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Comparative Study on Efficacy between Continuous Epidural Infusion of Ropivacaine and Levobupivacaine with Fentanyl as Adjuvant for Post Operative Analgesia

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ABSTRACT
The word "Pain" is derived from Greek term "Poine" (Penalty). Pain is not just a sensory modality, but it is an experience. The International association for the study of pain defines "pain as unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". Post-Operative pain forms an acute category of non-malignant pain producing range of detrimental acute and chronic effects. Post-Operative epidural analgesia is an effective and well accepted method of pain relief techniques to improve patient's outcome, early mobilization and ambulation which accelerate the post-operative recovery. Analgesia delivered through epidural infusion is a safe and effective method for management of acute post-operative pain. The present study is to compare post-operative analgesia with continuous epidural infusion of Ropivacaine (0.125%) and Levobupivacaine(0.125%)with Fentanyl asAdjuvant for 24hours.
Keywords:*Post-Operative Pain, Epidural Infusion, Ropivacaine, Levobupivacaine, Fentanyl*

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INTRODUCTION

Post-operative epidural analgesia is an effective and well accepted modality of pain relief techniques after abdominal surgeries. Post-Operative epidural analgesia improves patient's outcome. Early mobilization and ambulation accelerate post-operative recovery. Epidural Analgesia is often considered optimal post-operative analgesia after major lower abdominal or lower extremity surgery. Analgesia delivered through indwelling catheter is a safe and effective method for management of acute post-operative pain. The high quality of post-operative pain relief is the main concerns for the patients. It is also the ultimate goal of both national health policy and then specialty of Anesthesiology. Epidural infusion of local anesthetics alone is combined with Opioids may be used for post-operative analgesia. The location of action of local anesthetics in the epidural space includes spinal nerve roots, dorsal root ganglion or spinal cord itself. Ropivacaine is the monohydrate of the hydrochloride salt of 1-propyl-2,6-pipecoloxylidide and is prepared as pure S-enantiomer. Levobupivacaine is the pure S-enantiomer of racemic bupivacaine with lower cardiac and central nervous system toxicity. Levobupivacaine has better safety profile compared to racemic bupivacaine [2-5]. This study compares post-operative analgesia with continuous epidural infusion of Ropivacaine 0.125%with Fentanyl and Levobupivacaine 0.125% with Fentanyl for 24 hours in lower abdominal and lower limb surgeries.

MATERIAL AND METHODS

This is prospective randomized comparative study was conducted on 60 consecutive adult patients undergoing elective surgery under epidural anesthesia at Vinayaka Missions Kirupananda Medical College and Hospital, Salem. Institutional ethics committee approval was obtained, and informed consent was obtained from all these patients. All the patients were visited on the day before surgery. A detailed pre-anesthetic evaluation was carried out. They were explained in detail regarding the anesthetic procedure and about the methods to assess pain intensity by using Visual Analog Scale (VAS). Age between 18 and 60 years, patients undergoing elective or emergency lower abdominal surgeries were included. Patients with infection at the sight of injection, coagulation abnormalities, those with hypersensitive to local anesthetics and neurological or neuro-muscular disease were excluded from the study. Routine investigations like complete urine examination, complete blood picture, blood sugar, blood

urea, serum creatinine, serum electrolytes, electrocardiogram and chest X-ray was undertaken to rule out the presence of systemic illness. All patients had intra-dermal sensitivity test, only those with normal response were included. Preparation of the patient included the period of overnight fasting. Per-medication was done with oral tablet Alprazolam0.25 mg and tablet Pantoprazole 40mg at night. The sixty patients were randomly divided into 2 groups (Group A and Group B) of thirty each. Randomization was done by throwing lots.

Group A: Thirty patients received 0.125% Ropivacaine with Fentanyl 1 micro gram per ml at the rate of 8mlperhourinfusionfor 24hoursepidurally.

GroupB: Thirty patients received 0.125%Levobupivacaine with Fentanyl1microgram per ml at the rate of 8ml per hourinfusionfor24 hours epidurally.

Operation theatre was checked and emergency drugs, airway cart was kept ready. After shifting the patient into operation theatre, monitors were applied. Base line parameters were noted. IV access with18-gauge cannula secured and fluids started. With proper positioning of the patient under sterile aseptic precautions, after local skin infiltration, epidural catheter placed in epidural space with Tuohy needle byloss of resistance to air technique. Then, subarachnoid block performed using 25-guage Quincke babcock needle with 3cc of 0.5% hyper baric bupivacaine. Longer duration surgery or breakthrough intra-operative pain was managed with subsequent epidural top-ups with 0.5% bupivacaine.

Post-operatively patients allocated to each group received their test drug. Epidural infusion was started only when the patient complains of pain with VAS score of more than 3 and bromage scale 0. Patients were received their respective drugs with initial loading dose of 5ml followed by continuous infusion of test drug at 8ml per hour. 5ml bolus top-up of same test drug was given for rescue analgesia. VAS score at movement and at rest was recorded at 0-minute, 1 hour, 3 hours, 6 hours, 12 hours, 18 hours, and 24hoursalongwith other vitals. Patients were monitored for adverse effects.

Quantitative data were analyzed by ANOVA followed by unpaired 't' test. Qualitative data were analyzed using Chi square test. P value < 0.05 was taken as statistically significant. P value < 0.001 was taken as statistically highly significant.

RESULT

A total of sixty patients were included in his study. Patients were divided into 2 groups (Group A and Group B) each included thirty patients.

Group A: 0.125% of Ropivacaine with Fentanyl

Group B: 0.125% of Levobupivacaine with Fentanyl

The mean age, sex was comparable between the groups. The study was conducted with variable age in group A, group B with mean of 37.00+/-9.1689 and 39.900+/- 10.246 respectively.

Demographic Data was comparable between the 2 groups as shown in the table 1.

Table1:Statistical analysis of age

Group	No.of Patients	Age	f value	p value
A	30	37+/-9.16	0.601	0.6151
B	30	39.9+/-10.24		0.615

Sex Distribution

In group A and -group B, **t**he male patients were 25 and 25 respectively where as female patients were 5 and 5 respectively as shown in the table 2.

Table 2: Statistical Analysis Of Sex

Sex Distribution	Group A	Group B	Chi square	p value
Male	25	25	0.17	0.98
Female	5	5		

**Statistically not significant p value=0.98*

VAS Scoring at Rest

Pain intensity was assessed by VAS scoring. Before starting the infusion, baseline VAS scoring was matched between 2 groups and found to be statistically not significant (p value – 0.547). There was no-significant difference in pain scores before starting infusion. After 1 hour of infusion, there was reduction in pain score from baseline in both the groups. On comparison of VAS score among 2 groups, group B was found to be statistically significant reduction. After 3 hours of infusion, further reduction was seen in VAS scoring. Values were analyzed and statistically significant difference wasfoundin2groups.VAS scoring was comparable between both groups after 6 hours, 12 hours, 18 hours, and 24 hours of infusion. Statistically

significant difference exists between group A and group B as shown in table 3.

TABLE 3: Statistical Analysis of Vas Scoring at Rest

Time	Group A	Group B	f value	p value	Statistical Significance
0hr	7.16+/-0.37	7.10+/-0.48	0.71	0.54	NS
1hr	3.03+/-0.927	2.933+/-0.63	3.23	0.002	S
3hrs	1.83+/-0.87	1.70+/-0.74	4.11	0.008	S
6hrs	1.36+/-0.55	1.36+/-0.61	8.05	<0.0001	S
12hrs	1.40+/-0.67	1.30+/-0.59	2.98	0.003	S
18hrs	1.36+/-0.55	1.23+/-0.50	8.05	0.007	S
24hrs	1.30+/-0.53	1.1+/-0.40	5.23	0.002	S

*NS–Not-significant ,S–Significant

Heart rate

The base line heart rate before the start of infusion did not show the significant difference between both groups as shown in table 4.

TABLE4:Statistical analysis of heart rate

Time	Group A	Group B	f value	p value
0hr	79.96+/-9.56	79.60+/-8.00	1.7	0.28
1hr	78.06+/-8.99	77.50+/-8.16	1.76	0.15
3hrs	76.20+/-9.11	76.93+/-8.76	1.58	0.19
6hrs	74.76+/-8.77	74.13+/-9.10	1.59	0.19
12hrs	73.90+/-8.32	72.43+/-8.98	1.29	0.28
18hrs	72.90+/-8.09	72.13+/-8.86	1.875	0.13
24hrs	72.30+/-7.84	72.33+/-8.01	2.36	0.07

Systolic Blood Pressure

Before the start of infusion mean SBP was 116 and 118 in group A and group B respectively. After 1 hour,3 hours, 6 hours,12 hours, 18 hours, and 24hours were not statistically significant as shown in table 5.

TABLE5: Statistical Analysis of systolic blood pressure

Time	Group A	Group B	f value	p value
0hr	116+/-5.26	118+/-7.12	2.07	0.10
1hr	113.48+/-4.67	114.23+/-7.19	1.01	0.38
3hrs	111.58+/-4.84	113.23+/-7.55	0.86	0.46
6hrs	109.62+/-4.30	111.70+/-7.29	1.64	0.18
12hrs	109.27+/-4.82	109.43+/-7.20	2.05	0.10
18hrs	109.10+/-5.15	107.80+/-7.11	0.75	0.52
24hrs	107.86+/-4.83	107.40+/-6.75	1.48	0.22

Diastolic blood pressure

Before the start of infusion, DBP was 75.41 and 71.60 in group A and group B respectively. After 1 hour, 3 hours,6 hours,12 hours,18 hours, and 24 hours were not statistically significant as shown in table 6.

TABLE 6: Statistical analysis of diastolic blood pressure

Time	Group A	Group B	f value	p value
0hr	75.41+/-5.62	71.60+/-5.76	2.47	0.06
1hr	71.34+/-4.83	68.83+/-7.05	1.22	0.30
3hrs	69.96+/-6.16	67.23+/-5.47	1.75	0.15
6hrs	68.65+/-5.51	67.36+/-5.26	0.77	0.50
12hrs	67.58+/-5.72	65.70+/-5.35	2.37	0.07
18hrs	67.79+/-5.44	65.90+/-5.04	1.26	0.28
24hrs	67.03+/-4.95	63.76+/-5.96	2.28	0.08

Total no. of boluses required

Number of required in group A and group B were statistically significant as shown in table7.

TABLE 7: Statistical Analysis of Number of Boluses Required

No.of Boluses	Group A	Group B	f value
Mean+/-SD	1.7+/-0.96	1.033+/-0.80	8.54

Table 8. COMPLICATIONS

Complications	**Group A**	**Group B**
Nausea and Vomiting	2	1
Pruritis	-	-
Urinary retention	1	2
Hypotension	1	2

*ChiSquare–3.65, pvalue–0.30,NS

Table 9. Associated Motor Blockade

Group	**Motor Blockade**
A	0
B	2

DISCUSSION

The adequate management of post operative pain has been emphasized now a days. Epidural analgesia with local anesthetics is one of the most effective techniques used for post operative pain relief and may improve patient outcome. Epidural local anesthetics can block nociceptive input into the central nervous system with the addition of an epidural opioids providing an even greater analgesic effect. Although the combination of epidural opioid with local anesthetics is known to provide superior analgesia in the postoperative period, epidural ropivacaine has not been evaluated in combination with low-dose opioids or postoperative analgesia. Despite widely held impression that the combination of epidural local anesthetics and opioids provides superior analgesia with less untoward effects than epidural localanestheticsalonethemechanismofactionofepidurallyadministeredopioidsremainsunclear.

Spinal opioids exert their analgesic effects by reducing neurotransmitter release at the presynaptic level and by hyperpolarizing the membrane of dorsal horn neurons at the postsynaptic level. Epidural opioids have the advantage of producing analgesia without motor or sympathetic blockade. The mechanism of postoperative fentanyl analgesia after epidural administration is primarily systemic. Therefore, in clinical practice the objectives of co-administration of epidural opioids with subanesthetic concentrations of local anesthetics are important for three reasons: a reduction in the dose of both drugs, maintenance, orenhancement of the degree of pain relief and a reduction in the incidence of adverse effects caused by opioids and local anesthetics.

Epidural ropivacaine appears to be superior to its homologue bupivacaine because of decreased motorblockpotencymakingitlesstoxic.Theoptimalconcentrationofropivacainewhenusedaloneforepidurala nalgesia is 2 mg/ml. but this often gives inadequate analgesia or excessive motor block. If a combination of both local anesthetic and opioid is used with the addition of fentanyl it was found that the optimal concentration of fentanyl seems to lie in the range of 1-5 ug/mL. This combination can improve analgesia and allow the use of a 0.1% solution of epidural ropivacaine with a decreased risk of motor block.

R Whiteside *et al* [6]conducted a study on the effect of volume and concentration of epidural ropivacaine with fentanyl in treating postoperative pain following gynecological oncology surgery. They found that low concentration ropivacaine 0.1% with low dose Fentanyl 1 microgram/ml appears satisfactory compared with ropivacaine 0.2% with Fentanyl (2 is microgram/ml). So, in this present study we chosethe concentration of ropivacaine as 0.1%.Levobupivacaine, the pure S enantiomer of bupivacaine possess similar local anesthetic potency to the racemic parent bupivacaine, but with reduced cardiac and central nervous system toxicity. Epidural infusion of levobupivacaine provides excellent anesthesia and analgesia in clinical practice. For example, continuous epidural infusion of levobupivacaine with or without morphine has been shown to provide adequate postoperative analgesia in patients undergoingmajor abdominal surgery [5]. Murdoch *et al*[8] conducted a study to compare the postoperative analgesia efficacy of three different concentrations of levobupivacaine (0.0625%, 0.125% and 0.25%), which was given by epidural continuous infusion. It was concluded that 0.25% levobupivacaine provided better analgesia than 0.125% or 0.0625 % levobupivacaine in patients after orthopedic surgery [8]. However epidural continuous infusion of 0.25% levobupivacaine could result in a higher incidence of untoward effects particularly motor block than 0.125% or 0.0625% levobupivacaine [8]. Decreasing the concentration of levobupivacaine can reduce the incidence of side effects [8].

DA Scott et al[8] conducted a study of comparison of Epidural Ropivacaine infusion alone and in combination with 1, 2, and 4mg/mL. Fentanyl for seventy-two hours of postoperative analgesia after major abdominal surgery. They reported that opioid related side effects were predictably more common with 2 microgram/ml and 4 microgram/ml group patients with pruritus and nausea being most frequently reported [8]. In the present study we chose 1 microgram/ml Fentanyl, and the incidence of Pruritus was low. In the present study we compared between 0.125% ropivacaine and 0.125% levobupivacaine with 1 mcg/ml of Fentanyl as continuous epidural infusion for postoperative analgesia inthe lower abdominal surgeries. Changes in heart rate were similar in all the groups and no statistically significant difference was found. This may be due to the sub anesthetic concentration of local anesthetics and low dose fentanyl used in the present study. In the present study, statistically significant difference was not found in both systolic and diastolic blood pressure during 24-hour infusion of ropivacaine with Fentanyl and levobupivacaine with fentanyl. In the present study, hypotension was noted inonepatientin group A and two patients in group B which was statistically insignificant. Pruritis was not noted among 2 groups. Nausea and vomiting were noted in 1 patient in group B and 2 patients in group A. The difference was statistically not significant in the present study. Urinary retention was noted inonepatientin group A and two patients in group B which was statistically in significant.

In the present study, motor block was seen in one patient in group B and no motor block in groups A. Contrary to the present study. E. Sitsen *et al* [9]found no motor block in 0.125% levobupivacaine with Fentanyl group and Decosmo et al [10] found no motor block in levobupivacaine with Fentanyl group. Paraskevi *et al* [11] observed motor weakness in lower limbs in patients receiving 0.15% levobupivacaine and no weakness in patients receiving 0.15% ropivacaine and 0.15% ropivacaine with Fentanyl supporting present study Lin MC et al [12] observed significant motor block in patients receiving 0.1levobupivacainewithfentanylcomparedwith0.0625%plusFentanyl.

SUMMARY

The study was to compare quality of analgesia, hemodynamic changes, side effects, any associated motorblock consumed among 0.125% Ropivacaine with Fentanyl, and 0.125% Levobupivacaine with Fentanylwhen administered as continuous epidural infusion for 24 hours. Analgesia was superior in Levobupivacaine with Fentanyl infusion when compared to Ropivacaine with Fentanyl. Hemodynamic changes among groups were found not statistically significant throughout the study.

CONCLUSION

From this present study, it can be concluded that, Analgesia was more effective with Levobupivacaine with Fentanyl group when to RopivacainewithFentanylgroup.Pruritiswasnotobservedinanyofthegroups. Very few side effects seen which was not-significant.

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