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COMPARISON OF DEXMEDETOMIDINE AND BUPRENORPHINE AS AN ADJUVANT TO ROPIVACAINE IN EPIDURAL ANAESTHESIA FOR LOWER ABDOMINAL SURGERIES

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Abstract

Background: This study was done to compare the effects of buprenorphine and dexmedetomidine as an adjuvant to ropivacaine in epidural route for lower abdominal surgeries especially hernia surgeries. Sixty patients between 18 to 60 years of both gender of ASA status I and II scheduled for elective hernia surgeries satisfying the inclusion and exclusion criteria were selected randomly allocated into 2 groups as Group A and Group B. The were investigated for RBS, RFT, LFT, CBC, Platelet count, CXR & 12 lead ECG. **Group A** received dexmedetomidine (0.5ml) (50mcg) with 0.5ml sterile normal saline 15 ml of 0.75% ropivacaine through epidural catheter. **Group B** received buprenorphine 0.5ml (150mcg) with 0.5ml sterile normal saline with 15 ml of 0.75% ropivacaine through epidural catheter. Before commencement of the procedure, patients were instructed on the method of sensory and motor assessments. After adequate sensory blockade (T10) patient was positioned for surgery. Intraoperatively assessment of sensory and motor blockade was done at the end of each minute after injecting 16 ml of the study drug. The onset time for the sensory and motor blockade and the duration of sensory and motor blockade were recorded. Vitals parameters were observed throughout the procedure till 24 hours. In our study, the time to onset of sensory blockade was faster in buprenorphine group (mean time=7.87 minutes) than in dexmedetomidine group (mean time=8.73 minutes). The time to onset of motor blockade was faster in buprenorphine group (mean time= 10.3 minutes) than in dexmedetomidine group

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(mean time=16.8 minutes). The duration of sensory blockade was more in buprenorphine group (mean time=466 minutes) than in dexmedetomidine group (mean time= 319.37 minutes). The duration of motor blockade was more in buprenorphine group (mean time= 433.5 minutes) than in dexmedetomidine group (mean time=258.9 minutes). The duration of analgesia was more in buprenorphine group (mean time=491.3 minutes) compared to dexmedetomidine (mean time=331.8 minutes). There is statistically significant difference in hemodynamic parameters where Heart rate, systolic blood pressure, diastolic blood pressure was lesser in dexmedetomidine group compared to Buprenorphine group. Only 6 patients in group A had hypotension compared to 2 patients in group B and it was effectively managed with Inj. Ephedrine 6 mg I.V.

KEYWORDS: EPIDURAL, ROPIVACAINE, DEXMEDITOMIDINE, BUPREGESIC, LOWER ABDOMINAL SURGERIES.

Introduction

Epidural blockade is quickly becoming one of the most versatile and useful procedures in modern anaesthesia. When compared to general anaesthesia, it provides intense pain relief, reduces sympathetic response, eliminates airway trauma, avoids polypharmacy, early ambulation, and so on.

Subarachnoid block provides complete block, as well as complications such as hemodynamic changes due to intense sympathetic blockade and post dural puncture headache, whereas epidural anaesthesia has fewer of these complications.

Because of its similar analgesic properties, less motor blockade, and lower chance for cardiotoxicity, epidural ropivacaine has increasingly replaced bupivacaine.

Even though ropivacaine requires a slightly higher dose than bupivacaine to produce analgesic and anaesthetic effects, the addition of an adjuvant aids in lowering the local anaesthetic dose and increases the potency of local anaesthetics by enhancing and lengthening the blockade.

After major abdominal surgeries, alpha 2 adrenergic agonists have been used as an adjuvant to epidural local anaesthetics to enhance the quality of analgesia. Through both central and peripheral actions, they cause analgesia. An imidazole derivative called dexmedetomidine has a plasma elimination half-life of about two hours and is 1600 times more selective for Alpha 2 receptors than Alpha 1 receptors.

A very lipophilic semi-synthetic opioid is buprenorphine. It seems to bind to mu and kappa receptors with a lot of affinity. It attaches to the mu receptors slowly and releases itself slowly. Dexmedetomidine and buprenorphine were introduced as additives in this trial to lengthen the duration of analgesia.

Aim of the Study

To compare the effect of Dexmedetomidine and Buprenorphine as an adjuvant to Ropivacaine in Epidural anaesthesia for lower abdominal surgeries.

OBJECTIVES

PRIMARY OBJECTIVES:

1. Onset of sensory blockade
2. Onset of motor blockade

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3. Duration of sensory blockade
4. Duration of motor blockade

SECONDARY OBJECTIVES

1. Duration of analgesia
2. Hemodynamic parameters
3. Side effects

Materials And Methods

This randomised, double blinded study was conducted at Thiruvarur Medical College, Thiruvarur between February 2022 to September 2022 after obtaining approval from institutional ethical committee.

Selection Criteria

Inclusion Criteria:

- ASA physical status I and II
- Age between 18-60 years
- Both gender
- Patients undergoing elective hernia surgeries

Exclusion Criteria:

- ASA physical status III and IV
- Pregnant and lactating women
- Patient unwilling
- Local infection at the injection site
- Known sensitivity to local anaesthetics
- Any bleeding disorder and patient on anticoagulation
- Neurological and musculoskeletal disease

Methodology

Study design: Randomized double blinded study

Sample size: 60

Patient satisfying inclusion criteria were investigated for, Preoperative biochemical test (RFT, LFT)

- Hematological test (Hb%, TC, DC, Platelet count)
- Random blood sugar
- 12 lead ECG
- Chest X-ray

Patients were randomly divided into two groups

Group A

These patients receiving 0.75% Inj.Ropivacaine 15ml with Inj.Dexmedetomidine (0.5ml) (50mcg) with 0.5ml sterile normal saline. Total volume-16 ml

Group B

These patiens receiving 0.75% Inj.Ropivacaine 15ml with Inj.Buprenorphine 0.5ml (150mcg)

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with 0.5ml sterile normal saline. Total volume-16ml.

Standard monitors: Pulse oximetry for saturation (SpO2), Non Invasive Blood Pressure (NIBP), Electrocardiogram (ECG) were attached and baseline pulse rate, blood pressure, saturation were recorded.

Materials used for performing an epidural blockade were placed in a sterile tray which contained antiseptic solution in a bowl, gauze sponges, sponge holding forceps, sterile towel and drapes to prepare the area for asepsis.

A sterile epidural kit was kept ready with a 18G Tuohy needle, 19G calibrated epidural catheter, a LOR syringe for appreciating Loss of Resistance.

All patients were premedicated with T. Ranitidine 150mg and T. Alprazolam 0.5mg the night before the surgery to reduce the anxiety and were fasted for 8 hours.

An intravenous line was started before procedure with 18G cannula and crystalloid infusion at 10ml/kg over 15 minutes commenced. Oxygen at the rate of 4L/min was administered through face mask. Vital parameters were observed throughout the procedure at time intervals specified in the proforma.

Under aseptic precautions, Epidural block was done in sitting position using 18G Tuohy needle in L3-L4 interspace and Epidural space identified by Loss of Resistance technique and epidural catheter length was 5cm inside the epidural space. Test dose of 3ml of 1.5% Inj.Lignocaine 45mg with Adrenaline 15mcg (1:2,00,000) was given. After ruling out intravascular and intrathecal placements, the bolus drug solution of group A and group B was administered slowly. Vital parameters were continuously monitored and recorded at time intervals specified in the proforma.

Hypotension (SBP<90mmHg) was treated with Inj.Ephedrine 6mg i.v. Bradycardia (HR <60/min) was treated with Inj.Atropine 0.6mg i.v. Nausea and vomiting was treated with Inj.Ondansetron 4mg i.v.

Block Evaluation

Intraoperatively assessment of sensory and motor blockade was done at the end of each minute after injecting 16 ml of study drug. The onset time of sensory and the onset time of motor block were recorded.

Sensory blockade was assessed by pin prick method using a short beveled, blunt 22 gauge needle.

Onset of sensory blockade was defined as the time taken from the completion of epidural injection of till the patient did not feel the pin prick at T10 level.

Duration of sensory blockade was defined as the time taken from the loss of pain at T10 to the return of pain at T10 level.

Duration of analgesia was defined as onset of sensory block at T10 level to the time of incisional discomfort as reported by the patient.

Motor Blockade

Onset of motor blockade was defined as the time taken from completion of epidural injection to inability to raise the extended leg (Bromage 1 score) was registered.

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Duration of motor blockade was taken as the time from the onset of motor block till the patient with no motor blockade (Bromage 0)

Motor blockade in the lower limb was assessed using ***modified Bromage scale.***

0 – No motor blockade

1 – Inability to raise the extended leg

2 – Inability to flex the knee

3 – Inability to flex the ankle joint

Surgical incision was made only after achieving total loss of sensation at T10 level. Intra operatively HR, SBP, DBP were monitored and recorded at 5 mins,10 mis, 15 mins, 20 mins, 25 mins, 30 mins, 60 mins, 90 mins, 120 mins then at 3 hours, 4 hours, 6 hours, 12 hours and at 24 hours. At the end of surgery patients were shifted to the recovery room and subsequently to the post operative ward. The patients were instructed to inform the onset of incisional pain to the post operative ward nurse.

Postoperatively observations were made regarding duration of post operative analgesia, hemodynamic monitoring (NIBP & HR), episodes of intraoperative and postoperative side effects such as hypotension, bradycardia, desaturation (SpO2<90%) and respiratory depression (<10 breaths/min), pruritis, nausea vomiting noted and treated.

Observation And Results

Data Analysis

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t-Test. Categorical variables were analysed with the Independent t Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 17 and Microsoft Excel 2007.

Results

When statistically comparing age distribution, weight, sex distribution, ASA status between the two groups, were found to be statistically insignificant.

All the patients in group B attained sensory block at T10 with a mean time of 7.87±1.3 minutes and all the patients group A attained sensory block at T10 with a mean time of 8.73±1.4 minutes. Hence the time for onset of sensory block up to T10 was faster in group B when compared to group A, the p value being <0.02 is highly significant.

Table 1: Time to onset of sensory block at T10 (min) (a)

	Group	N	Mean	Std. Deviation	P Value
TIME TO ONSET OF SENSORY BLOCK AT	A	30	8.73	1.484	0.020
	B	30	7.87	1.306	0.020

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T10 (MIN)					

Table 1: Time to onset of sensory block at T10 (min) (b)

TIME TO ONSET OF	**Levene's Test for Equality of Variances**		**t-test for Equality of Means**						
SENSORY BLOCK AT T10 (MIN)	**F**	**Sig.**	**T**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
								Lower	**Upper**
	.101	.752	-2.401	58	.020	-.867	.361	-1.589	-.144

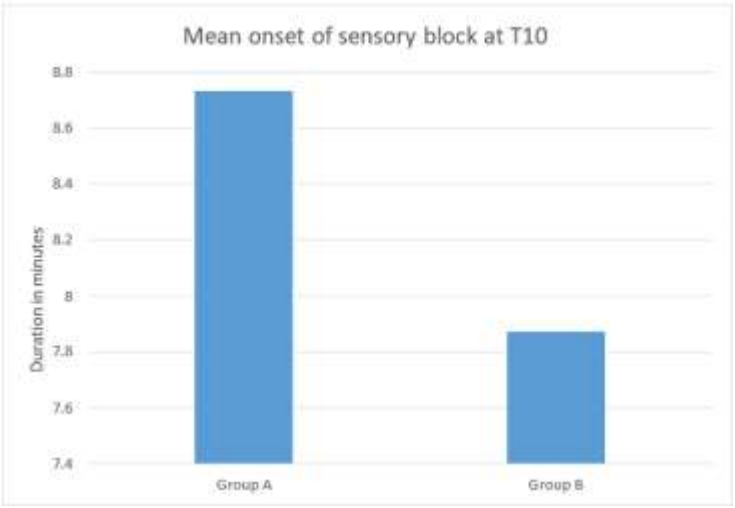

Figure 1: Comparison of mean time to onset of sensory block at T10

All the patients in group B attained motor block (Bromage 1) with a mean time of 10.3±1.2 minutes and all the patients in group A attained motor block (Bromage 1) with a mean time of 16.8±1.9 minutes. Hence the time for onset of motor block (Bromage 1) was faster in group B when compared to group A, the p value being <0.0001 is highly significant.

All the patients in group B had sensory blockade with a mean time of 466±14 minutes and all the patients in group A had sensory blockade with a mean time of 319±25 minutes. Hence the duration of sensory blockade was prolonged in group B when compared to group A, the p value being <0.0001 is highly significant.

All the patients in group B had motor blockade with a mean time of 433±10 minutes and all the patients in group A had motor blockade with a mean time of 258±5 minutes. Hence duration of motor blockade was prolonged in group B when compared to group A, the p value being <0.0001 and is highly significant.

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Table 2: Duration of motor blockade (min) (a)

	Group	N	Mean	Std. Deviation	P Value
DURATION OF MOTOR BLOCAKDE (MIN)	A	30	258.90	5.616	0.000
	B	30	433.50	10.598	0.000

Table 2: Duration of motor blockade (min) (b)

DURATION	**Levene's Test for Equality of Variances**		**t-test for Equality of Means**						
OF MOTOR BLOCAKDE (MIN)	**F**	**Sig.**	**T**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
								Lower	**Upper**
	22.725	.000	79.730	58	.000	174.600	2.190	170.216	178.984

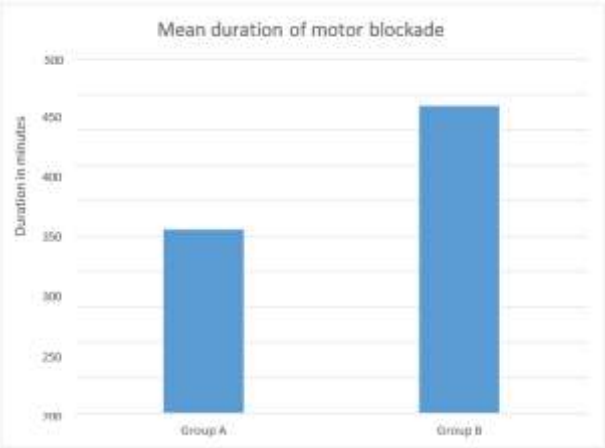

Figure 2: Mean time of duration of motor blockade

All the patients in group B had analgesia with a mean time of 491±14 minutes and all the patients in group A had analgesia with a mean time of 331±20 minutes. Hence the duration of

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analgesia was prolonged in group B when compared to group A, the p value being <0.024 is highly significant.

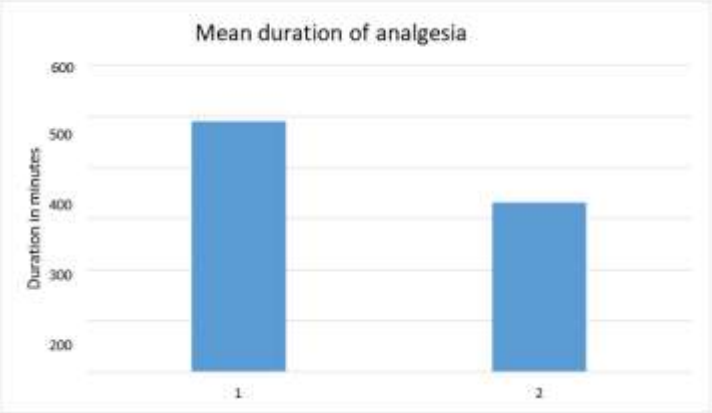

Figure 3: Duration of analgesia

There is statistically significant (p<0.05) difference between two drugs where heart rate is comparatively lesser in Dexmedetomidine group compared to Buprenorphine at 30 mins, 60 mins, 90 mins, 2 hours, 3 hours, 4 hours and at 6 hours.

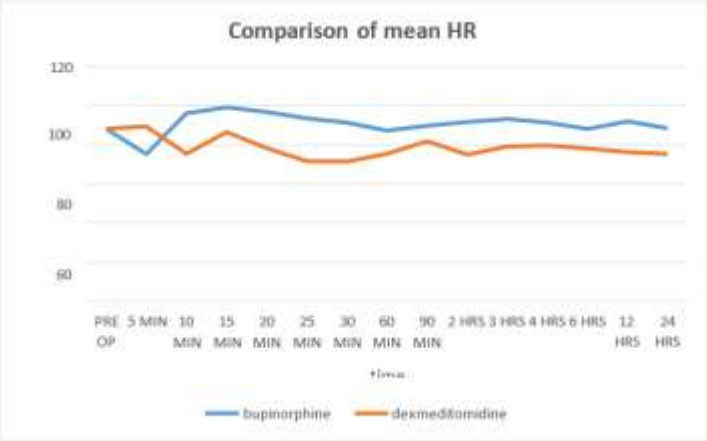

Figure 3: Comparison of mean Heart rate between two groups

There is statistically significant (p<0.05) difference between two groups where Systolic blood pressure is lesser in Dexmedetomidine group compared to Buprenorphine group at 10 mins, 15 mins, 20 mins, 30 mins, 2 hours, 3 hours, 4 hours and at 6 hours.

There is statistically significant (p<0.05) difference between two groups where Diastolic blood pressure is lesser in Dexmedetomidine group compared to Buprenorphine group at 10 mins, 15 mins, 25 mins, 30 mins, 2 hours, 4 hours and at 6 hours.

Only 6 patients in group A had hypotension compared to 2 patients in group B and it was effectively managed with Inj.Ephedrine 6 mg i.v. Only 3 patients in group B had nausea and 1 patient in group B had pruritis and it was effectively managed with Inj.Ondansetron 8 mg i.v. No other side effects noted in both groups.

Discussion

Post operative analgesia offers not only relief of pain but also decreases and mitigates the nociceptive impulses induced by trauma sometimes to blunt autonomic reflexes.

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Postoperative pain that is left untreated can occasionally have both immediate and long-term negative repercussions. Neuroendocrine reactions to pain result in an increase in sympathetic tone, increased catecholamine release, decreased anabolic hormone secretion, and increased catabolic hormone secretion. Other detrimental physiological effects such as hypercoagulability, immunosuppression, and a delay in the restoration of normal gastrointestinal function are further exacerbated by the neuroendocrine stress response. Particularly following abdominal and upper thoracic procedures, reduced postoperative respiratory function is seen.

Benefits of regional anaesthesia is not pain relief alone but also decrease in need of general anaesthetic, reduction in adverse events due to general anaesthetic agents, decreases neuro-hormonal stress responses, recover the gastro intestinal functions, decreases intraoperative blood loss and expand the defense mechanisms.

Enteral and parenteral analgesics used in postoperative analgesia, are linked to unwanted events like gastrointestinal bleeding, nausea and vomiting, also sometimes causes sedation, respiratory depression, thrombocytopenia, nephrotoxicity, hepatotoxicity, etc.

Many local anaesthetic agents like lidocaine, bupivacaine and ropivacaine have been used for epidural block. Drugs like opioids, clonidine, dexmedetomidine, midazolam and ketamine are used as adjuvant to local anaesthetics to increase the duration of analgesia, decrease the individual dose of the drug and thereby decreasing the unwanted adverse effects.

Understanding that the uptake into neural tissue is a function of the CSF concentration and perineural concentration in the epidural space, which is determined by the distribution of the drug in various tissues, is necessary to estimate the effectiveness of medications injected into the epidural space.

The duration of the drug's activity is dependent on how quickly it leaves the subarachnoid and epidural spaces. We use clinical estimation to determine the effects of medications on the onset, distribution, and duration of anesthesia because it is challenging to determine the epidural and CSF concentrations of drugs directly.

With the discovery of opioid receptors in the spinal space by Taksh and Rudy in 1976 these have been used as additives with local anaesthetics to hasten the block onset and prolong the duration of analgesia.

In this randomized double blinded controlled study, we compared the Alpha 2 agonist namely, Dexmedetomidine with Ropivacaine and Buprenorphine- opioid, which is a thebaine derivative and a partial mu agonist and antagonist with kappa receptor. Ropivacaine in epidural route for lower abdominal surgeries with respect to onset, duration and side effects.

This study was conducted in Sixty patients. Thirty of them were randomly assigned to Group A and received Dexmedetomidine 0.5 ml (50mcg) with 0.5ml sterile normal saline with 15 ml of 0.75% ropivacaine.

The remaining thirty patients were assigned to Group B and received Buprenorphine 0.5ml (150mcg) with 0.5 ml sterile normal saline with 15 ml of 0.75% ropivacaine

Onset Of Sensory blockade

In our study, the time to onset of sensory blockade at T10 level in buprenorphine group was 7.87±1.3 minutes when compared to 8.73 ±1.4 minutes in dexmedetomidine group with significant difference (p=0.02) statistically and clinically.

Sukhminder Jit Singh Bajwa *et al.,* compared dexmedetomidine

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1.5µg/kg and clonidine 2µg/kg with ropivacaine and found that the onset at T10 sensory level was significantly ($p<0.05$) earlier in dexmedetomidine group (8.52±2.36 min) than the clonidine group (9.72±3.44 min).

Onset of Motor blockade

The time to onset of motor block (Bromage 1) was 10.30±1.2 minutes in buprenorphine group and 16.6±1.9 minutes in dexmedetomidine group with significant difference ($p=0.001$) statistically and clinically.

The onset of complete motor block was also significantly ($p<0.05$) In studies by Dakshinamoorthy *et al.* and Santosh kumar *et al.* there was no significant statistical difference in the onset of sensory block between buprenorphine and fentanyl groups which is in contrast to our study though there was a clinically observable difference with a slightly faster onset in the fentanyl group when compared to buprenorphine group (Fentanyl 6.6 mins, Buprenorphine (7.53 mins).

Similarly there was a statistical significant difference even in the onset of maximal sensory block amongst the two groups. The time to onset of motor blockade and maximal motor blockade was also significant being faster in group A than in group B which is in contrast to the study by Santosh kumar *et al.* where no significant difference was found statistically though clinically there was a slightly faster onset in the fentanyl group by 0.3 minutes.

For onset of motor block, the determinants are diffusion through meningeal layers, penetration of neural tissue and distribution of the drug in various tissues. Dexmedetomidine being more lipophilic and having a favourable pKa produces earlier onset than clonidine. Dexmedetomidine alters its own pharmacokinetics at higher concentration by causing vasoconstriction, and decreasing volume of distribution thereby allowing more drug for penetration of neural tissue. This also explains the transient hypertension after rapid intravenous bolus dose of dexmedetomidine. However, vasoconstriction is not seen with lower concentrations of dexmedetomidine.

Buprenorphine is a thebaine derivative, mu-receptor agonist and kappa receptor antagonist. It is effective in relieving moderate to severe pain. Buprenorphine is a long-acting, highly lipophilic opioid, which has proved to be a promising analgesic, by the epidural and intrathecal route. It is found to be about 25 times more potent than morphine and has a low level of physical dependence. While compare to local anaesthetics, it offers good analgesia while allowing early ambulation of the patient by sparing sympathetic and motor nerves.

Duration of analgesia

In our study duration of analgesia was more in Buprenorphine group (491±14 minutes) than in Dexmedetomidine group (331±20 minutes) which was statistically significant ($p=0.0001$).

The duration of analgesia was significantly longer in the buprenorphine group (491±14 mins in group B when compared to 331±20 mins in group A (Dexmedetomidine) which was similar to the results in the study by Santosh kumar *et al.* (471 mins in fentanyl group and 766 in buprenorphine group). Similarly in the study by Shibani Padhy *et al.* also the duration of analgesia was significantly more in the buprenorphine group when compared to the fentanyl group (586 ± 26.1 mins for the buprenorphine and 218 ± 19.8 mins for fentanyl group). Similarly the duration of motor blockade was also significantly more prolonged in

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Buprenorphine group (433.5 +- 10.5 minutes) compared to 258.9+-5.6 minutes in Dexmedetomidine group.

Neogi et.al also did a comparative study between clonidine and Dexmedetomidine where they were used as adjuvants to ropivacaine for caudal analgesia in paediatric patients. They compared clonidine 1μg/kg and dexmedetomidine 1μg/kg as adjuvants to ropivacaine 0.25% for caudal analgesia. The mean duration of analgesia was 6.32±0.46 hours in ropivacaine, 13.17±0.68 hours in clonidine group and 15.26±0.86 hours in dexmedetomidine group. This finding was similar to our study where duration of analgesia was 11.25 hrs in dexmedetomidine group and 7.68 hrs in clonidine group where the difference was also statistically significant.

In the study done by Sukhminder Jit Singh Bajwa *et al.*, the time for first rescue top up was 342.88±29.16 minutes in dexmedetomidine group and 310.76±23.76 minutes in clonidine group and the difference was statistically significant ($p<0.05$).

The side effects noted in our study were hypotension, nausea and pruritis. 6 patients in Dexmedetomidine group and 2 patients in Buprenorphine group had hypotension which was treated with Inj.Ephedrine 6mg i.v. 3 patients in Buprenorphine group complained of nausea which was treated with Ondansetron 8mg i.v.

This is similar to the observations by Shibani Padhy in which 4 patients in fentanyl and 7 in buprenorphine group had nausea. These problems have been reported by Blanco *et al.* also.

We observed from our study that the onset of sensory blockade and motor blockade was earlier in buprenorphine group compared to dexmedetomidine group.

The duration of sensory and motor blockade and duration of analgesia was more in Buprenorphine group compared to Dexmedetomidine group.

Side effects like hypotension are less in buprenorphine group and nausea, pruritis were less in dexmedetomidine group. So, Buprenorphine is most useful adjuvant in epidural anaesthesia.

Conclusion

Buprenorphine are safe and effective adjuvants to epidural ropivacaine in patients undergoing lower abdominal surgeries compared with Dexmedetomidine. So, Buprenorphine being the better choice in view of its faster onset of action and longer duration of action.

Buprenorphine has early onset of sensory and motor blockade and prolonged duration of post operative analgesia, less hemodynamic changes compared with Dexmedetomidine. So, Buprenorphine is more useful adjuvant in epidural anaesthesia.

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