side effects of addition of clonidine and dexmedetomidine to intrathecal hyperbaric bupivacaine.

Objectives of the Study

To assess the synergistic effect and safety of adding Dexmedetomidine to 0.5% hyperbaric Bupivacaine compared with Clonidine to 0.5% hyperbaric Bupivacaine in subarachnoid block in elective lower abdominal surgeries, regarding

- Time of onset of sensory blockade
- Time of onset of motor blockade i.e., Modified bromage power 3
- Time to achieve maximum dermatomal level of sensory blockade
- Time for two segment regression from highest sensory level
- Time for rescue analgesia
- Time for regression to Modified Bromage 0 muscle power
- The occurrences of adverse drug reactions and side effect.

Materials and Methods

This was a randomized comparative study carried out in the Department of Anesthesiology and Critical care, Kempegowda Institute of Medical Sciences, Bangalore among two groups of 30 subjects each, from August 2020 to September 2021. Random sampling was done using computer generated random number tables. Group C (n=30) received 3 ml volume of 0.5% hyperbaric Bupivacaine and 50 μg clonidine in 0.5ml normal saline. Group D (n=30) received 3 ml volume of 0.5% hyperbaric Bupivacaine with 10 μg Dexmedetomidine in 0.5ml normal saline.

Inclusion Criteria

All the patients who were willing to give consent, of age group 18 and 60years of either sex, who belonged to ASA 1 and 2 posted for lower abdominal surgeries with.

1. Weight > 50 kg.
2. Height > 150cm.

Exclusion Criteria

1. Pregnancy and lactation.
2. Patients with obesity. BMI > 30
3. Patients having uncontrolled hypertension or Diabetes mellitus.
4. Patients having,
   i. Allergy to local anaesthetics , dexmedetomidine and clonidine
   ii. Local infection.
   iii. Severe hypovolemia.
   iv. Bleeding coagulopathy.
   v. Neurological disorder.
   vi. Raised intra cranial tension and deformities of spine.

Statistical Methods

Data was entered in Microsoft excel and analyzed using SPSS (Statistical Package for

Social Science, Ver.10.0.5) package. Microsoft word and Excel have been used to generate graphs, tables etc. The results were averaged (mean + standard deviation) for continuous data and number and percentage for dichotomous data were presented in tables. Proportions were compared using Chi-square (χ^2) test of significance. The student 't' test was used to determine whether there was a statistical difference between groups in the parameters measured.

Results

Demographic Profile

Table 1: Demographic profile - Age, height, weight of patients expressed as mean±SD and gender & ASA physical status as actual numbers

Sl. No	Variable		Group D	Group C	p-value
1.	Age (in years)		42.80 ± 11.622	39.9 ± 10.637	0.318
2.	Height (cm)		165.5 ± 5.638	164.0 ± 7.012	0.356
3.	Weight (kg)		66.5 ± 6.044	65.7 ± 8.417	0.687
4.	Gender	Male (No.)	24	23	0.754
		Female (No.)	6	7	
5.	ASA Physical Status	ASA- 1 (No.)	14	19	0.194
		ASA- 2 (No.)	16	11	

The mean age of the D group was 42.80 ± 11.622 and that of C group was 39.9 ± 10.637 which was comparable and the difference in the age in both group was insignificant with a p-value of 0.318. The majority of patients in group D belong to the age group of 41-50years (43.3%). The majority of patients in group C belong to the age group of 41-50years (43.3%). The mean ages of both the groups were comparable and difference in the age was insignificant. The mean height (cm) of the D group was 165.5 ± 5.6383 and that of C group was 164.0± 7.012 which was comparable and the difference in the height in both group was insignificant with a p-value of 0.356. The mean weight (kg) of the D group was 66.5 ± 6.044 and that of group C is 65.7 ± 8.417 which was comparable and the difference in the weight in both group was insignificant with a p-value of 0.687. There were 24 males (80%) and 6 females (20%) in group D and 23 males (76.7%) and 7 females (23.3%) in group C. Both the groups were comparable in gender distribution (with p-value of 0.754, which is insignificant). There were 14 ASA-1 (46.7%) &16 ASA-2 (53.30%) patients in group D and 19 ASA- 1 (63.3%) &11 ASA- 2 (36.7%) patients in group C. The ASA physical status of both the groups were comparable (with p-value of 0.194, which was insignificant)

Types and Duration of Surgery

8 patients (26.7%) of D group and 7 patients (23.3%) of C group underwent open appendicectomy.6 patients (20%) of D group and 6 patient (20%) of C group underwent Total abdominal hysterectomy.16 patients (53.3%) of D group and 17 patients (56.7%) of C group underwent open hernioplasty.

Duration of Surgery

The mean duration of surgeries the patients underwent in the D group was 80.83± 12.183 minutes and the C group was 79.67± 16.238 minutes. The difference in the duration of surgeries between the two groups was insignificant as the p-value was 0.754 which was insignificant.

Table 2: The onset and duration of sensory and motor blockade in minutes expressed as mean±SD.

Sl. No	Variable	Group D	Group C	p-value
1.	Onset of Sensory Blockade (min)	2.47±.629	3.67±.606	<0.001
2.	Onset of Motor Blockade (min)	8.40±.894	8.43±.858	0.883
3.	Time to achieve maximum sensory block level (min)	9.50±.820	8.70±1.662	0.019
4.	Time for two segment regression from highest sensory level (min)	120.67±10.483	94.67±10.417	< 0.001
5.	Time to rescue analgesia(min)	378.67±13.830	331.67±17.436	< 0.001
6.	Time for regression to Bromage 0 muscle power (min)	285.33±10.417	242.67±17.798	< 0.001

The Onset of Sensory Blockade

The mean onset of sensory blockade in the D group was 2.47±.629 minutes and that of C group was 3.67±.606minutes. The difference in onset of the sensory blockade was significant as indicated by the p-value of < 0.001.

The Onset of Motor Blockade

The mean onset of motor blockade in the D group was 8.40±.894 minutes and that of C group was 8.43±.858. The difference in onset of the motor blockade was insignificant as indicated by the p-value of 0.883.

Time to Achieve Maximum Sensory Blockade in Two Groups

The D group patients achieved the maximum sensory block level in mean time of 9.50±.820 minutes whereas the C group in 8.70±1.662 minutes. The difference in the time to achieve maximum sensory block level between the two groups was insignificant (p-value=0.019).

Two Segment Regression Time in Two Groups

The mean time taken for two segment regression from highest sensory level in D group was 120.67±10.483 minutes whereas it was 94.67±10.417 minutes in the C group. The difference in the time taken for two segment regression between the two groups was statistically highly significant with p value of <0.001.

Duration of Analgesia in Two Groups

The duration of analgesia as measured by the mean time to rescue analgesia in group D was 378.67±13.830 minutes and that for group C was 331.67±17.436 minutes. The difference in the time to rescue analgesia between the two groups was statistically highly significant (p value= <0.001).

Duration of Motor Blockade in Two Groups

The duration of motor blockade as measured by the mean time to Bromage -0 muscle power was 285.33±10.417 minutes in D group and 242.67±17.798 minutes in C group. The difference in duration of motor blockade between the two groups was highly significant statistically as indicated by p value of <0.001.

The Sedation Score

The sedation score as measured by Ramsay sedation scale was 2.47±0.507 in group D and 1.97±.556 in group C. The difference in sedation score between the two groups was highly significant statistically as indicated by p value of <0.001.

The SPO_2 Variability among the Two Groups

There was no significant difference between both the groups with respect to SpO_2.

The Heart Rate Variability among the Two Groups

The mean HR was comparable at all the timed intervals with no statistically significant difference between the two groups.

The Systolic Blood Pressure Variability in Two Groups

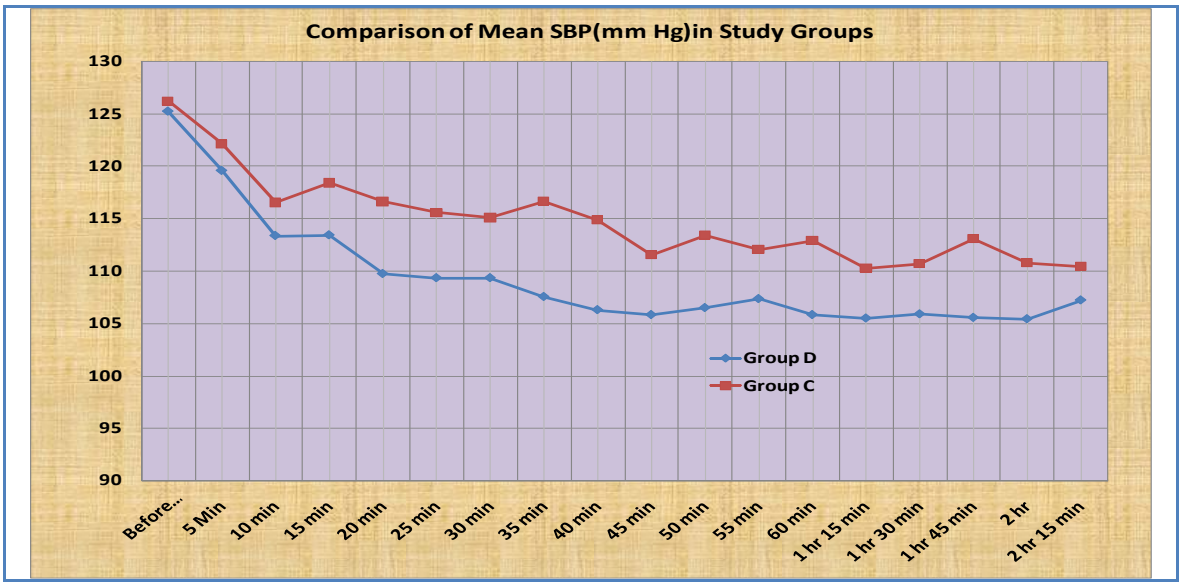

Figure 1: Comparison of SBP (mm Hg) in two groups studied

Systolic blood pressure (SBP) was recorded, every 5 minutes till the end of 1 hour and then every 15 minutes till the end of surgery in patients of both the groups. The mean SBP at these timed intervals was compared between both the groups and found that statistically significant difference in mean SBP was found at 35 and 40 minutes, with a greater fall in SBP in Group D than in Group C. The mean SBP was comparable at the other timed intervals. Clinically the mean SBP was lower in Group D as compared to group C.

The Diastolic Blood Pressure Variability in Two Groups

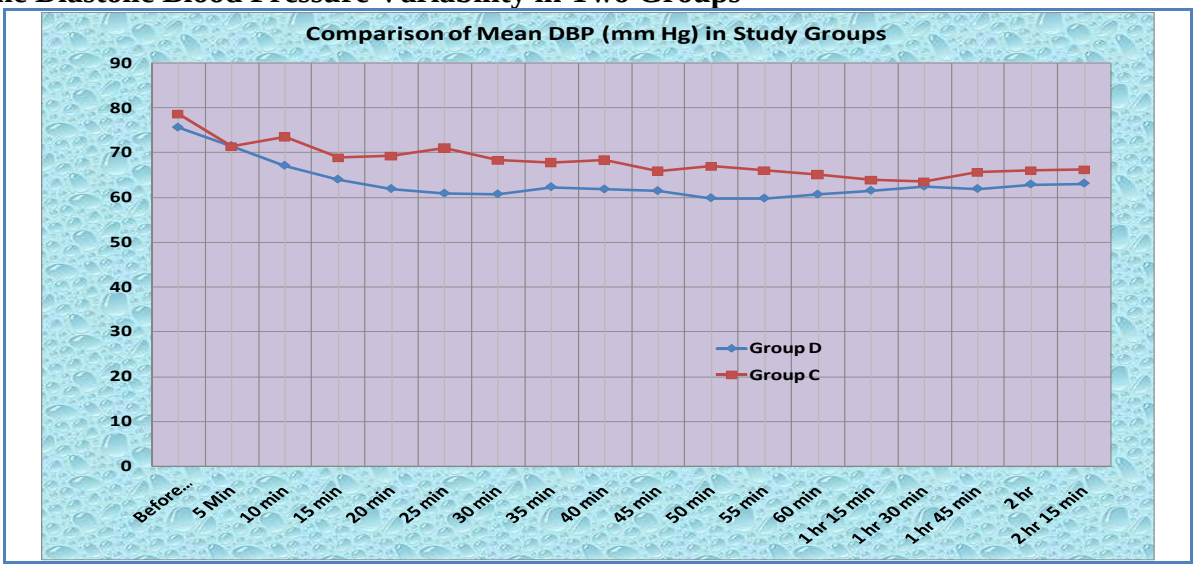

Figure 2: Comparison of DBP (mm Hg) in two groups studied

Diastolic blood pressure (DBP) was recorded, every 5 minutes till the end of 1 hour and then every 15 minutes till the end of surgery in patients of both the groups. The mean DBP at these timed intervals was compared between both the groups and found that statistically significant difference in mean DBP was found at 20, 25 , 30 and 50 minutes, with a greater fall in DBP in Group D than in Group C. The mean DBP was comparable at the other timed intervals. Clinically the mean DBP was lower in Group D as compared to group C

The Mean Arterial Blood Pressure Variability

Mean Blood Pressure (MBP) was recorded every 5 minutes till the end of 1 hour and then every 15 minutes till the end of surgery in patients of both the groups. When compared there was no significant difference between both the groups with respect to mean MBP at any of these timed intervals.

Occurrence of Adverse Events

There was no significant difference between both the two groups with respect to the intraoperative occurrence of hypotension and bradycardia. No patient had residual neurological deficit, post-dural puncture headache or transient neurological symptoms at the postoperative follow-up.

Discussion

The Onset of Sensory Blockade

The mean onset of sensory blockade in the D group was 2.47±.629minutes and that of C group was 3.67±.606minutes. The difference in onset of the sensory blockade was significant as indicated by the p-value of < 0.001. The onset of sensory block was faster with addition of dexmedetomidine to bupivacaine as compared with clonidine.

Manuraj VS, [2] et al, 2015 in a study titled "A comparative study of bupivacaine and bupivacaine with clonidine under spinal anesthesia in patient for total abdominal hysterectomy" found that onset of sensory block in patients receiving 50 µg clonidine with 3.5 ml of bupivacaine was 112.22 seconds. This was faster than the results of our study.

Onset of Motor Blockade

According to our study there is no statistical difference in the onset of motor blockade with addition of dexmedetomidine to bupivacaine as compared with clonidine. Kashif M. Madani et al, [3] in a study titled "Comparative study of different doses of dexmedetomidine in spinal anaesthesia in lower limb orthopaedic procedures" found the onset of motor with addition of 10 µg dexmedetomidine was 9.7+_3.2 minutes which was almost similar to our study.

Time to Achieve Maximum Dermatome Level of Sensory Blockade

According to our study there is no significant difference in the time to achieve maximum dermatome level of sensory blockade with addition of dexmedetomidine 10 µg to bupivacaine 3ml as compared with clonidine 50 µg. Kashif M. Madani et al [3] in a study titled "Comparative study of different doses of dexmedetomidine in spinal anaesthesia in lower limb orthopaedic procedures" found the time to achieve maximum dermatome level of sensory blockade with addition of 10 µg dexmedetomidine to bupivacaine 0.5% 2.5ml was 10.3+_3.3 minutes which was almost similar to our study.

Time for Two Segment Regression from Highest Sensory Level

According to our study addition of dexmedetomidine 10 µg to bupivacaine 3ml increases the time for two segment regression significantly as compared with clonidine 50 µg. Vidhi Mahendru et al, [4] 2013 in s study titled "A comparison of intrathecal dexmedetomidine, clonidine, and Fentanyl as adjuvants to hyperbaric bupivacaine for lower limb Surgery: A double blind controlled

study" found that the time to two segment regression of sensory blockade was significantly higher with dexmedotomidine group 146.7±20.5min and clonidine group 117.0±21.8 min and was statistically significant ($p < 0.001$). These results were similar to our present study.

The Time for Regression to Bromage-0 Muscle Power

According to our study addition of dexmedetomidine 10 µg to bupivacaine 0.5% 3ml increases the duration of motor block significantly as compared with clonidine 50 µg.

Kashif M. Madani et al, [3] in a study titled "Comparative study of different doses of dexmedetomidine in spinal anaesthesia in lower limb orthopaedic procedures" found that the total duration of motor blockade with addition of 10 µg dexmedetomidine to bupivacaine 0.5% 2.5ml was 273.3+_24.6 minutes which was almost similar to our study.

Total Duration of Analgesia

According to our study addition of dexmedetomidine 10 µg to bupivacaine 0.5% 3ml increases the duration of analgesia significantly as compared with clonidine 50 µg.

Manuraj VS, [2] et al, 2015 in a study titled "A comparative study of bupivacaine and bupivacaine with clonidine under spinal anaesthesia in patient for total abdominal hysterectomy" found that the total duration of analgesia in patients receiving 50 µg clonidine with 3.5 ml of bupivacaine 0.5% was 332.64 minutes. This was almost similar to the results of our study.

Variations in Vitals

2 patients in either group had bradycardia in the present study which was successfully managed with Inj. atropine 0.6 mg IV.

There was statistically significant difference in mean SBP at 35 and 40 minutes, with a greater fall in SBP in Group D than in Group C. The mean SBP was comparable at the other timed intervals. Clinically the mean SBP was lower in Group D as compared to group C but not statistically significant.

The mean DBP at these timed intervals was compared between both the groups and found that statistically significant difference in mean DBP was found at 20, 25, 30 and 50 minutes, with a greater fall in DBP in Group D than in Group C. The mean DBP was comparable at the other timed intervals. Clinically the mean DBP was lower in Group D as compared to group C but not statistically significant.

In 2007 Olfa Kabaachi et al, [5] used 1 µg/kg of Clonidine intrathecally added to Bupivacaine in adolescents 10-15 years of age.They found a prolonged duration of sensory block and analgesia without any adverse haemodynamic events recorded.

The Sedation Score

The sedation score as measured by Ramsey sedation scale was 2.47±0.507 in group D and 1.97±.556 in group C. The difference in sedation score between the two groups was highly significant statistically as indicated by p value of <0.001.

Conclusion

- Both 50 µg clonidine and 10µg dexmedetomidine when added to 0.5% hyperbaric bupivacaine provide prolonged sensory and motor block when added to intrathecal 0.5% bupivacaine.
- Onset of sensory block was delayed with clonidine 50 µg as compared with dexmedetomidine 10 µg when added to 0.5% hyperbaric bupivacaine. Onset of motor block was similar with both clonidine and dexmedetomidine
- Dexmedetomodine 10 µg produces longer duration of two segment regression time, sensory and motor block when compared to clonidine µg and thus it is better drug as compared to clonidine in terms of

duration of analgesia and duration of sensory and motor block when used as an adjuvant to 0.5% hyperbaric bupivacaine. Dexmedetomodine also provides greater sedation than clonidine which is optimal for neuraxial blockade.

- Both clonidine and dexmedetomidine provide good hemodynamic stability.
- Hence, we conclude that
- 10µg of Dexmedetomidine as adjuvant to intrathecal 0.5% bupivacaine provides better postoperative analgesia, longer duration of motor and sensory blockade, optimal sedation and is safe with regard to the haemodynamic variables and adverse effects when compared to 50µg of clonidine as an adjuvant to intrathecal 0.5% bupivacaine.

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