Comparative Analysis of the Efficacy of Epidural Dexmedetomidine and Clonidine with Bupivacaine in Patients Undergoing Infraumbilical Surgeries

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ABSTRACT

Introduction: Pain was defined by Mountcastle in the year 1968 as "that sensory experience evoked by stimuli that injures". It is a subjective feeling and failure to relieve pain in any procedure cannot be accepted, both ethically and morally, and adequate pain relief must be treated as basic human right. Pain relief both in peri-operative and post-operative period is the crux of anaesthesia. The aim of the study was to evaluate the efficacy of epidural Dexmedetomidine and Clonidine as an adjuvant to Bupivacaine in patients undergoing infraumbilical surgeries.

Material and Methods: Seventy (70) patients aged 20-60 years (ASA I-II) undergoing infraumbilical surgery were randomly allocated to two groups- Group BD receiving epidurally 15ml Bupivacaine (0.5%) + Dexmedetomidine (1mg/kg) and Group BC receiving 15ml Bupivacaine (0.5%) + Clonidine (1mg/kg). After securing I/V line, infusion started with R/L and under strict aseptic condition, patients were administered epidural block via 18G Tuohy needle in the sitting or lateral position at L_3-L_4 intervertebral space.

Results: We observed that the time taken for the onset of sensory block at T_{10} level, time for sensory block upto T_6 and the time taken for maximum motor block is less in Group BD compared to Group BC. Regarding the post-operative block, the time to sensory two segment regression, time to sensory regression to S_1, time for recovery of motor block and time to first rescue analgesia were more in Group BD compared to Group BC. And the difference between the two groups were significant ($p<0.001$).

Conclusion: On the basis of the findings of our present clinical study, we can come to conclusion that Dexmedetomidine is more effective epidural adjuvant compared to Clonidine in patients undergoing infraumbilical surgery.

Keywords: Epidural Anaesthesia, Dexmedetomidine, Clonidine, Sensory Block, Motor Block, Segmental Regression, Motor Block Recovery, Rescue Analgesia.

INTRODUCTION

Pain was defined by Mountcastle in the year 1968 as "that sensory experience evoked by stimuli that injures". The international association for the study of pain chaired by Merskey in the year 1979 defined pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." It is a sensation in a part of the body which is always undesirable and therefore is also a negative emotional experience.[1]

Pain is a subjective feeling. Failure to relieve pain cannot be accepted, both ethically and morally and adequate pain relief must be treated as a basic human right.[2]

The crux of anaesthesia is that of pain relief in both peri-operative and post-operative period. If the peri-operative and post-operative pain is not adequately controlled, various sequels may arise, such as raised blood pressure, tachycardia, delayed recovery, increase duration of hospital stay and increase possibility of chronic pain.

Numerous modalities for peri-operative and post-operative analgesia in abdominal surgeries have been used, like opioids, NSAIDS, Ketamine, wound infiltration by local anaesthetics, peripheral or regional nerve blocks, intravenous patient controlled analgesia etc. Of the different available modalities of analgesia, regional anaesthesia is an invaluable technique for peri-operative and post-operative analgesia because of its simplicity, effectiveness and safety. Epidural anaesthesia has appeared to be an efficient approach for anaesthesia and post-operative analgesia for infraumbilical surgery.

Since the beginning of the millennium, epidural analgesia was a highly preferable technique because in patient undergoing abdominal and thoracic surgery, epidural anaesthesia is associated with decrease pulmonary and cardiovascular morbidity and mortality.[3] Moreover, epidural analgesia and anaesthesia can alleviate pain for long duration and the added option of top-ups and continuous infusion of anaesthetic drugs through epidural catheter provides smooth recovery for thoracic, abdominal, gynaecological and orthopaedic surgeries.

For peri-operative anaesthesia and post-operative analgesia, one of the common methods used in infraumbilical surgeries is epidural anaesthesia[4] and commonly used drug is Bupivacaine. A major advance in improving the achievement of regional anaesthesia has been obtained by adding adjuvant

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to LA which acts by decreasing sensory input to CNS and also potentiates the effects of anaesthesia by increasing the duration of analgesia of LA drugs.[5] Adjuvant drug also lowers the incidence of LA toxicity by decreasing the dose requirement of LA agent.[6] Drugs which may be used as adjuvant are α2 -agonist, opioids, vasoconstrictors, ketamine, neostigmine etc.[7] Among the various adjuvants available for epidural anaesthesia, α2 -adrenergic receptor agonists is considered as a suitable adjuvant for its sedative, analgesic, hemodynamic stabilizing, peri-operative sympatholytic and anaesthetic sparing properties.[8]

Clonidine has been tried and tested as an adjuvant for epidural anaesthesia for over many years and the scope of α2–agonist in RA has broadened after the introduction of Dexmedetomidine.[9]

The aim of this prospective randomized study was to analyse Dexmedetomidine and Clonidine when used epidurally as an adjuvant to Bupivacaine in patients undergoing infraumbilical surgeries.

MATERIAL AND METHODS

After approval by institutional ethical committee and after obtaining informed written consent from patient, this prospective randomized clinical trial was conducted on 70 patients aged 20-60 years undergoing infraumbilical surgery under epidural anaesthesia at Assam Medical College and Hospital, Dibrugarh for a period of one year from July 2018- June 2019. All patients belonging to ASA I or II were included in the study. Patients with co-morbid conditions and those patients unwilling for the trial were excluded from the study.

The day before surgery, re-evaluation of the patient fitness and review of investigation done. The nature and procedure of the study was explained to the patients and written informed consent was obtained from each patient. All patients had routine preoperative fasting for 8 hours before surgery.

Patients were divided into two groups with 35 patients in each group. Group BD receiving 15ml Bupivacaine (0.5%) + Dexmedetomidine (1 mg/kg) epidurally and Group BC receiving 15ml Bupivacaine (0.5%) + Clonidine (1 mg/kg).

Patient's Preparation

On shifting the patient to OT, non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected and baseline values were recorded. I/V cannulation done and ringer's lactate infusion started.

Procedure

Under strict aseptic condition, patients were administered epidural block via 18G Tuohy needle in the sitting or lateral position at L3-L4 intervertebral space. Hanging drop technique was used to locate the epidural space and the catheter was secured 3-4 cm into epidural space. A test dose of 3ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200000 was injected. The catheter was then anchored in place on the back of the patient using adhesive tape. After 4-6 minute of administering the test dose, study drug was administered. The order of drug administration was randomized. Quasi random sampling was used in this study. Patients in Group BD received 15ml of 0.5% Bupivacaine and 1mg/kg of Dexmedetomidine and patients in Group BC received 15ml of 0.5% Bupivacaine and 1mg/kg of Clonidine.

The sensory level was assessed by response to pin-prick method. The variables observed and recorded for sensory block were, the time taken for onset of sensory block at T10 and the time taken for sensory block upto T6.

Motor weakness was evaluated using modified Bromage scale. The variable observed and recorded for motor block is, the time taken for complete establishment of motor block (Bromage 3)

The patients were positioned for surgery after 30minute of epidural administration of the drugs and after ensuring effective sensory and motor block.

Post operative block characteristics were assessed at 1hour interval till 7 hours, the characteristics that were assessed were mean time to sensory two segment regression, mean time to sensory regression to S_1, mean time for recovery of motor block (Bromage 1) and mean time for first rescue analgesia.

Post operative pain was assessed by 10-point verbal rating scale (VRS). VRS was measured every 60minutes postoperatively till patient complained of pain (VRS>4). Then rescue analgesia of 10ml of injection Bupivacaine 0.125% was administered via epidural catheter. The time for first rescue analgesia (starting from epidural drug administration to once the patient asked for additional analgesia or with VRS>4) was recorded.

Haemodynamic monitoring was done and adverse effects if any were noted and treated accordingly.

STATISTICAL ANALYSIS

The data collected was tabulated in Microsoft Excel worksheet and computer based analysis was performed using the Statistical product and service solution (SPSS) 20.0 software (SPSS, Chicago, Illinois, USA) and Microsoft Excel 2010. Results on continuous measurements are presented as mean ± standard deviation and are compared using student t test. Discreet data are expressed as number (%) and are analysed using chi square test. For all analysis, the statistical significance was fixed at 5% (p value < 0.05).

RESULTS

Demographic profile and ASA physical status of the patients in both the groups were comparable and the difference between the groups was statistically not significant (Table 1).

Table 2 shows the onset of sensory block at T10 level and time for sensory block upto T_6. It is observed that there was a highly significant difference between the two study groups. ($p< 0.001$).

Table 3 shows time for maximum motor block which was 18.57±1.85 mins in Group BD and 21.65±2.21 mins in Group BC. Thus a significant difference was observed in between the two groups.

Table 4 shows the time to sensory two segment regression,

Parameter	Group BD (Mean ± SD)	Group BC (Mean ± SD)	p value
Age (years)	35.06±11.04	36.86±8.73	0.451
Sex-M:F (%)	31.43:68.57	25.71:74.29	0.596
Weight (kg)	51.69±8.20	50.00±8.20	0.393
Height (cm)	153.94±2.60	154.46±2.60	0.388
ASA I:II (%)	74.29:25.71	77.14:22.86	0.780
Duration of surgery (minutes)	72.26±20.89	77.66±21.47	0.290

Table–1: Demographic Profile

Sensory Block	Group BD (Mean ± SD)	Group BC (Mean ± SD)	p value
Onset at T10 (minutes)	8.44 ± 1.77	10.63 ± 1.53	<0.001
Time for block upto T6 (minutes)	13.77 ± 1.68	15.38 ± 1.39	<0.001

Table–2: Sensory Block

	Group BD (Mean ± SD)	Group BC (Mean ± SD)	p value
Time for Maximum Motor Block	18.57 ± 1.85	21.65 ± 2.21	<0.001

Table–3: Time for Maximum Motor Block

Postoperative lock	Group BD (Mean ± SD)	Group BC (Mean ± SD)	p value
Time to Sensory Two Segment Regression	135.71 ± 4.43	124.77 ± 4.00	<0.001
Time to Sensory Regression to S1	320.43 ± 16.96	300.37 ± 15.46	<0.001
Time for Recovery Motor Block (Bromage1)	243.23 ± 10.20	217.74 ± 17.16	<0.001
Time to First Rescue Analgesia	341.09 ± 16.14	314.94 ± 19.14	<0.001

Table–4: Postoperative Block

Side Effects/Complications	Group BD (Mean ± SD)	Group BC (Mean ± SD)	p value
Hypotension	9 (25.71%)	8 (22.86%)	0.780
Bradycardia	4 (11.43%)	3 (8.57%)	0.690
Dizziness	2 (5.71%)	3 (8.57%)	0.321
Headache	1 (2.86%)	1 (2.86%)	1
Nausea	4 (11.43%)	4 (11.43%)	1
Vomiting	1 (2.86%)	1 (2.86%)	1
Shivering	3 (8.57%)	2 (5.71%)	0.321
Dry Mouth	6 (17.14%)	7 (20.00%)	0.094
Pruritis	0	0	–
Respiratory depression	0	0	–

Table–5: Side Effects/Complications

time to sensory regression to S_1, time for recovery of motor block and time to first rescue analgesia. Statistically highly significant (p value<0.001) is observed between the two study groups.

Regarding side effects, hypotension was the most common side effects in both the groups but there was no statistically significant difference between the study groups. (Table 5)

Bradycardia and shivering were observed more in Dexmedetomidine group compared to Clonidine group whereas dry mouth and dizziness were commonly observed in Clonidine group compared to Dexmedetomidine group but the findings were statistically comparable in both groups.

DISCUSSION

Epidural anaesthesia is a safe technique that provides surgical anaesthesia and post-operative pain control. Addition of adjuvant to local anaesthesia helps in providing better surgical anaesthesia and post-operative analgesia, with very little adverse effects.[10] Use of neuraxial opioids as adjuncts is associated with side-effects such as respiratory depression, nausea, pruritus etc. and hence α2-adrenergic agonists were assessed as an alternative.[11] Epidural administration of α2-adrenergic agonist is associated with anxiolysis, hypnosis, sedation sympatholysis and analgesia. Analgesia is produced by direct stimulation of pre and post synaptic grey matter of the spinal cord which inhibits the release of nociceptive

neurotransmitters.

This study was undertaken to evaluate the efficacy of epidural Dexmedetomidine and Clonidine with Bupivacaine n 70 patients undergoing infraumbilical surgeries at Assam Medical College and Hospital. The patients were divided into two groups (35 patients in each group), Group BD receiving Isobaric 0.5% Bupivacaine 75mg (15ml) + Dexmedetomidine (1mg/kg) and Group BC receiving Isobaric 0.5% Bupivacaine 75mg (15ml) + Clonidine (1mg/kg).

The study groups were comparable regarding demographic variables such as age, sex, height, weight, ASA grading and duration of surgery.

Regarding the onset of sensory block, Agarwal et al (2015)[9] observed the time for sensory block at T_{10} level and upto T_6 level for dexmedetomidine group to be 8.40 ± 2.92 minute and 13.4 ± 3.01 min respectively which was shorter compared to clonidine group which was 10.53 ± 2.38 min and 15.66 ± 2.38 min respectively.

In our study, the time for sensory block at T10 level and upto T6 level in dexmedetomidine group was 8.44 ± 1.77 min and 13.77 ± 1.68 min respectively which was shorter compared to clonidine group 10.63 ± 1.53 and 15.38 ± 1.39 min respectively. The difference between the two groups was significant (p value < 0.001). Our study thus correlated with the above study group.

Regarding the time taken for maximum motor block, Agarwal et al (2015)[9] observed that the time taken by Dexmedetomidine group is 18.80 ± 3.37 minute which was shorter than time taken by the Clonidine group which was 21.24 ± 3.46 minute. Their findings were statistically significant (p value < 0.05) and is in accordance with our study.

Shaikh et al (2018)[12] also observed a statistically significant (p value < 0.05) difference between the two groups. Their Dexmedetomidine group took 18.80 ± 3.37 minute and the Clonidine group took 21.53 ± 3.46 minute to reach maximum motor block. Their findings were in accordance with our study. In our study, the time for complete motor block was 18.57 ± 1.85 minute in dexmedetomidine group and 21.65 ± 2.21 minute in Clonidine group (p value < 0.001).

Bajwa et al (2011)[13] observed that the time to sensory two segment regression to be longer in Dexmedetomidine group 136.46 ± 8.12 minute compared to Clonidine group 128.08 ± 7.54 minute (p value < 0.05). Sheikh et al (2018)[13]also observed a statistically highly significant (p value = 0.00001) difference between the groups. Dexmedetomidine group took 136 ± 6.86 minute and Clonidine group took 124.97 ± 6.65 minute for sensory 2 segment regression. The above observations were in accordance with our study. In our study, the time to sensory to segment regression for Dexmedetomidine group was 135.71±4.43minute and in Clonidine was 124.77±4.00minute which was statistically highly significant (p value<0.001)

Agarwal et al (2015)[9] observed that the time taken for sensory regression to S1 in Dexmedetomidine group was 390.33±41.07minute which was longer compared to Clonidine group 360±29.27 minute (p value <0.05).

Shaikh et al (2018)[12] also observed a statistically significant (p value=0.0038) difference between the two groups. Their Dexmedetomidine group took 314.17±18.87minute and the Clonidine group took 298.73±20.68minute for sensory regression to S_1

The findings of the above study groups were in accordance with our study. We observed sensory regression to S_1 to be 320.43±16.96 in Dexmedetomidine group and 300.37±15.46 in Clonidine group which was statistically significant (p value<0.001)

Agarwal et al (2015)[9] observed recovery time of motor block to Bromage 1 in Dexmedetomidine group to be 314±38.78minute which was longer compared to Clonidine group 282.60±7.50minute. Their findings were statistically significant (p value0.05)

Shaikh et al (2018)[12] observed recovery time of motor blockage to Bromage 1 for Dexmedetomidine group to be 240.93 ± 16.54 minute which was longer compared to Clonidine group which was 160.17 ± 27.58 minute. Their findings were statistically significant (p value < 0.05).

The findings of the above study groups were similar to our study. In our study, we observed the time for recovery of motor block to Bromage 1 as 243.23 ± 10.2 minute in Dexmedetomidine group and 217.74 ± 17.16 minute in Clonidine group (p value < 0.05).

Agarwal et al (2015)[9] observed that the time for first rescue analgesia was 434.33 ± 50.83 minute in Dexmedetomidine group which was longer compared to Clonidine group which was 399.33 ± 32.80 minute (p value < 0.05).

Shaikh et al (2018)[12] also observed statistically significant (p value < 0.05) difference between the two groups. Dexmedetomidine group took 342.97 ± 18.05 minute and Clonidine group took 307.97 ± 22.54 minute for first rescue analgesia.

Their findings were in accordance with our study. We observed the time for first rescue analgesia to be 341.09 ± 16.14 minute in Dexmedetomidine group and 314.94 ± 19.14 minute in Clonidine group. The time to first rescue analgesia for patients receiving Dexmedetomidine was longer and statistically highly significant (p value < 0.001).

Regarding the hemodynamic effects, we observed fall in HR and MAP in both groups. Though the fall was more in Dexmedetomidine group but it was statistically insignificant (p value > 0.5)

Agarwal et al (2015)[9] found hypotension to be the most common side effects in both groups but did not find any statistically significant difference between the groups regarding adverse effects.

Shailesh et al (2017)[14] also observed fall in heart rate and Mean Arterial Pressure but no statistical difference between two groups was observed (p > 0.5). We have also observed fall in respiratory rate in both the groups but no statistically significant difference was seen between the two groups.

Shaikh et al (2018)[12] though observed a decreasing trend of heart rate and mean arterial pressure in both the groups, but was not statistically significant. There was also no statistical

difference regarding mean respiratory rate.

Hypotension was the most common side effects in both the groups in our study. Bradycardia and shivering were observed more in Dexmedetomidine group and dry mouth and dizziness in Clonidine group. Shaikh et al (2018)[12] found dry mouth to be the most common side effect in both the groups and found no statistical difference between the side effects in both the groups.

CONCLUSION

On the basis of the findings of our present clinical study, we can come to conclusion that Dexmedetomidine is more effective epidural adjuvant compared to Clonidine in healthy patients undergoing infraumbilical surgery.

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