Original Research Paper Medical Science

Intravenous Dexmedetomidine Prolongs Bupivacaine Spinal Analgesia - A Clinical Study

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KEYWORDS

AIMS AND OBJECTIVES
To evaluate the effects of intravenous Dexmedetomidine on the duration of block, hemodynamic changes and level of sedation in patients undergoing elective lower abdominal surgeries with 0.5% hyperbaric Bupivacaine.

METHODOLOGY
This clinical study was conducted on 60 patients of ASA grade 1&2 in the age group of 18 -45 years of either sex posted for elective surgeries in the General Surgery department under spinal anaesthesia after taking informed consent, at Sri Venkateswara Ramnarayana Ruia Government General Hospital, Sri Venkateswara Medical College, Tirupati, over a period of 12 months. After approval from the hospital ethical committee, a comparative study was carried out on 60 adult patients.

Patients were randomly divided on an alternative basis into 2 groups of 30 each.

Group "D" - received Dexmedetomidine IV bolus (1mcg/kg over 10 minutes) followed by infusion (0.5mcg/kg/hr)

Group"C" - received normal saline 0.9 % in 10 minutes, the same calculated volume as in group D

DESIGN:
A placebo controlled randomized controlled trial.

Inclusion criteria:
- ASA grade 1&2 patients
- Age group of 18 – 45 years
- Patients giving valid informed consent
- Those patients scheduled to undergo elective surgeries below the umbilicus under subarachnoid block in General Surgery Department of
- Sri Venkateswara Medical College. Tirupati.
- Exclusion criteria:
- Patient refusal.
- Patients with gross spinal abnormality, localized skin sepsis, haemorrhagic diathesis, or neurological involvement / diseases.
- Head injury cases.
- Patient receiving alpha-2 adrenergic receptor antagonists, calcium channel blockers, ACE inhibitors, having dysarrhythmias on ECG, body weight more than 120 kgs.

Method of study:
Pre anaesthetic check up was carried out preoperatively with a detailed history, general examination and systemic examination, airway assessment, spinal column examination were done.

The following laboratory examination were done in selected patients-
- Haemoglobin
- Urine analysis
- Blood sugar
- Blood urea
- Serum creatinine
- Coagulation profile
- Blood grouping and Rh typing
- ECG for patients over 40 years of age
- Chest X ray.

Vital Parameters:
HR, NIBP, SPO2, RR, ECG at 1, 2, 5, 10.15.20, 25, 30, 45, 60, …..240 mins.

Assessment of Sensory Blockade:
The onset of sensory block was tested by pin prick method using a hypodermic needle. The time of onset was taken from the time of injection of drug into SAS to loss of pin prick sensation.

The highest level of sensory block and time was noted. The time for 2 dermatomal segment regression of sensory level was noted. The duration of sensory blockade was taken as time from onset to time to return of pinprick sensation to S1 (heel) dermatomal area.

Assessment of Motor Blockade:
This was assessed by Bromage scale[1, 2, 3].

Modified Bromage Scale:
Grade 0 – Full flexion of knees and feet.

Grade 1 – Just able to flex knees, full flexion of feet.

Grade 2 – Unable to flex knees, but some flexion of feet possible.

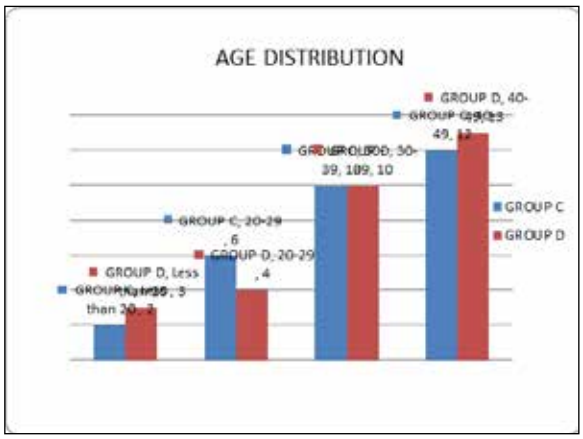
Grade 3 – Unable to move legs or feet.

Assessment of Sedation:
The level of sedation was evaluated introperatively and post operatively every 15 minutes using Ramsey level of sedation score.

Statistical analysis:
Statistical software SPSS version 16 was used for statistical analysis.

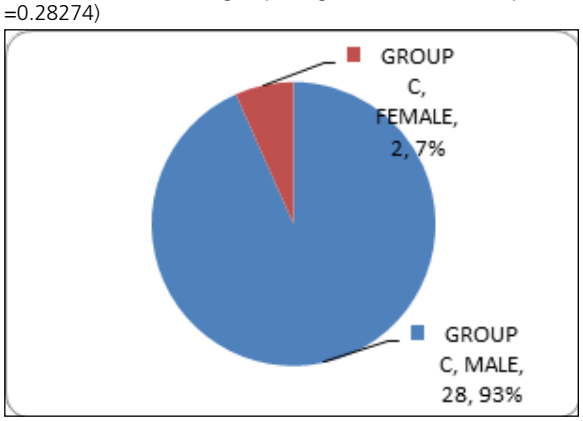
OBSERVATIONS AND RESULTS
Demographic data
Age :
The mean age in the Dexmedetomidine group was 34.960±9.14yrs as compared to 34.73±8.35yrs in the control group and the difference was statistically not significant (P val-

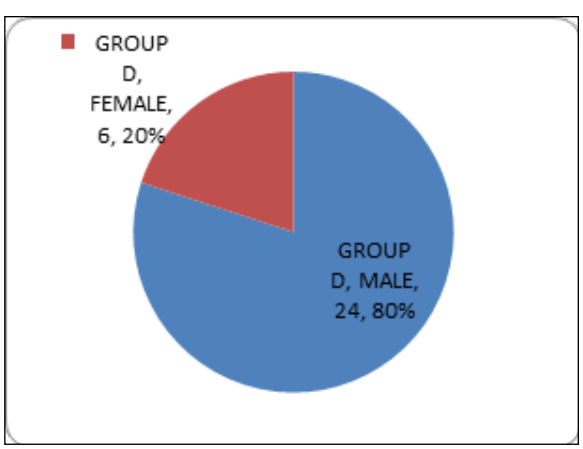
ue = 0.70313).



Bar diagram showing distribution of age in both the groups

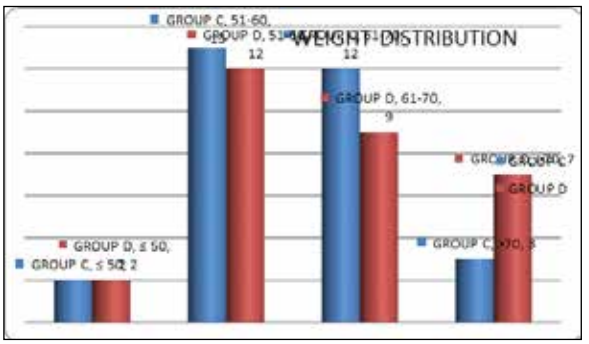
Gender :
Gender distribution in both the groups is summarized in table 3 and figure 21. There was no statistically significant difference between the two groups in gender distribution. (p value =0.28274)





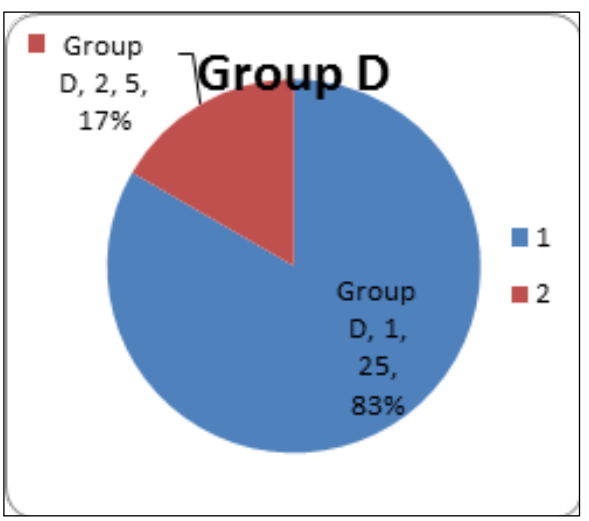
Pie diagrams showing Gender distribution in both the groups.

Weight :
The mean weight in the Dexmedetomidine group was 62.46±8.68kgs as compared to 60.46±8.02kgs in control group and the difference was statistically not significant (P value- 0.3500). There was no statistically significant difference in weight distribution.



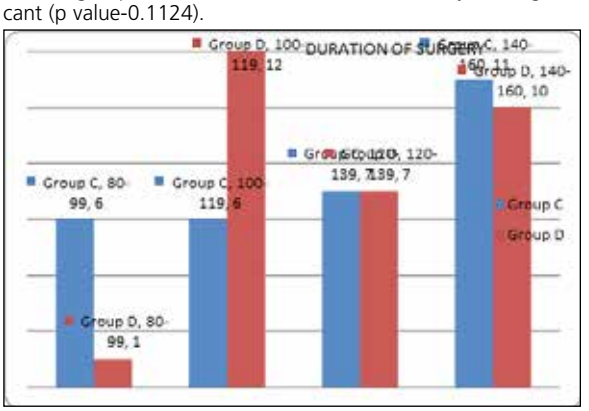
Bar diagram showing distribution of weight in both the groups.

ASA grade :
ASA grade in both the groups is summarized and there was no statistically significant difference between the two groups in ASA grade (p value=0.7386).



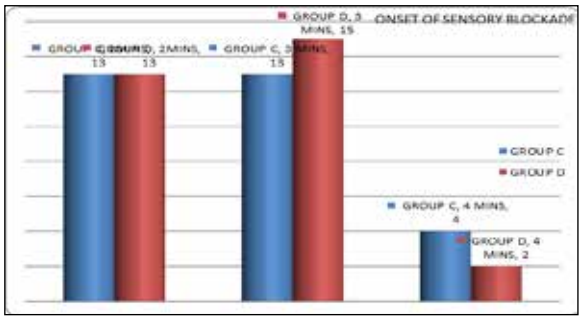
Pie diagrams showing ASA grade in both the groups.

Duration of surgery:
The mean duration of surgery in Dexmedetomidine group was 122.66+19.46mins as compared to 121+22.33mins in control group and the difference was statistically not significant (p value-0.1124).

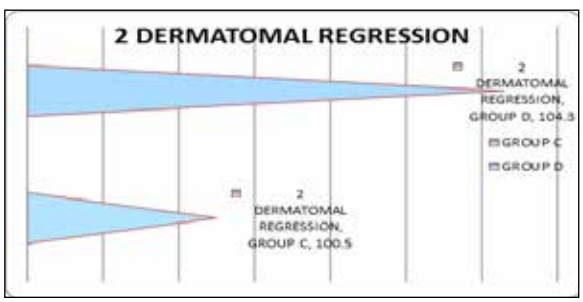


Bar diagram showing duration of surgery in both the groups.

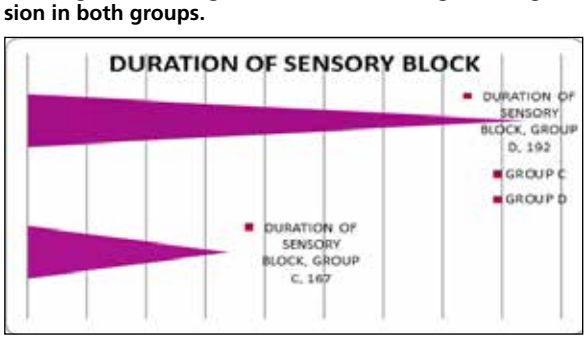
Onset of sensory block:
The mean duration of onset of sensory block in Dexmedetomidine group was 2.63 mins as compared to 2.7 mins in control group and the difference was statistically not significant (p value-0.834).



Bar diagram showing Onset of sensory block.



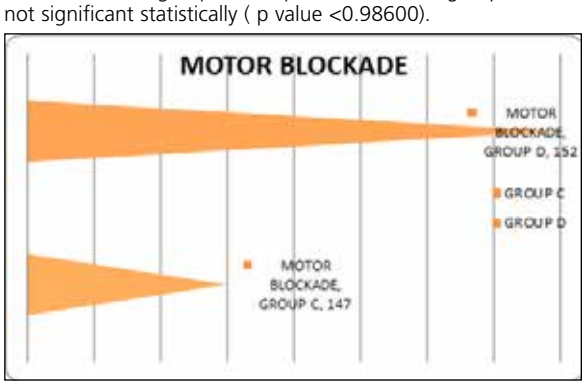
Bar diagram showing the duration of 2 segment regression in both groups.



Bar diagram showing the duration of sensory blockade

The duration of sensory blockade uptoS1 and duration of 2 segment regression of sensory blockade were slightly prolonged in Dexmedetomidine group as compared to control group (p value = 0.873 and 0.1743).which were statically not significant.

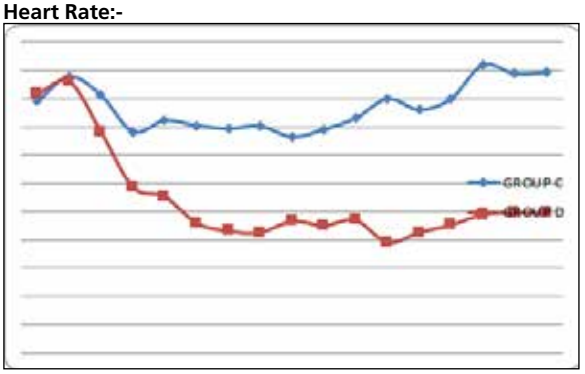
Duration of motor blockade:
The average duration of motor block regression to modified Bromage scale 0 were prolonged to a minor extent in Dexmedetomidine group as compared to control group but it is not significant statistically (p value <0.98600).



Bar diagram showing the duration of motor block in both the groups

Hemodynamic data:
The hemodynamic parameters taken into consideration were the Heart Rate, Blood Pressure (Systolic, Diastolic and Mean

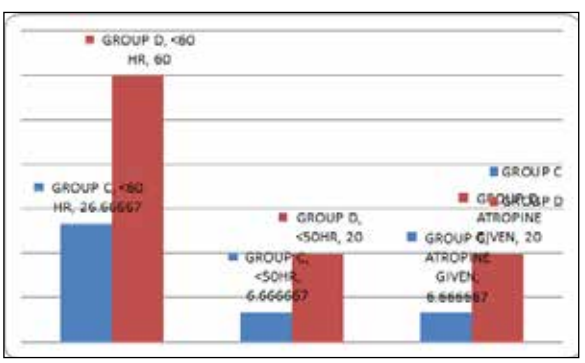
Heart Rate:-



Line diagram comparing the Heart rate in both the groups.

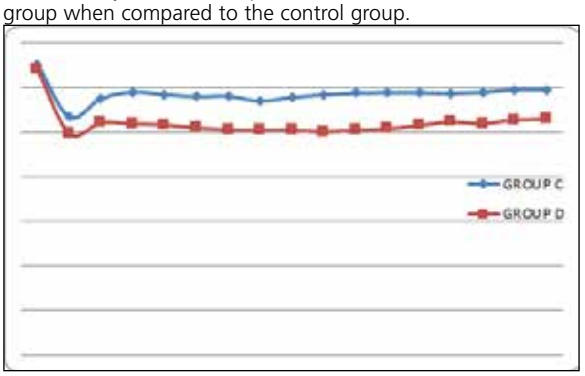
Between the groups:
The average heart rate was lower in Dexmedetomidine group (69.05±8.36) as compared to control group (75.46±9.16) (p value **< 0.001**).

Significantly higher number of patients in Dexmedetomidine group (6/30—20%) had transient intra operative heart rate <50/mt as compared to control group (2/30-6.66%) (p value-**0.00341**).



Atropine was required higher in Dexmedetomidine group (6/30-20%) as compared to control group (2/30-6.66%) (p value-0.00341) Bar diagram comparing the incidence of Bradycardia and requirement of Atropine in both the group in percentages.

Systolic Blood Pressure:
Between the groups:
The average intra operative SBP was lower in Dexmedetomidine group (104.13±6.25) as compared to control group (117.29±4.28) (p value-0.015003). There is significant decrease in systolic blood pressure in the dexmedetomidine group when compared to the control group.

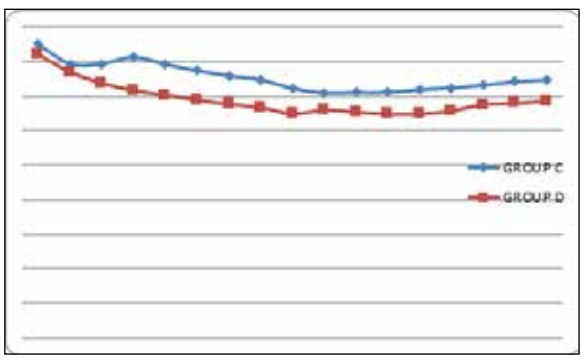


Line diagram comparing the Systolic Blood Pressure in both the groups.

There was significant difference in the intraoperative requirement of mephentermine in both the groups. Group D (9/30-30%) as compared to group C (4/30-13.33%) (P value 0.00724).

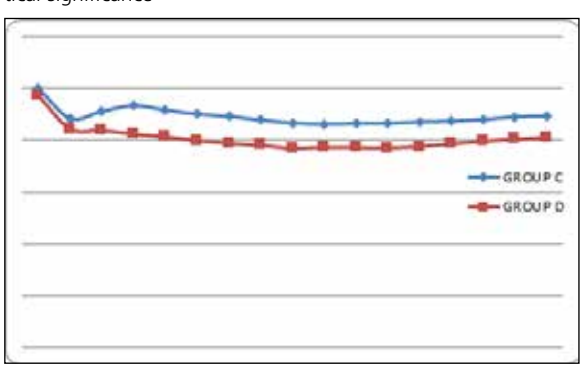
There was no significant difference in the intra operative requirement of total IV fluids between Dexmedetomidine and control group (1752±418.69vs 1592±317.43) (P value 0.134).

Diastolic Blood Pressure:
Between the groups:
The average intra operative DBP was lower in group D (69.09216±4.594847) as compared to control group (75.57059±3.992426) (p value 0.0001)



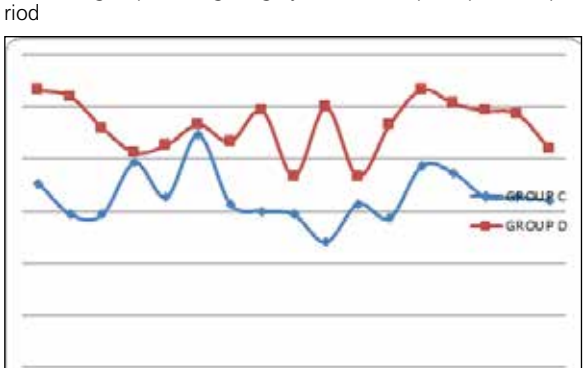
Line diagram comparing the Diastolic Blood Pressure in both the groups.

Mean Arterial Pressure:
The intra operative MAP after spinal blockade was lower in group D (80.77±4.73) as compared to group C (89.47±3.331628) (p value 0.373773) but there was no statistical significance



Line diagram comparing the Mean Arterial Pressure in both the groups Oxygen

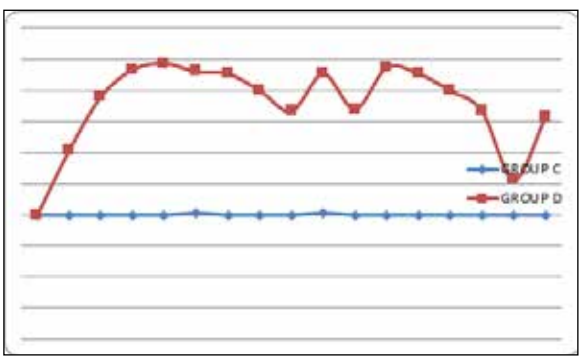
Saturation –SPO2
There was no significant difference in SPO2 levels between both the groups during surgery and in the postoperative period



Respiratory rate

There was no significant difference in the respiratory rates between both the groups during surgery and in the post operative period as shown in Figure 34. The average respiratory rate in the Dexmedetomidine group is about (14.81+0.26) where as in the control group it is (14.14+0.24) there was no significant change in the respiratory rate of both groups with a p value of (1.00) Line diagram comparing the average respiratory rate in both the groups.

Ramsay Sedation Score:
Ramsay sedation scores were significantly higher in group D (3.78±0.67) as compared to group C (2.00±0.01) (p value <0.0001).



Line diagram comparing the Ramsay Sedation Scores between the 2 groups.

Postoperative nausea and vomiting
Postoperative nausea and vomiting was noted in 2 patients (6.66%) in Dexmedetomidine group as compared to 1 patient (3.33%) in control group (p value 0.3091). There was no significant difference in both the groups

DISCUSSION
Different drugs like epinephrine, phenylephrine, adenosine, magnesium sulphate, sodium bicarbonate, Neostigmine and alpha2 agonists like Clonidine, Dexmedetomidine have been used as adjuvants to local anaesthetics to prolong the duration of spinal anaesthesia. Among them clonindine an alpha2 agonist is widely used by oral, intrathecal and intravenous routes as an adjuvant to prolong spinal anaesthesia. Recent studies have shown the efficacy of both intrathecal and intravenous Dexmedetomidine in prolonging spinal anaesthesia.

Dexmedetomidine is a more suitable adjuvant to spinal anaesthesia compared to Clonidine as it has more sedative and analgesic effects due to its more selective alpha 2.A receptor agonist activity. Dexmedetomidine has 8 times more affinity for α2 receptors than does Clonidine. Systemic and intrathecal injection of Dexmedetomidine produces analgesia by acting at spinal level, laminae VII and VIII of ventral horns. Jorm et al found that Dexmedetomidine has an inhibitory effect on the locus ceruleus located at the brainstem and dorsal raphe nucleus to produce sedation and analgesia. This supra spinal action explains the prolongation of spinal anaesthesia after intravenous Dexmedetomidine.

Sensory blockade
IV Dexmedetomidine significantly prolongs the sensory blockade of intrathecal Bupivacaine. In our study mean time for two dermatomal regression of sensory blockade was slightly prolonged in Dexmedetomidine group (104.33±7.85) as compared to control group (100.50±8.64) **(p value <0.873**). which is not significant prolongation in mean time for two dermatomal regression of sensory blockade was not in correlation to the study reported by others [Kaya et al[4] -145 ± 26 min vs 97 ±27 mins (**P < 0.001**), Tekin et al [9] -148.3 mins vs 122.8 mins (**P value < 0.001**) in Dexmedetomidine and control groups respectively]. Hong et al[5] reported that the mean time to two-segment regression was prolonged in Dexmedetomidine group [78 mins vs 39 mins for cold, 61 min vs 41 min

for pinprick for Dexmedetomidine group and control group respectively]. Similar results were reported by Elcıcek et al.[6]

The duration of sensory blockade i.e. time for regression to S1 dermatome was prolonged in Dexmedetomidine group [192.16 +18.60 min] compared to control group [167 ±13.42] (**P value < 0.1743**) in our study, which shows that there is definite average prolongation but not to a statistical significant prolongation in mean duration of sensory blockade in Dexmedetomidine group. It was reported by others [Al Mustafa et al[7]-261.5 ±34.8 min vs 165.2 ± 31.5 min (**P value < 0.05**), Whizar-Lugo et al[8]-(208±43.5 mins vs 137±121.9 mins (**P= 0.05**) in Dexmedetomidine and control groups respectively]. But our study shows no statistical significant prolongation.

Motor blockade

- IV Dexmedetomidine prolongs the motor blockade of intrathecal Bupivacaine.
- The regression time to reach the modified bromage scale 0 was prolonged in
- Dexmedetomidine group (152.69±15.48) as compared to control group (147.06±15.44) **(p value<0.9860),** which is not significant statistically**.**

Delay in motor block regression to Bromage Scale 0 was also reported in previous studies [Al Mustafa et al[7] - 199 ± 42.8 min in vs138.4 ± 31.3 min (**P value < 0.05**), Whizar-Lugo et al[8] 191±49.8 min vs 172±36.4 (P value- not significant), Tekin et al[9]- 215 mins vs 190.8 mins (**P value < 0.001**) for Dexmedetomidine group and control group respectively]. Elcıcek et al[6] and Hong et al[10] also found that complete resolution of motor blockade was significantly prolonged in Dexmedetomidine group. But contrary to all the above studies, Kaya et al[11] reported no significant prolongation in the duration of motor block in Dexmedetomidine group compared to control group .Our study also shows slight prolongation in motor block regression but not significant, supporting Kaya et al[11] report

Effect of Dexmedetomidine on heart rate

The mean heart rate was significantly lower in Dexmedetomidine group [69.05±8.36] as compared to control group [75.46±9.16] (**P value- <0.001**) in our study.

The lowest mean intra operative heart rate after subarachnoid block was significantly lower in Dexmedetomidine group [65.83±6.84] as compared to control group [73.30±10.25] (**P value < 0.001**). Significantly higher proportion of patients in Dexmedetomidine group [6/30- 20%] had bradycardia (heart rate < 50] as compared to control group [2/30-6.66%] (**P value 0.0034**). The lower HR observed in group D could be explained by the decreased sympathetic outflow and circulating levels of catecholamines that are caused by Dexmedetomidine .[11, 12]. Other studies support the finding that the bradycardia effect of Dexmedetomidine is long lasting when used as a premedication drug.[13,14] Like our study the mean heart rate was significantly lower in Dexmedetomidine group [69.05] as compared to control group [75.46] (**P value < 0.0001**) in the study done by Tekin M et al.[9] Higher incidence of bradycardia in Dexmedetomidine group [16.66%] compared to control group [8.3%] (P value 0.46) was reported by Al Mustafa et al.[7] Higher incidence of bradycardia in the present study is seen though the average duration of surgeries are nearly equal in both the groups [121 ± 22.33 min in control group and 122.66 ± 19.46 min in Dexmedetomidine group] requiring nearly equal dose of total Dexmedetomidine as compared to the study done by Al Mustafa et al[7] [42.8 ± 7.5 min in control group and 45.1 ± 8.3 min in Dexmedetomidine group] even though the study protocol of loading and maintenance dose of Dexmedetomidine were same. Whizar-Lugo et al[8] also reported higher incidence of bradycardia in Dexmedetomidine group [32%] compared to control group [20%].

Atropine was required in higher proportion of patients in Dexmedetomidine group [6/30-20%] as compared to control group [2/30-6.66%] (**P value 0.00341**) in the present study. Atropine requirement was found to be significantly higher in Dexmedetomidine group in other studies [Tekin et al[9]- 30%vs 6.6% (**P value < 0.001**), Hong et al[82] - 24.0% vs. 3.8% in Dexmedetomidine and control groups respectively]. Similar results were reported by Elcıcek et al.[8] Contrary to above studies Al Mustafa et al[7] reported no significant difference in atropine requirement between Dexmedetomidine [9%] and control groups [0%] (P value-0.65).

Effect of Dexmedetomidine on blood pressure

Lowest intra operative SBP after spinal block was significantly lower in Dexmedetomidine group [99.46±6.82] as compared to control group [106.93± 12.51] (**P value-<0.001**.) Average Post operative SBP was significantly lower in group D (105.86±5.37) as compared to group C (119.06±8.31) (**p value 0.004**).

Lowest intra operative DBP was significantly lower in group D (64.86±5.43) as compared to group C (71.0±2.50) (**p value 0.01**) . Average Post operative DBP was significantly lower in group D (68.63±5.50) as compared to group C (74.76±4.91) (**p value 0.036**).

Lowest intra operative average MAP in group D (76.96±3.55) as compared to group C (86.31±2.25) (**p value 0.022**). Average Post operative MAP was significantly lower in group D (81.04±4.42) as compared to group C (89.53±4.19) (**p value 0.0458**). Previous studies have shown that the hypotensive effect of Dexmedetomidine persists in the intra operative as well as in the postoperative period. Eliceck et al [8] reported significant decrease in mean arterial pressure after 20, 25, and 30 min after Dexmedetomidine infusion as compared to control group. Contrary to above studies and the present study, Al Mustafa et al[7]and Tekin et al[9] reported no significant difference in mean arterial pressures in Dexmedetomidine and control groups.

In the present study, there was significant difference in the number of patients requiring mephentermine for management of hypotension in both the groups [9/30 - 30% in Dexmedetomidine group when compared to control group 4/30 – 13.33% with P value 0.0072]. But, Tekin et al[9] reported no significant difference between groups in the number of patients who received ephedrine to treat hypotension. Though no significant difference in the incidence of hypotension was reported by others [Al Mustafa et al[7]- 0% vs 20% (p value-0.15), Whizar-Lugo et al[8] - 8% vs 4% in Dexmedetomidine and control groups respectively].

Total IV fluids administered in Dexmedetomidine group [1771.07 ± 332.1 ml] was significantly more as compared to control group [1653.33 ±216.13 ml] (P value of <0.0001). Similar to our study total IV infusion was more in Dexmedetomidine group [910.8 ± 280.1] compared to control group [864.5 ± 172.8] (**p value 0.025**) in the study done by Al Mustafa etal.

Ramsay sedation scores

In our study intra operative Ramsay sedation scores were significantly higher in Dexmedetomidine group [Mean-3.78±0.67] as compared to control group with [Mean-2] **(P value <0.001)**. Ramsay sedation score was 2 in all patients in control group and ranged from 2-5 in Dexmedetomidine group in the study done by Al Mustafa et al.[7] In their study the maximum score was 5 in 12% of patients, 4 in 79% of patients and 3 in 4% of patients. The maximum mean score of sedation [3.96 ± 0.55] was attained 30 min after starting Dexmedetomidine infusion. Hong et al[82]noted that the median sedation scores during surgery were 4 in the Dexmedetomidine group and 2 in the control group (**P value < 0.001**).

Postoperative nausea and vomiting

No significant difference in the incidence of post operative nausea and vomiting was noted between both the groups in

the present study 2/30 – 6.66% vs 1/30 – 3.33% in Dexmedetomidine and control groups respectively (p value 0.465

CONCLUSION

Supplementation of intravenous Dexmedetomidine had prolonged the duration of sensory and motor block of Bupivacaine spinal anaesthesia but it is not statistically significant. Dexmedetomidine caused significant decrease in heart rate, mean arterial and systolic blood pressures. The incidence of bradycardia is significantly high when intravenous Dexmedetomidine is used as an adjuvant to Bupivacaine spinal anaesthesia.

Dexmedetomidine induced significant bradycardia, which is transient and responded to atropine. The changes in blood pressure are without significant clinical impact and hypotension can be easily managed with bolus of IV fluids and mephentermine. All patients reached good sedation levels that enabled their cooperation and better operating condition for the surgeon without significant respiratory depression.

SUMMARY

This study was done in 60 adult ASA grade I/II patients undergoing surgeries under Bupivacaine spinal anaesthesia in Sri Venkateswara Ramnarayana Ruia Government General Hospital, Sri Venkateswara Medical College, Tirupati, over a period of 12 months. Patients were randomly allocated to Dexmedetomidine and control groups. Immediately after subarachnoid block with 3 ml of 0.5% hyperbaric Bupivacaine, patients in Dexmedetomidine group (group D) received a loading dose of 1 µg/kg of Dexmedetomidine intravenously by infusion pump over 10 mins followed by a maintenance dose of 0.5 µg/kg/hr till the end of surgery whereas the control group (group C) received an equivalent quantity of normal saline as loading and maintenance dose intravenously by infusion pump and served as control. The objective of the study was to compare the duration of sensory and motor block, sedation scores, intraoperative vitals of the patients.

Sensory blockade was checked with a hypodermic needle in mid axillary line and the time taken for the highest level of sensory blockade, two dermatomal regression from the maximum level and regression to S1 level were noted. Motor blockade was assessed by Modified Bromage Scale.

Time taken for motor blockade to reach Modified Bromage Scale 3 and regression of motor blockade to Modified Bromage Scale 0 was noted. The hemodynamic stability was assessed by heart rate, systolic, diastolic and mean arterial pressures. The level of sedation was evaluated using Ramsay Level of Sedation Scale.

We noted prolongation in the time for 2 dermatomal regression of sensory block, duration of sensory block and time taken for regression of motor blockade to modified Bromage scale 0. But this prolongation is not statistically significant. Dexmedetomidine resulted in significant decrease in heart rate, mean arterial/ systolic blood pressures. The incidence of bradycardia and requirement for atropine were significantly higher in Dexmedetomidine group. However, bradycardia was transient and responded well to atropine. The changes in blood pressure were without significant clinical impact and hypotension was easily managed with bolus of IV fluids and mephentermine. There was significant difference in the requirement of mepehentermine between the groups. Dexmedetomidine provided excellent sedation during surgery and sedation scores reached normal within 15 mins after stopping the drug.

We conclude that intravenous Dexmedetomidine is not so effective in prolonging the duration of motor and spinal blockade after Bupivacaine spinal anaesthesia. But it provides good sedation during surgery which quickly reverses after stopping the drug. It also provides good hemodynamic control. Bradycardia and hypotension after intravenous Dexmedetomidine are without significant clinical impact and can be easily managed. Dexmedetomidine does not cause significant respiratory depression.

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