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Original Research Article

Comparative Study of Postoperative Analgesia in Major Abdominal Oncosurgeries: Epidural Drug Combinations of Ropivacaine and Nalbuphine with Levobupivacaine and Tramadol

Kawade D. B[1], Damani K.[2], Chirde A.[3]

[1]Assistant Professor, Dr VitthalraoVikhe Patil Medical College and Hospital, Viladghat, Ahmednagar, Maharashtra, India

[2]Associate Professor, Dr VitthalraoVikhe Patil Medical College and Hospital, Viladghat, Ahmednagar, Maharashtra, India

[3]Resident, Dr VitthalraoVikhe Patil Medical College and Hospital, Viladghat, Ahmednagar, Maharashtra, India

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Corresponding author: Dr Kawade D.B

Conflict of interest: Nil

Abstract

Objective: To combat postoperative morbidity because of pain following major abdominal oncosurgeries, a prospective, double-blind, randomized study done in tertiary care hospital to compare the efficacy of postoperative analgesia by epidurally administered Levobupivacaine (0.1%) with Tramadol (50mg) and Ropivacaine (0.1%) with Nalbuphine (10mg).

Material and Methods: Study groups include patients of either sex, age 30 to 70 years, ASA I-II category planned for major abdominal oncosurgery. Randomization done into two equal groups as Levobupivacaine with Tramadol(Group LT) and Ropivacaine with Nalbuphine (Group RN). Preinduction lumbar epidural catheter was placed and then general anaesthesia was administered to all patients. Post operatively 10 ml solution made, containing 0.1% Levobupivacaine + 50mg Tramadol given in group LT and 0.1%Ropivacaine+ 10mg Nalbuphine given in group RN epidurally. Analgesic efficacy was evaluated using Visual Analogue Scale (VAS) at intervals of 15 min, 30 min, 1hr, 6hr, 12hr and 24 hr postoperatively.

Results: In group LT Visual Analogue Scale scores (VAS) were significantly higher after 6hrs than group RN. Also incidence of nausea and vomiting was less in group RN than in groups LT.

Conclusion: Epidurally administered Ropivacaine with Nalbuphine is more effective as compared to Levobupivacaine with Tramadol for managing postoperative pain in major abdominal oncosurgical procedures.

Keywords: Postoperative analgesia, epidural, levobupivacaine, tramadol, ropivacaine, nalbuphine, abdominal oncosurgery.

Introduction

Potential tissue damage that occurs during major abdominal oncosurgery may lead to postoperative pain and becomes major reason of patient's dissatisfaction [1,2]. Also if it is not controlled adequately may lead to chronic effects such as increased morbidity, pulmonary infection and hence prolonged hospital stay [2].

Although various analgesic methods have been recommended previously in patients undergoing major abdominal surgery, epidural analgesia is accepted as one of the best method for control of postoperative pain and it can be safely performed. Postoperative epidural analgesia helps in early ambulation, prevents DVT thus it has important role in postoperative recovery and early discharge.

However, the epidural analgesic agent and dosage also have important roles in the success of postoperative pain treatment [3]. Local anaesthetics are well known for its epidural analgesic effects. In recent years, levobupivacaine which is bupivacaine S (-) isomer that has a similar onset and duration of action as bupivacaine but with less toxic effects on the cardiovascular and central nervous system, is widely used [1]. Levobupivacine, ropivacine, bupivacaine are commonly used local anaesthethetics for epidural analgesia among which ropivacaine is reported toproduce less motor blockade than levobupicaine [4].

In postoperative period inadequately controlled pain increases the cardiovascular workload by activating the neuroendocrine and sympathetic nervous system. It delays mobilization, and thromboembolic events may occur. Postoperative pulmonary complications are also very common after major abdominal oncosurgeries such as atelectasis due to delayed ambulation and increased hospital stay further adds into increased postoperative morbidity and mortality [4].

Among the many options available for the control of postoperative pain, analgesia delivered through an indwelling epidural catheter is a safe and effective method for the management of acute postoperative pain. It can provide analgesia superior to systemic opioids. Apart from providing adequate pain relief, epidural local anaesthetics promoter convalescence by blunting autonomic and somatic reflexes to pain [3].

We propose to study postoperative pain relief with epidural combination of Levobupivacaine (0.1%) with Tramadol (50mg) in comparison with Ropivacaine(0.1%) with Nalbuphine (10mg) inpatients undergoing major abdominal oncosurgery. We aim to compare the onset and duration of analgesia, and other adverse effects of intermittent epidural.

Materials and Methodology

After obtaining the hospital ethics committee approval and written informed consent, we studied 60 ASA l-ll patients of either sex between 30 to 80 years scheduled for elective exploratory laparotomy for major abdominal oncosurgery under GA+EA over the period of one year (October 2021 to September 2022).

Exclusion criteria were patient refusal, contraindications to EA, allergy to LA, psychiatric disorders and coagulative disorder. Preoperatively patients randomly distributed using chit method in two equal groups of 30 each. 18G IV cannula was secured in preoperative room. Essential monitoring devices attached such as NIBP, ECG, and SpO2 and temperature probe. Premedication done with injection Ondansetron 0.1 mg /Kg. 16G epidural catheter was placed in L2-L3 space under all aseptic precautions with loss of resistance to air technique.

After securing epidural catheter, GA was given in all study group patients. Test dose has been given before administration of GA with 3ml lox 2% + adr (1:200000) and vitals monitored for changes if any to rule out accidental intravascular or intrathecal catheter placement. Postoperatively patient shifted to recovery room and then to wards. Patients were continuously monitored for pain(>3 on VAS scale). Postoperatively in group (LT), inj. Levobupivacaine 0.1% (9ml) + inj. Tramadol 50mg(1ml) and in group (RN), inj. Ropivacaine 0.1 %(9ml) + inj. Nalbuphine 10mg (1ml) was given as

epidural bolus. Pain assessment was done by using VAS score and side effects if any were monitored at interval of 15 mins, 30 mins, 1 hr, 6hrs, 12hrs and 24hrs respectively from the time of epidural bolus administration. Inj. Diclofenac 1 mg/kg was given as rescue analgesia to the patients with pain after decrease in analgesic effects epidural bolus after 6 to 8 hours.

Results

Table 1: Comparison of basic demographic data

Variable	Ropivacaine 0.1% + Nalbuphine 10 mg (10 ml)	Levobupivacaine 0.1% + Tramadol 50 mg (10 ml)	'p' value
Age (years)	64.10 ± 8.134	63.97 ± 6.941	0.946
Sex (M/F)	16/14	15/15	0.796

Table 2: Comparison of following parameters between two groups at 0 minute (before first epidural bolus)

Parameter	Group	Mean	SD	't' value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	91.47	9.797	0.074	0.941
	Levobupivacaine 0.1% + Tramadol 50 mg	91.27	10.973		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	141.80	7.170	2.497	0.816
	Levobupivacaine 0.1% + Tramadol 50 mg	141.00	17.291		
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	82.80	6.880	0.202	0.841
	Levobupivacaine 0.1% + Tramadol 50 mg	83.27	10.615		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	6.13	0.681	0.299	0.766
	Levobupivacaine 0.1% + Tramadol 50 mg	6.07	1.015		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	-	-	-	-
	Levobupivacaine 0.1% + Tramadol 50 mg	-	-		

Table 3: Comparison of following parameters between two groups at 10 minute (after first epidural bolus)

Parameter	Group	Mean	SD	't' value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	84.60	7.898	0.451	0.654
	Levobupivacaine 0.1% + Tramadol 50 mg	83.60	9.224		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	128.73	8.229	2.310	0.024*
	Levobupivacaine 0.1% + Tramadol 50 mg	120.20	18.483		
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	74.27	6.005	0.328	0.744
	Levobupivacaine 0.1% + Tramadol 50 mg	73.53	10.670		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	3.63	0.669	6.758	0.000**
	Levobupivacaine 0.1% + Tramadol 50 mg	2.50	0.630		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	-	-	-	-

	Levobupivacaine 0.1% + Tramadol 50 mg	-	-		

Table 4: Comparison of following parameters between two groups at 30 minute after first epidural bolus

Parameter	Group	Mean	SD	't' value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	79.87	7.754	0.223	0.824
	Levobupivacaine 0.1% + Tramadol 50 mg	80.33	8.421		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	116.27	9.878	1.117	0.269
	Levobupivacaine 0.1% + Tramadol 50 mg	112.73	14.234		
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	69.07	5.842	0.103	0.919
	Levobupivacaine 0.1% + Tramadol 50 mg	68.87	8.924		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	-	-	-	-
	Levobupivacaine 0.1% + Tramadol 50 mg	-	-		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	0.03	0.183	2.633	0.011*
	Levobupivacaine 0.1% + Tramadol 50 mg	0.27	0.450		

Table 5: Comparison of following parameters between two groups at 1 hour after first epidural bolus induction

Parameter	Group	Mean	SD	't' value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	79.07	7.961	2.332	0.023*
	Levobupivacaine 0.1% + Tramadol 50 mg	84.00	8.420		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	115.47	8.136	2.231	0.030*
	Levobupivacaine 0.1% + Tramadol 50 mg	110.00	10.674		
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	70.27	6.275	1.160	0.251
	Levobupivacaine 0.1% + Tramadol 50 mg	68.07	8.279		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	-	-	-	-
	Levobupivacaine 0.1% + Tramadol 50 mg	-	-		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	0.03	0.183	1.027	0.309
	Levobupivacaine 0.1% + Tramadol 50 mg	0.10	0.305		

Table 6: Comparison of following parameters between two groups at 6 hours after epidural bolus

Parameter	Group	Mean	SD	't' value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	81.80	8.652	1.670	0.100
	Levobupivacaine 0.1% + Tramadol 50 mg	85.20	7.039		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	131.27	10.245	1.659	0.103
	Levobupivacaine 0.1% + Tramadol 50	126.13	13.503		

	mg				
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	77.33	5.762	0.259	0.797
	Levobupivacaine 0.1% + Tramadol 50 mg	77.73	6.209		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	3.83	0.747	0.705	0.484
	Levobupivacaine 0.1% + Tramadol 50 mg	3.97	0.718		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	0.00	0.000	1.000	0.321
	Levobupivacaine 0.1% + Tramadol 50 mg	0.03	0.183		

Table 7: Comparison of following parameters between two groups at 12 hours after epidural bolus

Parameter	Group	Mean	SD	't' value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	83.20	9.286	2.283	0.026*
	Levobupivacaine 0.1% + Tramadol 50 mg	88.80	9.707		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	135.33	12.685	0.365	0.716
	Levobupivacaine 0.1% + Tramadol 50 mg	134.00	15.456		
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	80.53	4.696	1.336	0.187
	Levobupivacaine 0.1% + Tramadol 50 mg	82.67	7.378		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	4.80	0.610	2.246	0.028*
	Levobupivacaine 0.1% + Tramadol 50 mg	5.30	1.055		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	0.03	0.183	1.000	0.321
	Levobupivacaine 0.1% + Tramadol 50 mg	0.00	0.000		

Table 8: Comparison of following parameters between two groups at 24 hours after epidural bolus

Parameter	Group	Mean	SD	't'value	p value
Pulse	Ropivacaine 0.1% + Nalbuphine 10 mg	87.27	10.576	1.603	0.114
	Levobupivacaine 0.1% + Tramadol 50 mg	91.33	9.011		
SBP	Ropivacaine 0.1% + Nalbuphine 10 mg	141.93	12.622	0.392	0.696
	Levobupivacaine 0.1% + Tramadol 50 mg	140.47	16.135		
DBP	Ropivacaine 0.1% + Nalbuphine 10 mg	81.40	7.030	2.504	0.015*
	Levobupivacaine 0.1% + Tramadol 50 mg	86.00	7.202		
Pain score	Ropivacaine 0.1% + Nalbuphine 10 mg	5.30	0.702	2.965	0.004**
	Levobupivacaine 0.1% + Tramadol 50 mg	6.07	1.230		
Nausea	Ropivacaine 0.1% + Nalbuphine 10 mg	-	-	-	-
	Levobupivacaine 0.1% + Tramadol 50	-	-		

	mg				

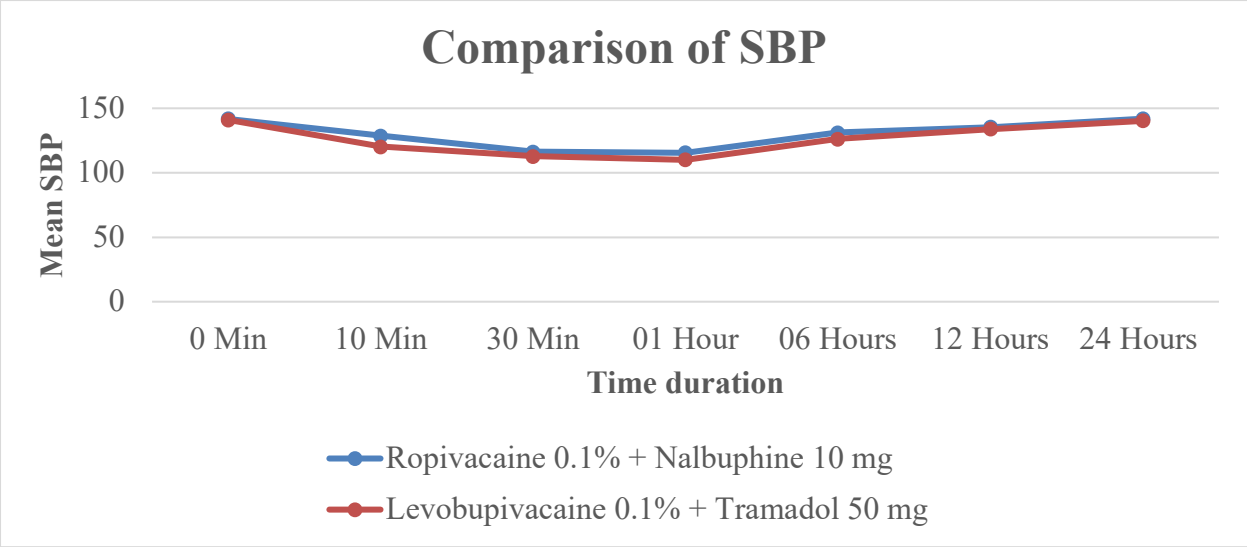

Figure 1: Comparison of Mean Systolic Blood Pressure (SBP) for two groups at different time intervals

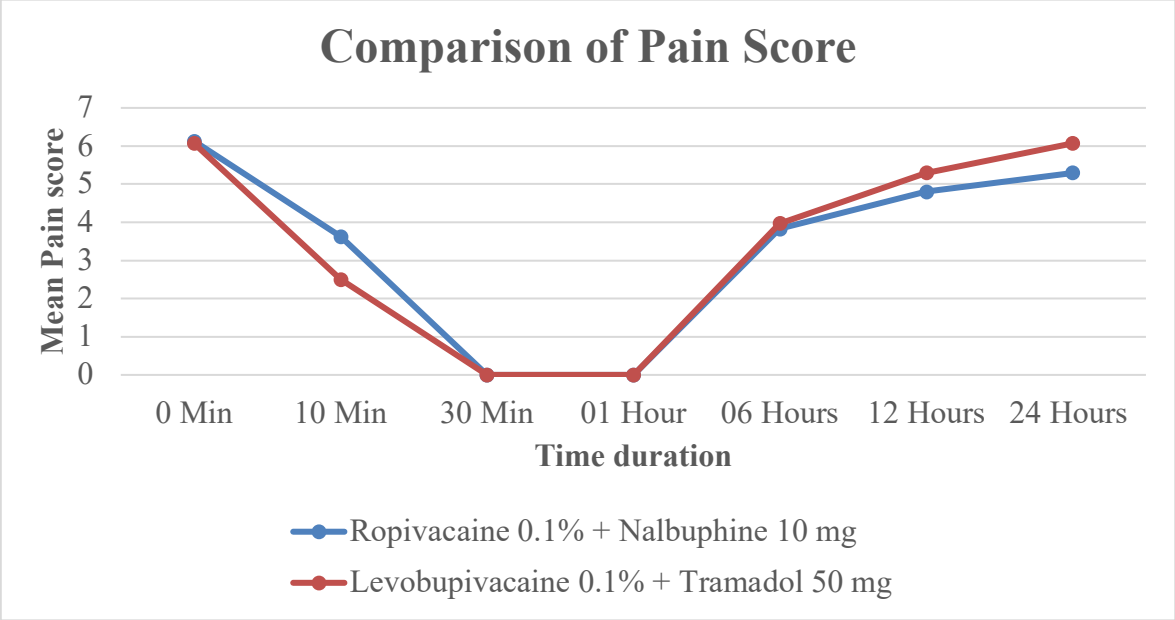

Figure 2: Comparison of Mean Pain score for two groups at different time intervals

Statistical Analysis

Data collected was analysed using SPSS statistical software version 22.0. Quantitative data was expressed as mean and standard deviation while qualitative data was expressed as frequency and percentage. Unpaired *t*-test was used to compare the means of two groups for quantitative variables and chi-square test was used for qualitative variables. All statistical tests used at 5% level of significance. *P* value less than 0.05 was considered statistically significant.

There were 30 participants in each group. Group RN who received Ropivacaine 0.1% + Nalbuphine 10 mg (10ml) and group LT who received Levobupivacaine 0.1% + Tramadol 50 mg(10ml) as postoperative epidural bolus. The age and sex were matched for both the groups with

no statistically significant difference found ($p > 0.05$).

Before epidural bolus, the parameters compared in both the groups were pulse, systolic blood pressure (SBP), diastolic blood pressure (DBP) and pain score. All these parameters were equal in both the groups with no statistical significant difference found. After postoperative epidural bolus, side effects in both the groups were also compared in addition to the above parameters.

At 10 minutes after epidural bolus, mean SBP was more in the group RN who received Ropivacaine 0.1% + Nalbuphine 10 mg as compared to the group LT who received Levobupivacaine 0.1% + Tramadol 50 mg. The difference found was statistically significant ($p = 0.024$). Similarly pain was statistically more in first group RN as compared to second group LT ($p < 0.001$).

30 minutes after epidural bolus, there was no statistical significant difference between all the parameters except side effects and there was no pain observed in either of the groups. Nausea was more in the group who received Levobupivacaine 0.1% + Tramadol 50 mg.

At 01 hour after epidural bolus, though the mean pulse rate was significantly more in group LT ($p = 0.023$), the mean SBP was more in group RN.

At 06 hours after epidural bolus, there was no statistical difference between all the parameters but pain score was significantly more in the group LT. Hence rescue analgesic requirement was more in LT grou pat 12 hours and 24 hours as compared to group RN ($p = 0.028$ and 0.004 respectively).

Discussion

In recent yearsfor major abdominal surgeries, regional anaesthesia methods have become popular. Analgesic concentrations of local anaesthetic with opioids can be effectively used for postoperative pain control which improves overall surgical outcome and decreases morbidity. In particular, epidural anaesthesia can provide effective intraoperative anaesthesia as sole anaesthetic technique or along with general anaesthesia. Postoperatively epidural catheter can be effectively used for analgesia and also decreases intravenous drug requirements for pain control.

Epidural analgesia technique for postoperative analgesia has been used as one of the first choice method in patients undergoing major abdominal surgery [3,5]. Therefore in our study, we used it as a technique of choice for postoperative analgesia in patients who were posted for major abdominal oncosurgeries like ovarian malignancy, gastrointestinal malignancy and malignancies of urogenital organs etc. under epidural with general anaesthesia.

In present study, our aim was to compare postoperative analgesia to provide subjective comfort and minimum side effects with epidural drug combinations, Levobupivacaine + Tramadol & Ropivacaine + Nalbuphine.

As study focuses on the long term efficacy of the epidural drug combinations, Group RN shows better and long term pain control lasting for the 6hrs in comparison to Group LT i.e. 4-5hrs. This is aligned to study Dipti Saxena et. al [6]. “Comparative study of duration of analgesia with epidural bupivacaine and bupivacaine with tramadol in lower limb surgeries” that epidural administration of local anaesthetic with opioids can provide very good analgesia during and after surgical procedures of lower extremity.

Ropivacaine was the drug of interest for postoperative epidural infusion because of its lower toxic potential as compared with Bupivacaine [7]. Study results indicate that delayed onset time of the Ropivacaine + Nalbuphine but it gave better long lasting analgesic effect. This helps in managing

the postoperative pain as compared to Levobupivacaine + Tramadol.

In present study, local anaesthetic drugs used were of aminoamide class. However bupivacaine is the most commonly used local anaesthetic for postoperative analgesia. It has high lipid solubility and high protein binding. It has more cardiotoxic effects as compared to levobupivacaine because once it gets bind to cardiac conduction fibres recovery is slow, this makes the resuscitation of patient difficult [4]. On the other hand, ropivacaine and levobupivacaine showed lesser cardiotoxicity than bupivacaine and quicker recovery from blockade.

We chose levobupivacaine and ropivacaine in our study as local anaesthetics drugs because of less cardiotoxic potential.

The use of opioids in the epidural or subarachnoid space for managing postoperative pain is based on the knowledge that opioid receptors are present in the substantia gelatinosa of the spinal cord [9].

In previous study Turkoglu Z. *Et al*, [3] they used morphine and tramadol as a additive to Levobupivacaine for patient controlled analgesia and they found less consumption of Levobupivacaine when used opioid as additive to local anaesthetic. So, we decided to use Ropivacaine with Nalbuphine and Levobupivacaine with Tramadol to compare postoperative analgesia of these two combinations.

Present study was prospective, double blind randomised control trial. In this study we compared Ropivacaine(0.1%) +Nalbuphine (10mg) and Levobupicaine (0.1%) +Tramadol (50mg) epidurally 10 ml volume of each in patients posted for major abdominal oncosurgeries for postoperative pain management. We have studied onset of action, duration of analgesia, requirement of rescue analgesia, haemodynamic responses and associated adverse effects like nausea, vomiting, pruritus and hypotension if any.

The demographic profile in both the groups was comparable and statistically insignificant. P value<0.9 (Table 1).

At the end of surgery i.e. at 0 min before giving epidural bolus we compared systolic BP (SBP), diastolic BP (DBP), Pulse rate (PR) and pain score. As shown in Table 2mean SBP, DBP, PR and pain score measured by VAS were comparable and statistically insignificant.

By using double blind method, epidural boluses of Ropivacaine(0.1%) +Nalbuphine (10mg) and Levobupicaine (0.1%) +Tramadol (50mg) 10 ml volume of each given in group RN and group LT at 0 min. Table 3 showed the comparison of SBP,DBP, PR, Pain score and side effects the difference found was statistically significant ($p = 0.024$). Similarly pain and SBP was statistically more in first group RN as compared to second group LT ($p < 0.001$). This shows that onset of action in group RN is slower than group LT which is statistically significant. This finding is in oppose with the previous literature that the onset of action of Ropivacaine is earlier than Levobupivacaine as per Chen W [10]which may be due to addition of Nalbuphine and needs further study.

After 30 min of epidural bolus, there was no statistical significant difference between all the parameters. In either of the groups VAS score was 0 and there was no clinically significant pain complaints from patients. However in the group who received Levobupivacaine 0.1% + Tramadol 50 mg and the most common side effects observed was nausea which is also clinically insignificant(Table 4). Our study findings were comparable with the previous studies, Senard M.*et al* [9] where they used epidural Levobupivacaine (0.1%) or Ropivacaine (0.1%) combined with morphine in patients posted for abdominal surgeries and the found that both the local anaesthetics were equianalgesic.

Continuous monitoring was done for same parameters including VAS score and side effects, at 1 hr after epidural bolus though the mean pulse rate was significantly more in group LT (p = 0.023), the mean SBP was more in group RN, i.e. the group who received Ropivacaine 0.1% + Nalbuphine 10 mg (p = 0.030) which is clinically insignificant. However mean VAS score was 0 in both the groups (Table5).

At 06 hours after epidural bolus, there was no statistical difference between all the parameters but pain score was significantly more in the group LT who received Levobupivacaine 0.1% + Tramadol 50 mg at 12 hours and 24 hours than group RN (p = 0.028 and 0.004 respectively)(Table 6,7,8). Mean SBP was in group RN = 131.27mmhg and group LT = 126.13mmhg. DBP was in group RN = 77.33 mmhg and in group LT =77.73 mmhg. Mean PR was in group RN=81.80/minand in group LT = 85.20/min which was statistically insignificant. Importantly, VAS score was more in group LT= 3.97 than group RN =3.83 which found to be statistically and clinically significant as shown in Table 6,7,8 we observed that duration of action of epidural bolus in group RN was more than group LT.

Conclusion

Epidurally administered Ropivacaine with Nalbuphine found more effective as compared to Levobupivacaine with Tramadol for managing postoperative pain in major abdominal oncosurgical procedures.

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