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COMPARISON OF DEXMEDETOMIDINE 2 MCG WITH CLONIDINE 50 MCG ADDING TO 12.5 MG OF 0.5% HEAVY BUPIVACAINE FOR SPINAL ANAESTHESIA IN LOWER ABDOMINAL SURGERIES.

KEYWORDS: Dexmedetomidine, Clonidine, Blood pressure, Heart rate,

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ABSTRACT *Context: Comparison of Dexmedetomidine 2 MCG with Clonidine 50 MCG adding to 12.5MG of 0.5% Heavy Bupivacaine for Spinal Anaesthesia in Lower Abdominal Surgeries.*

AIM: aim of our study was to compare the Dexmedetomidine 2 MCG with Clonidine 50 MCG adding to 12.5MG of 0.5% Heavy Bupivacaine for Spinal Anaesthesia in Lower Abdominal Surgeries.

Settings and Design: The present prospective study was carried out in a territory care Teaching

Hospital. A total of 60 patients of ASA I and II undergoing lower abdominal Surgery Under

spinal Anaesthesia was enrolled in this study. Patients were randomly divided in to two Groups,

Group C (Clondine group) and Group D (Dexmedetomidine) with 33 patients in each group.

Materials and Methods: Patients in group C received 2.5ml of 0.5% hyperbaric Bupivacaine with 50 µg of Clonidine. Patients in group D received 2.5 ml of 0.5% hyperbaric Bupivacaine with 2 µg of Dexmedetomidine.

Statistical Analysis Used: Data were Analyzed using MS Excel software and SPSS software for determining the statistical significance. Analysis of Variance was used to study the significance of mean of various study parameters between the two groups. Student's t test was used to compare the two groups on mean values of various parameters. The p-value <0.05 is considered significant.

Results: In our study, patients remained hemodynamically stable in both Dexmedetomidine and Clonidine groups. Patients in Clonidine group had a greater fall in heart rates than in Dexmedetomidine groups, and the difference was statistically significant. There was no much fall in blood pressure and heart rate when compared to the baseline values.

Conclusion: Addition of Dexmedetomidine 2µg to 0.5% heavy Bupivacaine intrathecally produced faster onset of sensory blockade, longer duration of analgesia and motor blockade and better haemodynamic stability than Clonidine 50µg

INTRODUCTION

Spinal anaesthesia is commonly employed for lower abdominal surgeries. Various adjuvants have been used to prolong the analgesic effect of Bupivacaine.

An adjuvant (from Latin, adjuvare: to aid), is a pharmacological or immunological agent that modifies the effect of other agents, such as a drug or vaccine[1].

Adjuvants are drugs that increase the efficacy or potency of other drugs when given concurrently. Neuraxial adjuvants are used to improve or to prolong analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their dose sparing effects, neuraxial adjuvants are also utilized to increase the speed of onset of neural blockade, improve the quality and prolong the duration of neural blockade[2].

Neuraxial adjuvants include Opioids, α-2 adrenoceptor agonists, N-methyl-D-aspartate (NMDA) antagonists, cholinergic agonists and vasoconstrictors.

Intrathecal α-2 agonists have become very popular among surgeons and anaesthesiologists as an adjuvant to Bupivacaine. Results of the previous studies show that addition of either of these two agents intrathecally significantly prolongs the duration of both sensory and motor analgesia of hyperbaric Bupivacaine[3].

Clonidine has been used extensively and studied as an adjuvant to Bupivacaine in almost all the types of nerve blocks. The mechanism of action of Dexmedetomidine differs from Clonidine as it posses selective alpha 2 adrenoceptor agonistic activity especially for the 2A subtype of this receptor, which causes it to be a much more effective sedative and analgesic agent than Clonidine[4].

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.

METHODS AND MATERIALS

This study was conducted at Kurnool Govt. General Hospital, Kurnool on 60 patients of ASA I and II undergoing lower abdominal surgeries.

STUDY DESIGN

This study was done in a prospective double blinded randomized manner.

SELECTION OF CASES

Inclusion criteria

- Patients in age group of 20 to 50 yrs
- ASA – I & II

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- Lower abdominal surgeries.

Exclusion criteria
- ASA – III & IV
- Patient refusal
- Renal / hepatic dysfunction
- Allergy to drugs
- Contra indication to sub arachnoid block.
- Treatment with alpha 2 adrenergic antagonists
- Labile hypertension

60 patients were included in this double blinded randomized controlled study. Patients were divided into 2 groups.

Patients in group C received 2.5ml of 0.5% hyperbaric Bupivacaine with 50µg of Clonidine.

Patients in group D received 2.5 ml of 0.5% hyperbaric Bupivacaine with 2µg of Dexmedetomidine.

PREANAESTHETIC EVALUATION
Patients included in the study underwent thorough pre operative evaluation which included the following.

HISTORY
History of underlying medical illness, previous surgery, anaesthesia and hospitalization are noted. Patients were advised overnight fasting.

PHYSICAL EXAMINATION
- General condition of the patient
- Vital signs
- Height and weight
- Examination of CVS,RS, CNS and vertebral column
- Airway assessment

INVESTIGATIONS
Hb, PCV, BT, CT, RFT, blood sugar, ECG, CXR, platelet count, blood grouping and cross matching were done.

Patients who satisfied the inclusion criteria were explained about the nature of the study and the anaesthetic procedure.

Written informed consent was obtained from all patients included in the study.

HOW DOUBLE BLINDING WAS DONE
Allotment of cases was done by computerized lots. The consultant who made the drug combination took no further part in the study. I performed the subarachnoid block and made intraoperative observations. Postoperatively in the recovery room, observations were done.

TECHNIQUE
In the OT, appropriate equipment for airway management and emergency drugs were kept ready. Patient was shifted from premedication room to the OT after giving oral Alprozalam 0.5mg 2hrs prior to surgery. The horizontal position of the operating table was checked and patient shifted to the table, I.V.line was started and intra venous fluids started. NIBP, SpO2 , ECG leads were connected to the patient. Pre operative baseline systolic and diastolic BP, PR, SpO2 and RR were recorded. SAB and done and observations were made in all the patients involved in the study. Under strict aseptic precautions a midline lumbar puncture was performed using a 25G Quincke needle in lateral decubitus position. The patient was then immediately placed in supine position. Lumbar puncture was successful in first attempt in almost all patients. The time for intrathecal injection was considered as 0 and the following parameters were observed – onset of sensory blockade was taken as loss of sensation to temperature by spirit swab at L2 level. Onset of motor block was taken as Bromage scale 1. Respiratory rate, sedation and any other complications were observed.

VITAL SIGNS AND SIDE EFFECTS
The PR, systolic and diastolic BP, SpO2 and RR were recorded pre operatively, 0 min, 5 min, 15 min, 30 min, 60 min and 90 min and at the end of surgery. Hypotension was defined as fall in systolic BP > 30 % from baseline or MAP <60 mmHg. This was managed with inj. Ephedrine 6mg increments. Bradycardia was defined as HR <50 /min and this was managed with Inj.Atropine 0.01mg/kg i.v.

Respiratory depression defined as RR< 8/min and or SpO2 <85%. This was planned to be managed with bag and mask ventilation or intubation and IPPV if necessary. Blood loss more than the allowable loss was replaced with blood. The occurrence of sedation was assessed using Ramsay sedation scale.

ASSESSMENT IN RECOVERY ROOM
Patient was shifted to recovery room after completion of surgery, the vital signs were recorded, every 30 mins interval. Sensory and motor block assessments were done every 15 mins till recovery of pin prick sensation to L1 and BROMAGE scale of 1 respectively. Patients were shifted to post operative ward after complete resolution of motor blockade.

ASSESSMENT OF PAIN AND DURATION OF ANALGESIA
In the recovery room pain assessment using VAS were done every15 mins . At the end of surgery, the degree of pain was assessed using VAS scale till VAS score >4 was reached. Whenever the patient complained of pain and rescue analgesic Inj. Diclofenac 75mg i.m was given. Duration of effective analgesia was defined as time interval between onset of SAB and the time to reach VAS >=4.

Patients were monitored for 24 hrs to detect the occurrence of side effects - respiratory depression, nausea, vomiting, dry mouth and pruritis. Patients were also enquired about the occurrence of Transient neurological symptoms which was described as pain / paresthesia in the buttocks, legs or pain radiating to lower extremities after initial recovery from SAB within 72 hrs.

RESULTS
STATISTICAL ANALYSIS:
All recorded data were entered using MS Excel software and analysed using SPSS software for determining the statistical significance. Analysis of Variance was used to study the significance of mean of various study parameters between the two groups. Student's t test was used to compare the two groups on mean values of various parameters. The p-value <0.05 is considered significant.

Data is presented as mean ± SD or numbers (n).
Group-D = Dexmedetomidine group
Group-C = Clonidine group

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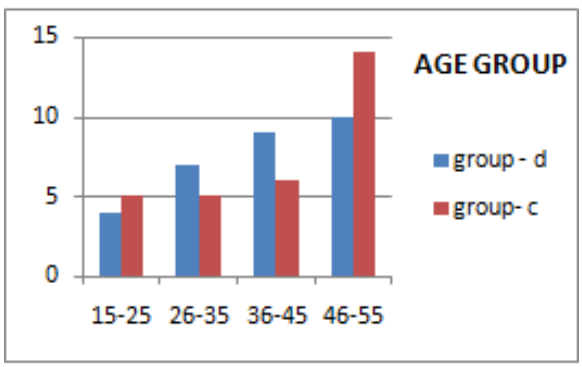
DEMOGRAPHIC DATA

Variables	Group D	Group C
Age (yrs)	40.8 ± 9.17	39.5 ±11.43
Sex (F/M)	12/18	13/17
Height (cms)	156.6 ± 4.85	161.4 ± 4.65

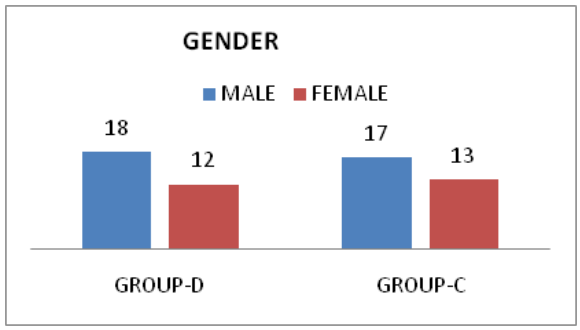
The demographic data reveals that all 3 groups are comparable in age, height, and sex ratios. There is no statistically significant difference between the groups with regard to demographic data

AGE DISTRIBUTION AMONG TWO GROUPS



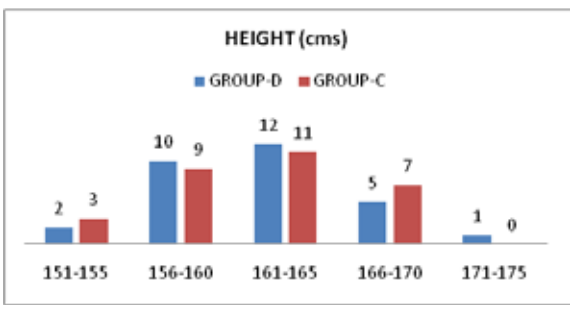
There is no statistical significance among the groups with respect to age

GENDER DISTRIBUTION AMONG TWO GROUPS



There is no statistical significance among the groups with respect to gender

HEIGHT DISTRIBUTION AMONG TWO GROUPS



There is no statistical significance among the groups with respect to height.

Onset and duration of sensory and motor blockade among two groups

	GROUP-D	GROUP-C	t- VALUE	p-VALUE
DURATION OF SURGERY (min)	116 ± 64.7	161 ± 70	0.4873	0.660
ONSET OF SENSORY BLOCKADE (sec)	83 ± 32.42	115± 39.35	3.4377	0.0011
ONSET OF MOTOR BLOCKADE (sec)	191.2± 98.04	141.7±51.75	2.5939	0.0120
DURATION OF ANALGESIA (min)	374.34±44.54	302.5±29.18	7.3897	0.0001
DURATION OF MOTOR BLOCK (min)	317 ± 32	220 ± 48	9.2096	0.0001
MAXIMUM SENSORY LEVEL ACHIEVED	T6 ± 1.2	T6 ± 1.2	0.000	1.000

There is no significant difference in the duration of surgery in both the groups.

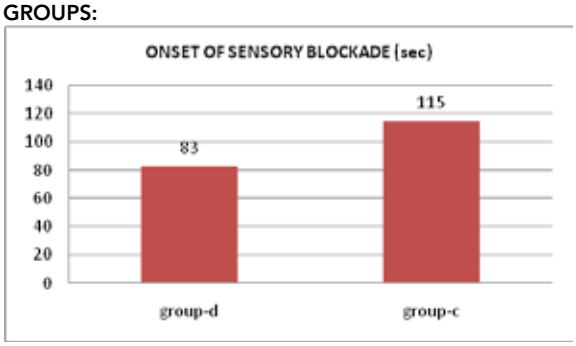
There is significant difference in the duration of analgesia, duration for duration of motor block and onset of sensory and motor blockade.

The **onset of sensory blockade** was shorter in Dexmedetomidine group than in Clonidine group.

The **onset of motor blockade** was delayed in Dexmedetomidine group when compared to Clonidine group.

The **duration of analgesia and motor blockade** was more for Dexmedetomidine group than Clonidine group.

ONSET OF SENSORY BLOCKADE (sec) AMONG TWO GROUPS:



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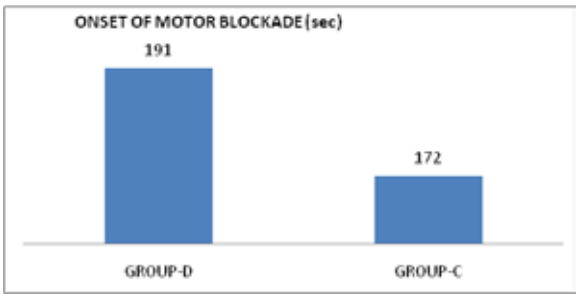
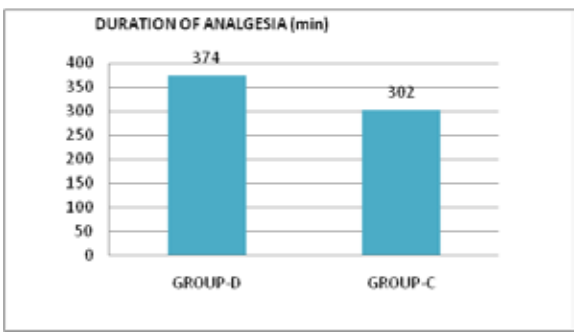
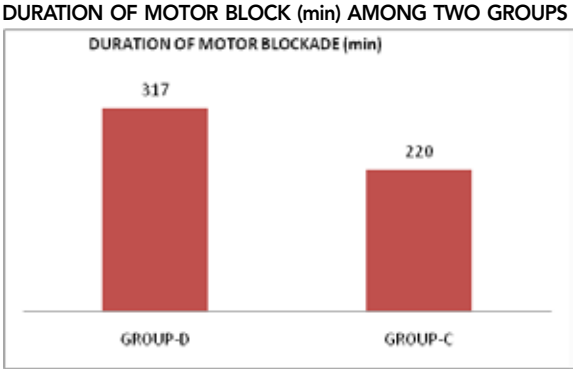
ONSET OF MOTOR BLOCKADE (sec) AMONG TWO GROUPS



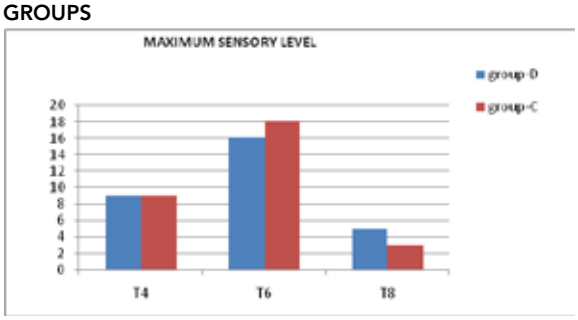
DURATION OF ANALGESIA (min) AMONG TWO GROUPS:



DURATION OF MOTOR BLOCK (min) AMONG TWO GROUPS



MAXIMUM SENSORY LEVEL REACHED AMONG TWO GROUPS



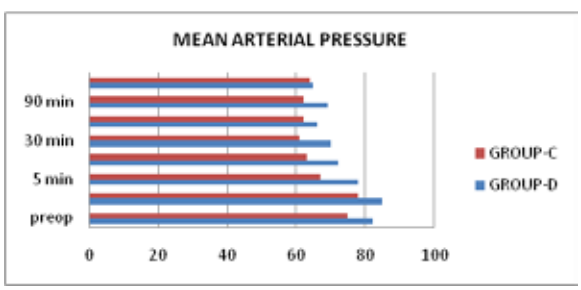
VARIATIONS IN PULSE RATE AMONG TWO GROUPS

	GROUP-D	GROUP-C	t-VALUE	p-VALUE
PRE OP	81.7 ± 18.6	75.3± 10.3	1.6487	0.1046
0 MIN	85.1 ± 20.9	78.2 ± 12	1.5682	0.1223
5 MIN	77.6 ± 22.7	67.2± 9.8	2.3039	0.0248
15 MIN	71.6 ± 17.4	63.3± 8.9	2.4102	0.0191
30 MIN	69.7 ± 15.7	61.3± 8.0	2.7043	0.0090
60 MIN	66.1± 14.2	62.5± 7.5	1.3984	0.1673
90 MIN	65.6± 14.5	62.3± 7.1	1.2216	0.2269
EOS	68.9 ± 11.8	63.5± 7.46	2.1235	0.0380

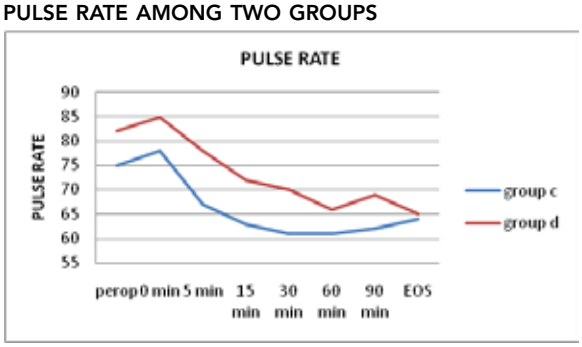
VARIATIONS IN MEAN ARTERIAL PRESSURE AMONG TWO GROUPS

	GROUP-D	GROUP-C	t-VALUE	p-VALUE
PRE OP	96.1 ± 9.4	93.4 ± 6.4	1.4735	0.1460
0 MIN	110.0±11.6	92.3 ± 9.6	6.9368	0.0001
5 MIN	84.3± 10.56	81.4 ± 9.12	1.2214	0.2269
15 MIN	80.1± 12.11	77.6 ± 9.23	1.0954	0.2778
30 MIN	80.8 ± 9.7	78.9 ± 10.4	0.7863	0.4349
60 MIN	76.4 ± 7.7	80.6 ± 9.67	1.9215	0.0596
90 MIN	78.6±8.78	80.2 ± 9.9	0.9097	0.3667
EOS	79.7±11.21	81.3 ± 9.0	0.7708	0.4440

MEAN ARTERIAL PRESSURE AMONG TWO GROUPS



PULSE RATE AMONG TWO GROUPS



RESPIRATORY RATE AMONG TWO GROUPS

RESPIRATORY RATE	GROUP-D	GROUP-C	p-VALUE
PREOP	14 ± 1.04	14 ± 1	>0.05
0 MIN	14 ± 1.4	14 ± 1.1	>0.05
5 MIN	14 ±0.81	14 ± 1.26	>0.05
15 MIN	14 ± 0.8	14 ± 1	>0.05
30 MIN	13 ± 0.8	14 ±1	>0.05
60 MIN	13 ± 0.6	13 ± 0.9	>0.05
90 MIN	13 ± 0.8	13 ± 0.94	>0.05
EOS	13 ± 0.73	13 ± 0.95	>0.05

COMPLICATIONS AMONG TWO GROUPS

	Nausea	Bradycardia	Hypotension	Sedation
GROUP-D	1	2	3	1
GROUP-C	1	3	4	1

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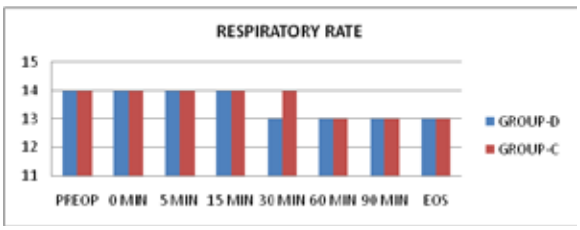
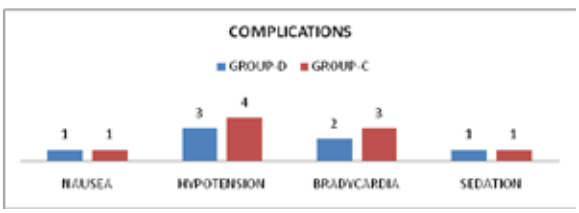
RESPIRATORY RATE AMONG TWO GROUPS



COMPLICATIONS AMONG TWO GROUPS



DISCUSSION

Dexmedetomidine and Clonidine, are alpha-2 adrenoceptor agonist agents initially prescribed for hypertension and intravenous sedation. Gradually the role of these two agents extended beyond wards to operation theatre for the provision of intraoperative and postoperative analgesia and sedation. Though there are sufficient studies on addition of Clonidine to local anaesthetics both epidurally and intrathecally, intrathecal and epidural characteristics of Dexmedetomidine have been studied mainly in animals and there is scarcity of literature about intrathecal use of Dexmedetomidine in humans.

When we compared the Dexmedetomidine and Clonidine with each other, we found that onset of motor block was delayed with Dexmedetomidine as compared to Clonidine .The difference was statistically insignificant [191.23 ± 98.04 sec in group D vs 171.75 ± 57.75sec in group C , p=0.2]. Onset of sensory block was delayed with Clonidine as compared to Dexmedetomidine [83 ± 32.42 sec in group D Vs 115 ± 39.35 sec in group C, p=0.001]. The difference was statistically significant. Dexmedetomidine produced significantly longer duration of sensory and motor block as compared to Clonidine. Regression time of sensory block was 374.34 ± 44.54 min for Dexmedetomidine as compared to 302.5 ± 29.18 min for Clonidine. Regression time to reach Bromage 1 was 317 ± 32 min for Dexmedetomidine as compared to 220 ± 48 min for Clonidine. When we searched the literature we found that very few authors have compared intrathecal Dexmedetomidine to Clonidine.

Rampal Singh and Aparna Shukla compared the effects of intrathecal Clonidine and Dexmedetomidine on sensory analgesia and motor block of hyperbaric Bupivacaine. Ninety adult patients of ASA grade I and II were divided into three groups of thirty patients each. Group A, B and C patients received inj. bupivacaine (15 mg) intrathecally with normal saline, with clonidine (50 mcg) and with Dexmedetomidine (5 mcg) respectively. Pulse rate and noninvasive blood pressure was recorded after every 5 minutes. Degree of motor block (Bromage scale), time to reach sensory block to T8 level (cold alcohol swab) ,time of regression of sensory block to S1 dermatome and time to reach Bromage 1 was assessed. Onset time of sensory and motor block was greater in group B and C. Regression time of sensory block to S1 dermatome was significantly higher in group A vs B, group A vs C and group B vs C (210.0+32.69 min , 268.93+62.75 min and 404.43+114.83 min for group A,B and C respectively). Regression time to reach bromage 1 was significantly high in group B and C as compared to A (172.11+29.77 min , 231.93+70.57 min and 309.93+101.71 min for group A, Band C respectively) [group B vs C : t=3.451; p=0.001]. Heart rate and mean arterial pressure remained at significantly lower level in Group B and Group C as compared to Group A. They concluded that though both Clonidine and Dexmedetomidine prolonged duration of sensory and motor block of Bupivacaine, Dexmedetomidine is better in terms of longer duration of action.

Sukhminder Jit Singh Bajwa compared Dexmedetomidine and Clonidine in epidural anaesthesia. The patients were randomly allocated into two groups; ropivacaine + Dexmedetomidine (RD) and ropivacaine + Clonidine (RC), comprising of 25 patients each. Group RD was administered 17 ml of 0.75% epidural Ropivacaine and 1.5 µg/kg of Dexmedetomidine, while group RC received admixture of 17 ml of 0.75% Ropivacaine and 2 µg/kg of Clonidine. They concluded that addition of Dexmedetomidine to Ropivacaine as an adjuvant resulted in an earlier onset (8.52 ± 2.36 min) of sensory analgesia at T10 level as compared to the addition of Clonidine (9.72 ± 3.44 min). Dexmedetomidine not only provided a higher dermatomal spread but also helped in achieving the maximum sensory anaesthetic level in a shorter period (13.14 ± 3.96 min) compared to Clonidine (15.80 ± 4.86 min). Modified Bromage scale 3 was achieved earlier (17.24 ± 5.16 min) in patients who were administered Dexmedetomidine as adjuvant.

G. E. Kanazi studied the effect of low-dose Dexmedetomidine or Clonidine on hyperbaric Bupivacaine. In a prospective, double-blind study, 60 patients undergoing transurethral resection of prostate or bladder tumor under spinal anaesthesia were randomly allocated to one of three groups. .Group B patients received 12 mg of hyperbaric Bupivacaine, group D patients received 12 mg of Bupivacaine supplemented with 3mcg of Dexmedetomidine and group C patients received 12 mg of Bupivacaine supplemented with 30 mcg of Clonidine. The mean time of sensory regression to the S1 segment was 303 ± 75 min in group D, 272 ± 38 min in group C and 190 ± 48 min in group B (B vs. D and B vs. C, $P < 0.001$). The regression of motor block to Bromage 0 was 250 ± 76 min in group D, 216 ± 35 min in group C and 163 ± 47 min in group B (B vs. D and B vs. C, $P < 0.001$).They opined that Dexmedetomidine (3 mcg) or Clonidine (30 mcg), when added to intrathecal Bupivacaine, produces a similar prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation.

In our study, patients remained hemodynamically stable in both Dexmedetomidine and Clonidine groups. Patients in Clonidine group had a greater fall in heart rates than in Dexmedetomidine groups, and the difference was statistically significant. There was no much fall in blood pressure and heart rate when compared to the baseline values.

Mahmoud M. Al-Mustafa added Dexmedetomidine to spinal Bupivacaine for urological procedures. He compared 5mcg (group D5) and 10 mcg (groupD10) of Dexmedetomidine added to 12.5 mg Bupivacaine to Bupivacaine 12.5 mg with normal saline (control group). The author found that the mean time of sensory block to reach T10 dermatome was 4.7±2.0 minute in D10 group, 6.3±2.7 minute in D5 group and 9.5± 3.0 minute in control group. The mean time to reach Bromage 3 scales was 10.4±3.4 minute in D10 group, 13.0±3.4 minute in D5 group and18.0 ± 3.3

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minute in control group. Regression time to reach S1 dermatome was 338.9±44.8 minute in D10 group, 277.1±33.2 minute in D5 group and165.5 ± 32.9 minute in control group. Time to reach Bromage 0 was 302.9±36.7 minute in D10 group, 246.4.1±24.7 minute in D5 group and140.1 ± 32.3 minute in control group. They opined that Dexmedetomidine has dose dependent effect on onset and regression of sensory and motor block.

Subhi M. Al-Ghanem, evaluated the onset and duration of sensory and motor block as well as operative analgesia and adverse effects of Dexmetedomidine (5 µg) or Fentanyl (25 µg) given intrathecally with plain 0.5% Bupivacaine (10mg) for spinal anaesthesia. Patients in Dexmedetomidine group (D) had significant longer sensory and motor block as compared to patients in fentanyl group (F). The time to reach the maximal sensory block was 19.34± 2.87 min. for group D and 18.39 ±2.46 min. for Group F (p = 0.126) The onset time of modified Bromage 3 motor block was also not different between group D and F; 14.4± 6.7 and 14.3 ±5.7 min. respectively (P = 0.93).The mean time of sensory regression to S1 was 274±73 min in group D and 179±47 min in group F (P < 0.001). The regression time of motor block to reach modified Bromage 0 was 240±60 min in group D and 155±46 min in group F (P< 0.001). Hypotension was mild to moderate in both groups except one patient in group F, who had a blood pressure less than 90 mmHg, and required 36 mg ephedrine to restore his blood pressure They concluded that in women undergoing vaginal reconstructive surgery under spinal anaesthesia, 10 mg plain Bupivacaine supplemented with 5 µg (microgram) Dexmedetomidine produces prolonged motor and sensory block compared with 25 µg Fentanyl.

Van Tuij, added various doses of Clonidine (0, 15 or 30 µg) to 5 mg hyperbaric Bupivacaine and evaluated their effect on the duration of the motor block, analgesic quality and ability to void .They opined that addition of 15 and 30 µg of Clonidine increased the motor block duration by 25 and 34 min, respectively and also resulted in better analgesic quality.

Strebel S et al. examined the dose-response relationship of intrathecal Clonidine at small doses (<or=150 µg) with respect to prolonging Bupivacaine spinal anaesthesia.. Eighty orthopaedic patients were randomly assigned to receive 18 mg of isobaric 0.5% Bupivacaine intrathecally plus saline (Group 1), Clonidine 37.5 mcg (Group 2), Clonidine 75mcg (Group 3), and Clonidine 150mcg (Group 4). Duration of the sensory block (regression below level L1) was increased in patients receiving intrathecal Clonidine, 288 ±62 min (Group 1, control), 311 ± 101 min in Group 2, 325± 69min in Group3, and 337±78min in Group 4 .They concluded that small doses of intrathecal Clonidine (<or=150 µg) significantly prolongs the anaesthetic and analgesic effects of Bupivacaine in a dose-dependent manner.

CONCLUSION

On the basis of the observations made during this study and their analysis, the following conclusion was drawn:

Addition of Dexmedetomidine 2µg to 0.5% heavy Bupivacaine intrathecally produced faster onset of sensory blockade, longer duration of analgesia and motor blockade and better haemodynamic stability than Clonidine 50µg.

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