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Original Research Article

A comparative study of intravenous dexmedetomidine and clonidine as pre-emptive analgesia to intrathecal bupivacaine in subarachnoid block - A randomized double blind study

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ABSTRACT

Introduction: Several drugs and drug regimens are used as adjuncts to local anaesthetics for neuraxial blockade in order to enhance its efficacy. In recent times novel drugs, adrenergic agonists like dexmedetomidine and clonidine are extensively used. Very few studies have compared the equipotent doses of both the drugs when given as pre-emptive analgesia. This study compares the efficacy of pre-emptive intravenous dexmedetomidine and clonidine for prolongation of bupivacaine spinal anaesthesia.

Materials and Methods: This is a prospective double-blind comparative study conducted at a tertiary care center from January 2021 to May 2022. 90 participants satisfying inclusion criteria were chosen after obtaining ethical Committee approval and informed consent. Study participants were randomly divided into two groups. Group C (n=45) received clonidine 0.5mcg/kg IV and Group D (n=45) received 0.5mcg/kg IV over 10mins following which subarachnoid block was given with hyperbaric bupivacaine 0.5% 15mg intrathecally. The following parameters were measured as onset, duration of sensory and motor blockade, duration of analgesia and number of rescue analgesics given in the postoperative period.

Results: Onset of sensory blockade (2.40+ 0.81) and motor blockade (2.78+ 0.88) was significantly faster in group D when compared to group C. Sensory blockade duration in group C and D was (100.22+ 11.38) and (129.33+ 13.55) respectively and was statistically significant. Similarly, Motor blockade duration was prolonged in group D (156.67+ 12.25) than in group C (121.78+ 14.35). Mean duration of analgesia in group D (169.51+19.23) and group C (143.8+18.78) illustrated statistically significant difference.

Conclusion: Dexmedetomidine when given as a pre-emptive analgesia enhances the effectiveness of bupivacaine by prolonging its duration of action when compared to clonidine at given doses.

1. Introduction

Regional anesthesia or Neuraxial blockade are extensively used for lower extremities and lower abdominal surgeries. Due to use of minimal drugs, less postoperative pulmonary complications and cost effectiveness, spinal blockade remains first choice. However, shorter duration of anaesthetic blockade is its disadvantages. [1]

To enhance the effectiveness of local anaesthetic agents and prolong the duration of anaesthesia and analgesia various drugs and drug regimens are used as adjuvants like opioids, but it has acute side effects which includes nausea, vomiting, itching, respiratory distress, and urinary statis. [2] Alpha-adrenergic agonists such as dexmedetomidine and clonidine are novel, used through intrathecal, epidural or intravenous route to enhance the effectiveness of subarachnoid block in terms of both sensory and motor blockade. [3,4]

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Clonidine, a partial alpha 2-adrenoreceptor agonist when administered intrathecally, is highly efficacious and safer drug. An alpha 2-adrenoreceptor agonist, i.e., dexmedetomidine has eight to ten times $\alpha 2/\alpha 1$ selectivity ratio greater than clonidine.[5] As per data clonidine is relatively 1.5 to 2 times more potent than dexmedetomidine in terms of similar dose.[6]

Till date very few researches have studied the equivalent dose of above mentioned drugs. Henceforth, the research was conducted to determine the effectiveness of dexemedetomidine and clonidine when given as pre-emptive analgesia in terms of onset and duration of bupivacaine spinal anaesthesia, duration of analgesia and time required to receive the first rescue analgesia. The article was previously presented as a paper at the ISACON 2022 National conference, Shillong, on November 26^{th}, 2022.

2. Materials and Methods

This was a prospective double-blind comparative study conducted on 90 patients undergoing elective lower abdominal and lower limb surgeries at a tertiary care centre, between January 2021 to May 2022. Institutional ethics committee clearance was obtained before starting the study (IEC no: SDUMC/KLR/IEC/616/2020-21). Written informed consent was obtained taken from patients, for participation in the study. Patients aged 18-60 years of either sex belonging to ASA physical status 1 and 2 were included in the study. Patients with ischemic heart disease, renal disease, uncontrolled diabetes and hypertension, spinal deformities, coagulopathies, previous neurological disorders, allergy to study drugs and parturients were excluded from the study.

Patients satisfying the inclusion criteria underwent pre anaesthetic evaluation including thorough physical and systemic examination 1 day prior to the surgery. Patients were randomly distributed into group D and group C based on a computer generated tables of random numbers. On the day of surgery group D received Dexmedetomidine 0.5mcg per kg IV and group C received Clonidine 0.5mcg per kg IV, to ensure blinding both the groups received 10ml of normal saline. The drug was premixed to a total volume of 10ml and given IV over 10min duration as a single bolus dose. Five minutes after administrating the study drug in both the groups, subarachnoid block was performed and hyperbaric Bupivacaine 0.5% 15mg was administered intrathecally. Both patients and treating anaesthesiologist involved in the study were blinded and recordings were taken by an anaesthesiologist who was unaware of groups. Post operatively VAS score was recorded in post operative period at 1^{st}, 4^{th}, 8^{th}, 12^{th} and 24^{th} hour. If the VAS score was 3 or more inj. Diclofenac 75mg intramuscularly was given and number of doses given were recorded.

2.1. Parameters recorded

1. Sensory blockade- onset was assessed by time taken to attain highest dermatome level and recovery time by 2 segment regression was assessed by using sterile pin prick method in mid axillary line on both sides.
2. Motor blockade- was assessed by modified Bromage scale at the time of highest dermatome level and duration was the time to return to grade-1 on modified Bromage scale
3. Time of 1^{st} rescue analgesia and number of doses required in 24 hours post- operative period based on VAS score.
4. Hemodynamic parameters- HR, SBP, DBP, MAP, SPO2.

2.2. Statistical analysis

Based on a study conducted by Reddy VS et al.[2] the minimum required sample size to find the difference in mean duration of onset of sensory blockade was calculated as 44 subjects in each study group. Hence, we considered 45 subjects in each group and a total sample size of 90 was calculated with alpha error of 5%, 95% confidence limit and power of 80%. Collected data were entered into Microsoft Excel (Windows 10) and analysis was done using the Statistical Package for Social Sciences (SPSS version 25.0; Chicago). Continuous variables were shown as mean, S.D, categorical variables were shown as percentage. For statistical analysis, Independent t test, and Chi square test was applied. P-value <0.05 was considered as statistically significant.

3. Results

All 90 patients completed the study without any complications or dropouts. Among the study participants, 45(50%) were in group C and rest of the 45(50%) participants were in group D. The mean age of group C was (45.62 ± 10.75) and group D was (41.60 ± 12.16) the difference was statistically insignificant (p-value 0.1). The baseline vitals and mean duration of surgery were comparable among groups but was statistically insignificant (Table 1)

Pre-emptive intravenous administration of dexmedetomidine in Group D resulted in faster onset of sensory blockade (2.40+ 0.81) in comparison to Group C (3.80+ 0.84) and is statistically significant (p-value 0.0001). Highest sensory blockade level was achieved in Group D (T4+1) than in Group C (T6+1).

Onset of motor blockade was faster in Group D (2.78+ 0.88) contrary to Group C (4.47+ 0.79) and was found to have statistically significant difference. Sensory blockade duration was prolonged in Group D (129+ 13.55 mins) than in Group C (100.22+ 11.38 mins), similarly Mean motor blockade duration was prolonged in Group D (156.67 ±

Table 1: Comparison of demographic variables like age, weight of the study population, baseline hemodynamic variables and duration of surgery

Variables	Group C (n=45)	Group D (n=45)	p-value
Age (in years)	45.62 ± 10.75	41.60 ± 12.16	0.1
Weight (in kgs)	63.00 ± 6.58	61.53 ± 5.49	0.25
Baseline HR (in bpm)	85.84 ± 7.79	85.82±9.67	0.99
Baseline SBP (in mmhg)	126.91±7.81	126.13±8.71	0.657
Preop DBP (in mmhg)	83.51±6.53	80.27±9.32	0.059
Preop MAP (in mmhg)	97.84±7.63	96.13±8.45	0.316
Preop SPO2 (%)	99.47±0.66	99.58±0.65	0.426
Duration of surgery (mins)	105±18.78	105.22±18.56	0.933

HR- heart rate, SBP- systolic blood pressure, DBP-diastolic blood pressure, MAP- mean arterial pressure, SPO2- Peripheralcapillary oxygen saturation

12.25) when compared to Group C (121.78 ± 14.35) and was statistically significant. The duration of analgesia was longer in Group D (169+ 19.23mins) than in Group C (143+ 21.22mins) and this illustrated a statistically significant difference. The mean total No. of rescue analgesics received in first 24hrs was more in Group C (3.22+ 0.67) in comparison to Group D (1.69+0.71) and is statistically significant (Table 2).

The trend of mean HR observation shows that heart rate in group D was lower than group C, but at any given point heart rate was always >60bpm which indicates hemodynamic stability. At 5^{th} minute after spinal anaesthesia, there was decrease in HR of about (80.73±8.57) bpm in Group C and (72.07±10.09)bpm in group D and this difference was statistically significant (p-value 0.0001) (Figure 1).

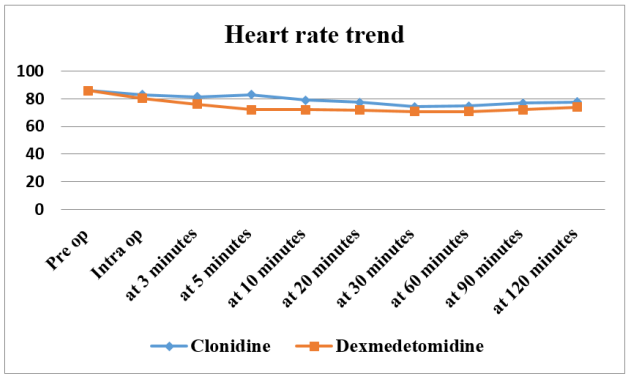

Fig. 1: Line diagram depicting heart rate trend

The trend of mean MAP in study results illustrated a non-significant difference in both groups excluding at 60 mins after spinal block where MAP was significantly lower (P=0.042). Peri-operative MAP was above 75mmHg, indicating hemodynamic stability (Figure 2).

The mean postoperative VAS score showed increasing trend in both Group C and D, but it was more in Group C than Group D. Except at 1^{st} hr, at the remaining time periods mean difference was significant in between the

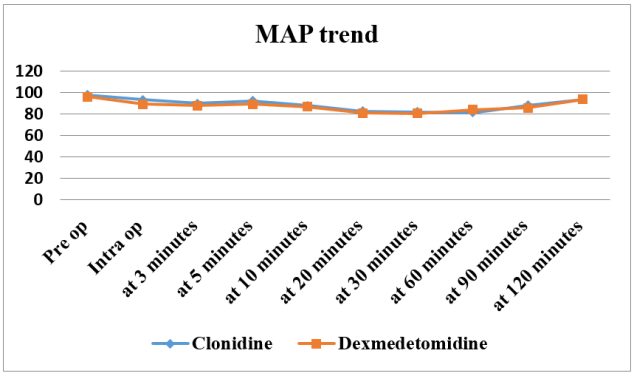

Fig. 2: Line diagram depicting MAP trend

groups (Figure 3).

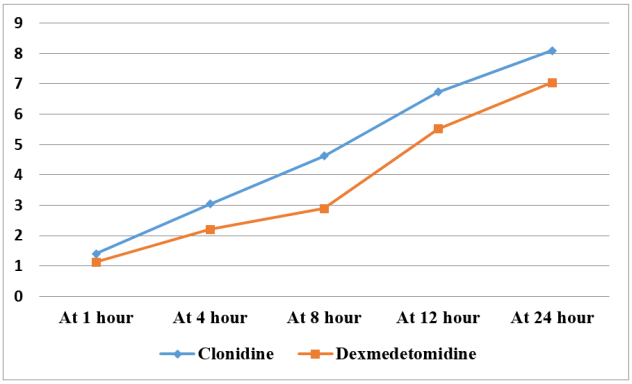

Fig. 3: Line diagram depicting VAS scores at 1^{st}, 4^{th}, 8^{th} , 12^{th} and 24 hrs post-operatively

4. Discussion

The study conducted involved 90 participants with 45 subjects each in group C and group D. The demographic variables of the subjects with respect to age and weight were comparable but illustrated insignificant difference among the groups.

Table 2: Comparison of mean onset, duration of sensory and motor blockade, highest sensory blockade, duration of analgesia and total no. of rescue analgesia in 24hrs

Variables	Group C (n=45)	Group D (n=45)	p-value
Sensory blockade onset(mins)	3.80 ± 0.84	2.40 ± 0.81	0.0001*
Highest level of blockade(segments)	T6±1	T4±1	-
Motor blockade onset(mins)	4.47±0.79	2.78±0.88	0.0001 *
Duration of sensory blockade(mins)	100.22±11.38	129.33±13.55	0.0001*
Duration of motor blockade(mins)	121±14.35	156.67±12.25	0.0001*
Duration of analgesia (mins)	143.80±21.22	169.51±19.23	0.0001*
No. of rescue analgesia	3.22+ 0.67	1.69+0.71	0.0001*

In the present study dexemedetomidine and clonidine when given as pre-emptive analgesia via intravenous route over 10 minutes prior to spinal anaesthesia showed a faster mean onset of sensory and motor blockade of bupivacaine spinal blockade in group D when compared to group C and the difference among the groups were statistically significant (p-value 0.0001). Hemodynamic parameters were found to be stable in both groups. In a study conducted by Chavi Sethi et al,[7] authors stated similar results when dexmedetomidine was given intravenously at 0.5mcg/kg before subarachnoid block with hyperbaric bupivacaine.

In a study by Sasha MM et al. authors concluded that Dexmedetomidine given by intramuscular route prior to spinal anaesthesia increases the duration of anaesthesia by prolonging the sensory and motor block.[8]

Reddy VS et al[2] compared premedication dose of intravenous dexmedetomidine at 0.5mcg/kg and clonidine at 1mcg/kg, found that that sensory block was higher and also the first postoperative analgesic request was prolonged with dexmedetomidine. The present study results showed a similar results, where a blockade till T4+ 1 was achieved with dexmedetomidine.

Mean VAS score between Group C, and Group D except at 1 hour, at remaining time periods was significant, which was similar to study by Raushan R, and Prakash A.[9] Highest VAS scores were seen in Group C than Group D, similar results were seen in a study conducted by Ganesh M, and Krishnamurthy D study,[4] authors concluded that as an adjunct to bupivacaine spinal anesthesia intrathecal dexmedetomidine is superior to clonidine.

Mean duration of analgesia was determined by the time for first rescue analgesic requirement in the post-operative period, which was (143.8 ± 21.22) in group C when compared to (169.51 ± 19.23) in group D. duration of analgesia between the groups were distinctive and stastically significant. Similar results were reported in a study conducted by Bamel S et al[10] when dexmedetomidine and clonidine is given as single dose of 1mcg/kg and 2mcg/kg IV respectively over 20 minutes showed prolonged duration of postoperative analgesia with dexmedetomidine, the results were consistent with a study by Patil KN et al.[11]

In a study a conducted by Khare A et al,[12] clonidine and dexmedetomidine was given as infusion at 1.5mcg/kg and 0.75mcg/kg respectively over 15 min before spinal anesthesia was given. The study results illustrated that dexmedetomidine fasten the onset of sensory and motor blockade, prolongs the duration of sensory and motor block and duration of analgesia was significantly prolonged ($p<0.001$). The study results were similar to the present study conducted.

5. Conclusion

We hereby conclude from the study that, pre-emptive administration of dexmedetomidine at 0.5μg/kg IV over 10mins prior to spinal anaesthesia has better hemodynamic stability, quicker sensory and motor blockade onset, extended sensory block and motor block period. Dexmedetomidine also provides better analgesia in comparison to clonidine as duration of analgesia was higher and VAS score were lower and requiring lesser rescue analgesia in Dexmedetomidine group.

6. Conflict of Interest

Nil.

7. Source of Funding

Nil.

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