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A Comparative Study of Nalbuphine and Fentanyl as Adjuvant to Thoracic Epidural Ropivacine for Post Operative Analgesia in Laparotomy Surgeries

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Abstract: ***Background: A prospective, double-blind, randomized studywas carried out to compare the quality of postoperativeanalgesia and side-effect profile between epidurally administered fentanyl and nalbuphine as an adjuvant to 0.2%ropivacaine. Postoperative pain therapy for abdominal surgeries is important far beyond the perioperative period because sensitization to painful stimuli can cause postoperative morbidity. Materials and Methods: A total of 60 patients between the age of 18 and 65 years of American Society of Anesthesiologists (ASA) Class I E and II E who underwent laparotomy surgeries were randomly allocated into three groups. Group 1 received 13 ml of 0.2% ropivacaine with 10mg (1ml) nalbuphine (Total volume 14 ml), Group 2 received 13 ml of 0.2% ropivacaine with 50µg (1ml) fentanyl in epidural catheter (Total volume 14 ml) and Group 3 received 14 ml of 0.2% ropivacaine in thoracic epidural catheter. Quality of analgesia, cardiorespiratory parameters, side-effects, and the need of rescue intravenous analgesia were observed. Results: Mean VAS score was lower in G 1 (0.75±0.91) and it was statistically significant when compared to G 2 (1.35±0.99) and G 3 (1.55±1.05), (p value = 0.035). Thus the requirement of 24 hours rescue analgesic in term of number was lower in G 1(0.50±0.61) when compared to group 2 (0.85±0.67)and group 3 (2.20±0.70), which was statistically significant.(p value = 0.0001). Systolic BP, diastolic BP and mean arterial BP were maintained and comparable in all three groups during first 24 hours of postoperative period (p value >0.05). Pulse rate was rate was lower and it was statistically significantly in first 15 minutes in group 3 as compared to group 1, group 2. (p value < 0.05) However after that pulserate was comparable in all three groups during first 24 hours of postoperative period (p value > 0.05). Side effects were comparable in group 1, group 2 and group 3 and werestatistically insignificant. (p value > 0.05). Conclusion: Thoracic epidurally administrated ropivacaine with nalbuphine is more effective than ropivacaine with fentanyl for postoperative analgesia up to 24 hours of the postoperative period in laparotomies .***

Keywords: fentanyl, emergency laparotomy, nalbuphine,postoperative analgesia, ropivacaine, thoracic epidural

1. Introduction

Pain is an unpleasant feeling often caused by intense or damaging stimuli. It has been defined by the International

Association for the Study of Pain (IASP) as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.[1]
Pain is the most common and anticipated problem during postoperative period. The inadequate postoperative pain control especially in upper abdominal surgeries results in reduced pulmonary compliance, inability to breathe deeply or cough forcefully leading to retention of secretions, atelectasisand pneumonia.[2]

The ‘gate control theory’ proposed that the spinal cord was a potential target site for modulation of pain signals. This changed the concepts about nociceptive transmission and laid the foundation for further research into dorsal horn opioid pharmacology. This led to the discovery of opioid receptors and the subsequent identification of dorsal horn opioid receptors by radioligand techniques. Epidural opioids acting through the spinal cord receptors hasten the onset, improve the quality of the block, have a dose sparing effect on local anaesthetics as well as prolong the duration of analgesia.[3]

Epidural analgesia has been shown to promote early mobilization, reduce the time for tracheal extubation, pulmonary morbidity, rehabilitation time and length of hospital stay.[4,5] Various adjuvants are used in epidural anaesthesia to enhance and prolong duration of postoperative analgesia . Opioids in combination with local anesthetics as an adjuvant are synergistic and can improve the analgesia andreduce the adverse effects of both classes of drug.[6] The epidural administration of parent opioids like morphine has been associated with lower efficacy and

undesirable side- effects such as nausea, vomiting, pruritus, respiratory depression and urinary retention.[7] Thoracic epidural analgesia is frequently used for major thoracic and abdominalprocedures.[8]

Both fentanyl and nalbuphine are opioid analgesics. Fentanyl is an opioid agonist and acts on μ-opioid receptors. [9] Nalbuphine is partial opioid agonist-antagonist with strong k-receptor agonism and weak μ-receptor agonist and antagonist activity. [10]

The aim of our study is to compare fentanyl with nalbuphine as adjuvant to thoracic epidural ropivacaine for postoperative analgesia in laparotomy surgeries.

2. Materials and Method

The Prospective, randomized comparative study was conducted in the Department of Anaesthesia, PBM hospital, S. P. Medical College, Bikaner. All Patients who were scheduled to undergo laparotomies under general anaesthesia were evaluated during the course of study, after obtaining approval from institutional ethical committee and writteninformed consent from the patients. Inclusion criteria were patient who were willing & able to provide written informed consent to participate in the study and patient older than 18 years & less than 65 years. Exclusion criteria were patients of American Society of Anaesthesiologist (ASA) > II class, contraindication to epidural anesthesia, allergy to local anesthetic, cardiac disease, psychiatric disease, respiratory distress, hemodynamic instability, acid-base disorders, and history of drug abuse.

Methodology

Patients were randomly assigned into three groups-

Group 1 - Received 13 ml of 0.2% ropivacaine with 10 mg (1ml) nalbuphine in epidural catheter (Total volume 14 ml).
Group 2 - Received 13 ml of 0.2% ropivacaine with 50ug (1ml) fentanyl in epidural catheter (Total volume 14 ml).
Group 3 - Received 14 ml of 0.2% ropivacaine in epidural catheter. Randomization was done by using computer-generated random number table.

Anaesthesiologists involved in the study recorded the group randomization separately. The anaesthesiologist conducting the case and recording the data remained unaware of the drug administered. All patients following evaluation & relevant laboratory investigations were taken up for anaesthesia. All patient's vital parameters were monitored using multiparameter monitor having pulse oximetry, electrocardiogram and non-invasive blood pressure. Intravenous line was secured with 18-gauge IV cannula. Patients were hydrated preoperatively using Ringer Lactate solution.

Patients were positioned in left lateral or sitting position based on their convenience. Best interlower thoracic space betweenvertebras T10, T11, T12 were identified & infiltrated using 2% lignocaine as local anaesthesia. Epidural needle 16G wasinserted with bevel facing upwards & it was pushed till it pierced interspinous ligament.

Stylet was removed and 10 ml LOR (loss of resistance) syringe was attached to hub of needle which was advanced slowly with pressure exerted on air column through plunger of LOR syringe and epidural space was identified using loss of resistance technique in LOR syringe.

Careful aspiration was done to make sure that duramater is notpunctured. If CSF is aspirated, LOR syringe was removed andreintroduced into different space.

If no CSF is aspirated then LOR syringe was removed and18G multi-orifice epidural catheter was threaded through needle into epidural space and epidural needle was removed carefully over catheter and catheter was positioned in cephalad direction and careful aspiration was done again to check for blood or CSF.

A small test dose of local anaesthetic 2ml of 2% lidocaine with adrenaline was injected via epidural catheter to rule out any signs of intrathecal (motor block) or intravascular placement (tachycardia) of catheter.

All cases of exploratory laparotomy were conducted under general anaesthesia with standard protocol using glycopyrrolate and fentanyl as premedication drugs. Inj. Propofol (2mg/kg) iv for induction and inj. Vecuronium (0.1mg/kg) iv to facilitate endotracheal intubation. Sevoflurane and inj. Vecuronium (0.01 mg/kg) iv were used for maintenance of general anaesthesia. Intraoperatively patient's heart rate, mean arterial pressure (MAP), SpO_2, ECG, end-tidal CO_2 and urine output were monitored. Intraoperative fluid and blood loss was replaced using Ringer Lactate solution and packed red cells. After completion of skin closure and dressing patient was extubated after adequate reversal with inj. neostigmine(0.05mg/kg) and inj. glycopyrrolate (0.01 mg/kg) and was shiftedto postoperative recovery room under continuous monitoring. Once the patient complains of pain (visual analog scale [VAS] of >3), the study was started. Initial dose of drug according to each group was given via epidural catheter. Epidural top up was repeated 6 hourly for 24 h. During the study period, patient's heart rate, MAP, respiratory rate and VAS score were noted at 15 min after the drug administration and 2 hourly for the first 6 h and then 6 hourly for the next 18 h. Side-effects such as nausea, vomiting, respiratory depression, motor blockade (Bromage scale >1), deep sedation (Ramsay sedation score >3), shivering and pruritus were noted. All patients were given rescue analgesic (injection diclofenac 75 mg i.v) whenever they complain of pain or VAS score >3 before the next epidural top up. Hypotension (fall in systolic blood pressure >20% of baseline) was treated with fluid boluses and injection mephentermine 6 mg i.v bolus. Bradycardia (heart rate <50/min) was treated with 0.02 mg/kg of injection atropine. Nausea and vomiting were treated with 0.1 mg/kg of i.v ondansetron. Postoperative maintenance i.v fluids were givenas per body weight.

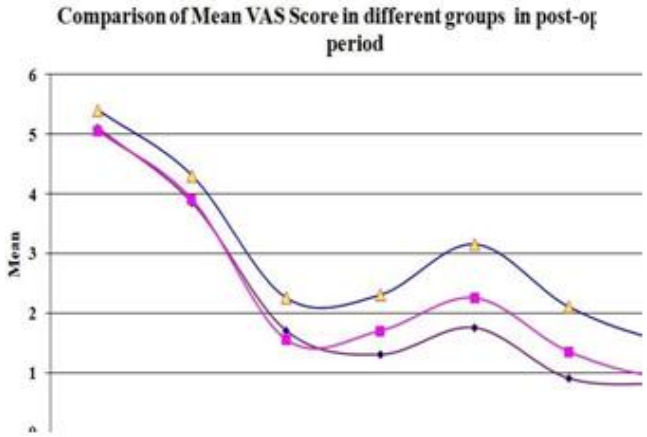
Data collection & analysis

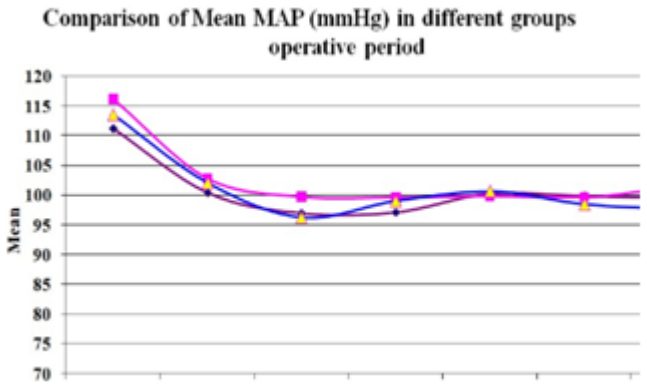
Data was coded and recorded in MS Excel Software. Descriptive statistics was elaborated in the form of means

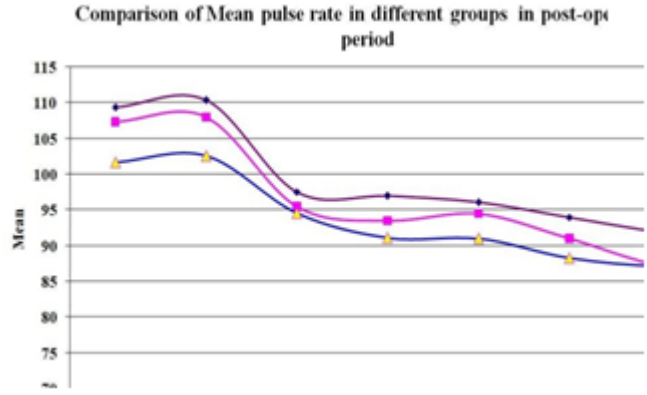
and standard deviations for continuous variables, frequencies and percentages for categorical variables. Group comparisons were made using one way anova test for normally/non- normally distributed continuous data and chi-square test for categorical variables. Primer was used for analysis. P<0.05 was taken as the cut-off for statistical significance.

3. Result

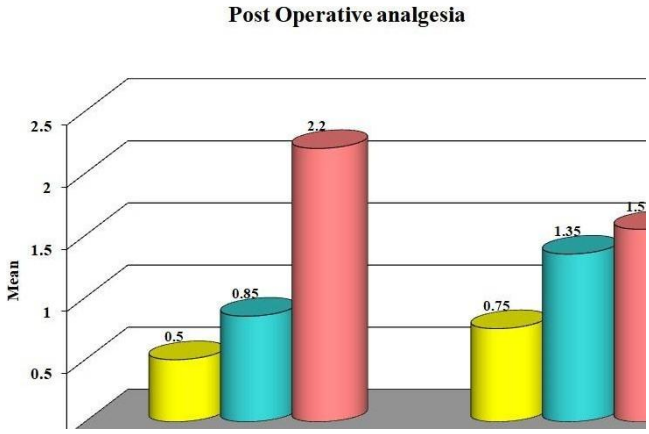
Mean VAS score was lower in group 1 (0.75±0.91) and it was statistically significant when compared to group 2 (1.35±0.99) and group 3 (1.55±1.05), (p value = 0.035).







Systolic BP, diastolic BP and mean arterial BP were maintainedand comparable in all three groups during first 24 hours of postoperative period (p value > 0.05). Pulse rate was rate was lower and it was statistically significantly in first 15 minutes in group 3 as compared to group 1, group 2. (P value < 0.05) However after that pulse rate was comparable in all three groups in 24 hours of postoperative period (p value > 0.05). Side effects were comparable in group 1, group 2 and group 3 and were statistically insignificant. (p value >0.05).



The requirement of 24 hours rescue analgesic in term of number was lower in group 1 (0.50±0.61) when compared to group 2 (0.85±0.67) and group 3 (2.20±0.70), which was statistically significant. (p value = 0.0001).

Table 1: Post operative analgesia

Variables	Group 1 n=20Mean ±SD	Group 2 n=20 Mean ±SD	Group 3 n=20 Mean ±SD	p value
Mean VAS Score	0.75±0.91	1.35±0.99	1.55±1.05	0.035
Number of rescue analgesics in 24 hours	0.50±0.61	0.85±0.67	2.20±0.77	0.0001

4. Discussion

Pain is the most common and anticipated problem during postoperative period. The inadequate postoperative pain control especially in upper abdominal surgeries results in reduced pulmonary compliance, inability to breathe deeply or cough forcefully leading to retention of secretions, atelectasis and pneumonia.[2]

Epidural analgesia has been shown to promote early mobilization, reduce the time for tracheal extubation, pulmonary morbidity, rehabilitation time and length of hospital stay.[5] Opioids as epidural adjuvants to local anesthetics improve the quality of analgesia and provide a nalbuphine as adjuvant to thoracic epidural ropivacaine for post-operative analgesia in laparotomy surgeries.

Thoracic epidural for post laparotomy pain

The surgical incision for laparotomies extends from subxiphoid level to supra-pubic level (T7-L1). Hence, we inserted epidural catheter at best lower thoracic intervertebral space between T10-T12 level. We gave constant drug volume of 14 ml in all three groups for the study. It is based on the previous studies by Saravana Babu et al.[11].

Quality of postoperative analgesia

In our study, postoperative analgesia was assessed with help of VAS score. The test drugs were given when the VAS score was more than 3 because just after extubation,

intraoperative anesthetic drugs made patients to bear some pain due to residual analgesia and hypnosis. Dose-sparing effect. Fentanyl is an opioid agonist and acts on μ-opioid receptors.[9] Nalbuphine is partial opioid agonist- antagonist with strong k-receptor agonist and weak μ-receptor agonist and antagonist activity.[10]We compared fentanyl with

Table 2: Comparison of Mean VAS Score in different groups in post-operative period

VAS Score	Group 1 n=20 Mean ±SD	Group 2 n=20 Mean ±SD	Group 3 n=20 Mean ±SD	p value
0 Min	5.10±0.55	5.05±0.60	5.40±0.60	0.132
15 Min.	3.85±1.04	3.90±0.72	4.30±0.57	0.159
2 Hours	1.70±0.73	1.55±0.69	2.25±0.64	0.005
4 Hours	1.30±0.73	1.70±0.92	2.30±1.13	0.005
6 Hours	1.75±0.91	2.25±0.85	3.15±0.75	0.0001
12 Hours	0.90±1.12	1.35±1.04	2.10±0.97	0.002
18 Hours	0.80±1.06	0.95±0.76	1.55±1.10	0.046
24 Hours	0.75±0.91	1.35±0.99	1.55±1.05	0.035

Although VAS score started decreasing after 15 minof drug administration in all three groups, it was significantly lower in G 1 than G 2 and G 3 at 2 hours (P value = 0.005), 4 hours (P value =0.005), 6 hours (P value =0.0001), 12 hours (P value =0.002), 18 hours (P value 0.046) till 24 hours (P value 0.035) postoperatively. The need of rescue analgesia (injection i.v diclofenac 75 mg.) was also significantly lower (p value 0.0001) in group 1 when compared to group 2 and group 3 during the first 24 hours postoperatively. This shows that ropivacaine with nalbuphine provides better analgesic property than ropivacaine with fentanyl, which leads to decreased need of rescue analgesia in the postoperative periodupto 24 hours.

Table 3: Distribution of cases according to Number of rescue analgesics in 24 hours

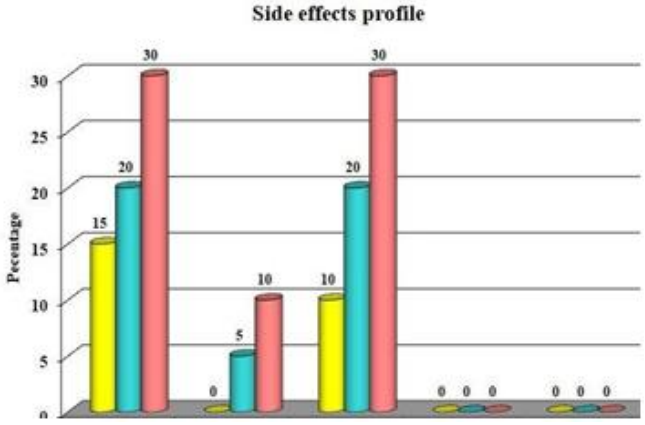
Number of rescue analgesics in 24hours	Group 1 N=20 n (%)	Group 2 N=20n(%)	Group 3 N=20n(%)	p value
0	11 (55)	5 (25)	0 (0)	0.0001
1	8 (40)	14 (70)	4 (20)	
2	1 (5)	0 (0)	8 (40)	
3	0 (0)	1 (5)	8 (40)	
Total	20 (100)	20(100)	20 (100)	

Our study results on quality of analgesia are similar to the previous studies by Chatrath et al.[12] and Babu S[11] where addition of nalbuphine to local anesthetics provided effective postoperative epidural analgesia when compared to other opioids.

Postoperative Hemodynamics

In our study systolic BP, diastolic BP and mean arterial BP were maintained due to lower concentration of ropivacaine 0.2% (which only blocks pain impulses and spares autonomic and motor blockade) and were comparable in all three groups during first 24 hours of postoperative period (p- value > 0.05). These findings were similar to the studyresults of Babu S[11]and Goma et al.[13].

In our study pulse rate was significantly lower in first 15 minutes in group 3 as compared to group 1& group 2. (P Value< 0.05) However after that pulse rate was comparable in all three groups during first 24 hours of postoperative period (p value > 0.05)



Postoperative side-effects:

The side-effects in all three groups were comparable as none of the patients had motorblockade or respiratory depression. In our study most side effects like nausea, vomiting, shivering, hypotension following 1st dose of epidural drug. Most side effects were seen in group 3 (15 cases) followed by Group 2 (10 cases) and least in group 1 (5 cases) and they were comparable and statistically insignificant (p value>0.05).

These finding were similar to the study result of Goma[13]et al. where side effects were less common in nalbuphine group but the difference was insignificant.

5. Conclusion

Thoracic epidurally adminstrated ropivacaine with nalbuphine is more effective than ropivacaine with fentanyl for postoperative analgesia up to 24 hours of the postoperative period in laparotomies.

Conflicts of Interest: Nil

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