

Comparative Study of Epidural Nalbuphine Versus Intravenous Nalbuphine for Postoperative Analgesia in Patients Undergoing Infraumbilical Surgeries

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Conflict of interest: Nil

Abstract:

Introduction: Postoperative pain is an important component of perioperative care and inadequate analgesia can adversely affect recovery, mobilization and overall patient comfort. Opioids remain an important option for postoperative pain management. Nalbuphine, a mixed κ -opioid receptor agonist and μ -opioid receptor antagonist, provides effective analgesia with a relatively low incidence of respiratory depression and other opioid-related adverse effects. It can be administered by different routes, including epidural and intravenous routes. Epidural administration may provide prolonged analgesia through a more localized spinal opioid effect. The present study was undertaken to compare epidural nalbuphine with intravenous nalbuphine for postoperative analgesia following infraumbilical surgeries under spinal anaesthesia.

Methods: This hospital-based prospective, randomized, double-blind study was conducted over two years, from November 2017 to October 2019, after ethical committee approval. Seventy patients of either sex, aged 18–60 years, belonging to ASA physical status I–II and undergoing infraumbilical surgery under spinal anaesthesia with 0.5% hyperbaric bupivacaine were enrolled. Patients were randomized into two groups of 35 each. Group A received epidural nalbuphine 10 mg diluted in 10 mL normal saline, while Group B received intravenous nalbuphine 10 mg diluted in 10 mL normal saline at the end of surgery. Postoperative pain was assessed using the Visual Analogue Scale (VAS), sedation using the Ramsay Sedation Scale, and rescue analgesia was administered with diclofenac 75 mg IM when VAS was ≥ 4 . Haemodynamic parameters, respiratory rate, SpO₂ and adverse effects were monitored for 24 hours.

Results: The demographic characteristics and duration of surgery were comparable between the groups. Haemodynamic parameters, including SBP, DBP, MAP, HR, respiratory rate and SpO₂, showed no statistically significant differences during the 24-hour postoperative period. Mean postoperative VAS scores were significantly lower in the epidural group than in the intravenous group ($p < 0.05$). The mean duration of postoperative analgesia was significantly longer with epidural nalbuphine (475.43 ± 39.58 min) compared with intravenous nalbuphine (379.71 ± 36.33 min; $p < 0.001$). Rescue analgesic requirements were also significantly lower in the epidural group, with 1–2 doses required compared with 2–3 doses in the intravenous group ($p < 0.05$). Mean Ramsay Sedation Scale scores were 1.40 ± 0.48 in Group A and 2.42 ± 0.48 in Group B ($p = 0.001$). Hypotension, bradycardia and nausea/vomiting occurred only in the intravenous group, while no respiratory depression, urinary retention or urticaria was observed in either group.

Conclusion: Epidural administration of nalbuphine 10 mg provided superior postoperative analgesia compared with intravenous administration in patients undergoing infraumbilical surgeries under spinal anaesthesia. Epidural nalbuphine resulted in lower postoperative pain scores, longer duration of analgesia and reduced rescue analgesic requirement, with fewer observed adverse effects. Thus, epidural nalbuphine may be an effective and well-tolerated option for postoperative analgesia in this patient population.

Keywords: Nalbuphine; Epidural analgesia; Intravenous nalbuphine; Postoperative pain; Infraumbilical surgery; Spinal anaesthesia; Rescue analgesia; VAS score.

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Introduction

Nature has placed mankind under the government of two sovereign masters – PAIN AND PLEASURE JEREMY BENTHAM (1748-1832). Postoperative pain relief is important aspect of pain management and has humanitarian role. The surgical stress response peaks during postoperative period and has major effects on all body systems. So, analgesia is main demand of all patients postoperatively. The pain-free and stress-free postoperative period definitely helps in early mobilization and recovery, thereby reducing morbidity and mortality. There has been a radical improvement in the quality of pain relief ever since W.T.G. Morton demonstrated anaesthesia. There is still scope to make analgesia not only more effective but also less hazardous. Postoperative analgesia is essential to provide comfort, restoration of functions like breathing, body movements and communication effectively in all of these procedures.

Infraumbilical surgeries are commonly performed surgeries in general population which includes orthopaedic procedures, gynaecological procedures and also surgical procedures. Central neuraxial blockade in the form of spinal anaesthesia is very popular for infraumbilical surgeries. Spinal anaesthesia consists of temporary blockade of neuronal transmission when local anaesthetics injected near nerve fibers. Additional benefits include modulation of the stress response to surgery, reduction in blood loss, decreased incidence of thromboembolism, decreased pulmonary compromise (particularly in patients with advanced pulmonary disease), avoidance of general anaesthesia (GA) which also avoid airway manipulations, ability to monitor patient's mental status, less incidence of post-operative nausea and vomiting, and early ambulation and recovery.

Combined spinal epidural anaesthesia technique (CSEA) has given a new dimension to regional anaesthesia by using single segment "needle-through-needle" technique in which drugs can be administered through epidural catheter for postoperative analgesia. Intravenous route is also commonly used for giving rapid boluses and titrable doses which provides steady blood levels and the duration is dose dependent as drugs are directly introduced into circulation.

Spinal anaesthesia with 0.5% hyperbaric Bupivacaine is routinely administered for lower abdominal surgeries. Bupivacaine Hydrochloride is a widely used long-acting amide local anaesthetic. It was first synthesized in 1957 by Ekenstam at A.B. Bafars laboratories Sweden. It has high potency, slow onset (5-8 min) and long duration of action (1.5 – 2 hrs). (1-4)

Opioids are the mainstay in the postoperative pain management. Opioid analgesic activates opioid

receptors located on the primary afferent neuron, resulting in the activation of pain modulating systems, their activation may either directly decrease neurotransmission or inhibit the release of excitatory neurotransmitters. Opioid receptors are abundantly expressed in the substantia gelatinosa, where substance P release from the primary sensory neuron is inhibited by opioids.(5) Opioid receptors are classified as mu, delta and kappa (6), the action of mu receptor agonist are invariably analgesic, whereas those of kappa receptor agonist can be either analgesic or antianalgesic.

Nalbuphine is new semisynthetic opioid drug like pentazocine with less side effects and less abuse potential. It is FDA approved drug. Nalbuphine is k receptor agonist and μ receptor antagonist. It is equipotent with morphine on milligram basis and three times more potent than pentazocine, it is one forth as potent as nalorphine as an antagonist. The plasma half-life of Nalbuphine is 5 hours and in clinical studies the duration of analgesic activity has been reported to range from 3 to 6 hours. Nalbuphine in contrast to other centrally acting opioid analgesic has minimal respiratory depressant effect because it is an opioid with mixed partial k receptor agonist & mu receptor antagonist. Incidence of side effects of opioids like pruritis and postoperative nausea vomiting are minimized with use of nalbuphine. Epidural and intravenous nalbuphine are both commonly used. The rationale for combination of opioids and local anaesthetics is that these two types of drugs eliminate pain by acting at two different sites. Local anaesthetics act at the nerve axon and opioid at the receptor site in the spinal cord.

Thus, we conducted the present study to compare the effect of epidural nalbuphine versus intravenous nalbuphine administered for postoperative analgesia in patients undergoing infraumbilical surgeries under spinal anaesthesia.

Material and Methods

The present study was a hospital based prospective, randomized double blind study to evaluate comparative study of epidural nalbuphine versus intravenous nalbuphine for postoperative analgesia in patients undergoing infraumbilical surgeries amongst ASA I and II patients, both sexes, age- 18-60 years undergoing infraumbilical surgeries under spinal anaesthesia with Bupivacaine. All Surgeries performed in Tertiary Care Centre during the study period after approval from ethical committee. The study was conducted over period of two year from November 2017 to October 2019

Sample Size: Sample size is calculated according to previous reference studies, when number of rescue analgesia used in postoperative period is taken, as the main result in the event of at least 35 patients in each group, is calculated by Open Epi-Version 3

online software, a 10% difference could be determined between the group at 80% power and 5 % significance ($\alpha = 0.05$, $\beta = 0.80$) using standard formula. Using double blind randomized study method, the randomization done by flipping the coin (toss). The Anaesthesiologist & patient were blinded to the group and to the drugs.

Inclusion Criteria: patients age - 18 – 60 years, both male and female, height – 150 to 170 (cms), weight – 50 to 80 (kgs), ASA physical status I-II, Normal liver and renal function tests and patient being scheduled for infraumbilical surgeries under spinal anaesthesia with Bupivacaine.

Exclusion Criteria: Patient refusal, Bleeding disorders, Mental disorders, Allergy to local anaesthetics, opioids and hypnotics, Morbid obesity, Abnormal LFT, KFT, Haemodynamic instability, Contraindications for spinal anaesthesia and patients with Neurological & cardiac problems.

Study Tools: All patients were monitored using multipara monitor for Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR), Respiratory Rate (RR) and SPO2 (Arterial saturation of oxygen).

Preoperative Preparation: A thorough pre-anaesthetic evaluation was done including history, laboratory investigations, ECG, CXR, recorded and general examination one day prior to the surgery. Demographic parameters such as age, sex, ASA grade, weight, height, BMI and type of surgery noted. All patients were monitored with multipara monitors for systolic BP, diastolic BP, mean BP, Heart Rate (from ECG), Respiratory rate and oxygen saturation. Randomization done by flipping the coin (toss) into 2 groups:

Group A: Patients received Epidural Nalbuphine 10 mg diluted in 10 ml normal saline at the end of surgery performed under spinal anaesthesia with 3.5 ml of 0.5% Bupivacaine heavy.

Group B: Patients received Intravenous Nalbuphine 10 mg diluted in 10 ml normal saline at the end of surgery performed under spinal anaesthesia with 3.5 ml of 0.5% Bupivacaine heavy.

Anaesthesia Technique:

1) Group A: Technique of giving combined spinal epidural- Under all aseptic precautions, painting and draping of back using Tuohy needle epidural space was obtained by loss of resistance to syringe

employed. The desired volume of drug, Bupivacaine 0.5% heavy, was then instilled through long fine needle (25G). The spinal needle then withdrawn and epidural catheter was inserted in the standard manner. After 30 minutes, test dose with 3 ml of 1.5% of Lignocaine with epinephrine (1:200000) given to detect any inadvertent intravascular or intrathecal placement of epidural catheter. At the end of surgery, patients received Epidural Nalbuphine 10 mg diluted in 10 ml normal saline.

2) Group B: Technique of giving spinal anaesthesia - Under all aseptic precautions, painting and draping of back done. After feeling for the landmarks (iliac crest corresponding to either L4 vertebral body or L4-L5 interspace), 25 G Quinckes Spinal needle inserted through L3-L4 interspace till subarachnoid space obtained by loss of resistance A small pop was felt as the dura is punctured, and the correct position was confirmed when cerebrospinal fluid seen dripping from the spinal needle. The desired volume of drug, Bupivacaine 0.5% heavy, was then instilled. The spinal needle then withdrawn. Duration of surgery noted. At the end of surgery, Patients received Intravenous Nalbuphine 10 mg diluted in 10 ml normal saline.

Post-operative period: At the end of surgery, the studied drug was administered. Group A received Epidural Nalbuphine 10 mg diluted in 10 ml Normal Saline and Group B received Intravenous Nalbuphine 10 mg diluted in 10 ml Normal Saline. Monitoring was done at the time of administration of epidural and intravenous nalbuphine and every 5 min for 10 min, then every 10 min for 30 min, every 30 min upto 2 hrs, for every 2 hrs upto 8 hrs, and every 4 hourly till 24 hrs. (0,5,10,20,30,60,90min,2hr,4hr,6hr,8hr, 12hr,16hr,20hr,24hr)

Patients were followed postoperatively for pain scores, sedation scores and incidence of side effects.

1) Pain scores- Visual Analogue Scale (VAS) using Numerical Rating Scale technique giving score 1-10. The NPRS is a segmented numeric version of the visual analog scale (VAS) in which a respondent selects a whole number (0–10 integers) that best reflects the intensity of his/her pain. The common format is a horizontal bar or line. Similar to the VAS, the NPRS is anchored by terms describing pain severity extremes.

2) Sedation scores- Ramsay sedation scale

Response	Level
Awake and Anxious, agitated or restless	1
Awake, Co-operative, accepting ventilation, oriented, or tranquil	2
Awake, responds only to commands	3
Asleep, brisk response to light, glabellar tap, or loud noise	4
Asleep, sluggish response to light, glabella tap, or loud noise	5
Asleep, no response to light, glabella tap, or loud noise.	6

3) Requirement of rescue analgesic in 24 hours:

Rescue analgesia given with Inj Diclofenac 75 mg IM when VAS $\geq$ 4. Patients were followed up for 24 hours to assess the requirement of rescue analgesic. Total requirement of rescue analgesic, Inj Diclofenac 75mg IM is calculated. The duration of postoperative analgesia was considered the time of first request for postoperative analgesia after surgery.

4) Side Effects: Following side effects were recorded for 24 hrs – hypotension, bradycardia, nausea & vomiting, respiratory depression, urinary retention, pruritis (Urticaria).

Results

We recruited 35 subjects per group as per the sample size. There were no dropouts or failed spinal cases. The patient was assigned to one of the following groups using randomization chart. **Group A:** Patients received Epidural Nalbuphine 10 mg diluted in 10 ml normal saline at the end of surgery performed under spinal anaesthesia with 3.5 ml of 0.5% Bupivacaine heavy. **Group B:** Patients received Intravenous Nalbuphine 10 mg diluted in 10 ml normal saline at the end of surgery performed under spinal anaesthesia with 3.5 ml of 0.5% Bupivacaine heavy.

Table 1: Comparison between the groups according to Mean MAP

Table 1: Comparison between the groups according to Mean MAP					
Mean MAP (mmHg)					
Time Interval	Group A		Group B		P value
	Mean	SD	Mean	SD	
00 Min	83.98	5.092	84.69	4.88	0.13
05 Min	81.57	5.952	82.77	4.634	0.87
10 Min	80.43	4.165	81.94	4.576	0.2
20 Min	84	6.678	83.37	5.23	0.08
30 Min	82.49	4.359	81.97	4.127	0.79
60 Min	85.17	4.011	85.17	4.134	0.1
90 Min	85.77	4.151	86.4	4.216	0.34
02 hrs	87.23	5.501	88.17	4.611	0.89
04 hrs	88.45	4.88	89.23	4.44	0.08
06 hrs	88.31	6.516	90.4	5.209	0.19
08 hrs	87.62	6.759	88.31	5.24	0.3
12 hrs	87.32	4.764	87.29	4.688	0.43
16 hrs	85.98	4.98	84.26	4.395	0.65
20 hrs	88.38	4.799	82.8	4.727	0.09
24 hrs	82.73	4.512	81.69	4.371	0.23

(p value $>$ 0.05 statistically not significant)

Mean arterial pressure (MAP) changes at all time intervals postoperatively from 0 min to 24 hours

were found to be comparable and statistically not significant (p $>$ 0.05) between the two groups. (Test-unpaired t test)

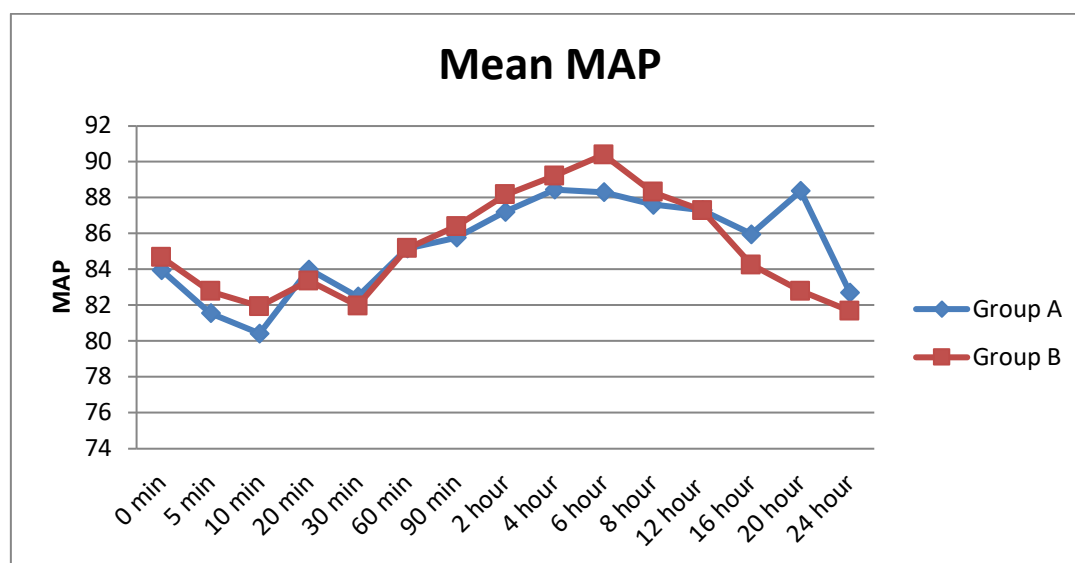
**Chart 1: Comparison between the groups according to Mean MAP**

Table 2: Comparison between the groups according to HR
Heart Rate (beats per min)

Time Interval	Group A		Group B		P value
	Mean	SD	Mean	SD	
00 Min	70.91	18.939	65.94	17.486	0.25
05 Min	91.83	119.49	89.54	119.98	0.93
10 Min	73.26	19.799	67.66	18.74	0.22
20 Min	72.74	20.065	71.26	19.005	0.75
30 Min	74.91	20.939	72.69	20.511	0.65
60 Min	73.43	20.411	74.34	21.096	0.85
90 Min	72.57	19.826	73.66	20.81	0.82
02 hrs	72.23	19.678	71.37	20.997	0.86
04 hrs	72.4	19.243	70.4	19.059	0.66
06 hrs	74.17	19.247	72.57	19.002	0.72
08 hrs	73.77	19.28	70.4	18.258	0.45
12 hrs	76.57	20.353	71.37	19.194	0.27
16 hrs	73.89	20.158	72.63	19.231	0.79
20 hrs	74.86	19.789	73.71	19.3	0.8
24 hrs	81.03	5.496	78.91	5.685	0.11

(p value > 0.05 statistically not significant)

Mean heart rate (HR) changes at all time intervals postoperatively from 0 min to 24 hours were found

to be comparable and statistically not significant (p > 0.05) between the two groups. (Test- unpaired t test)

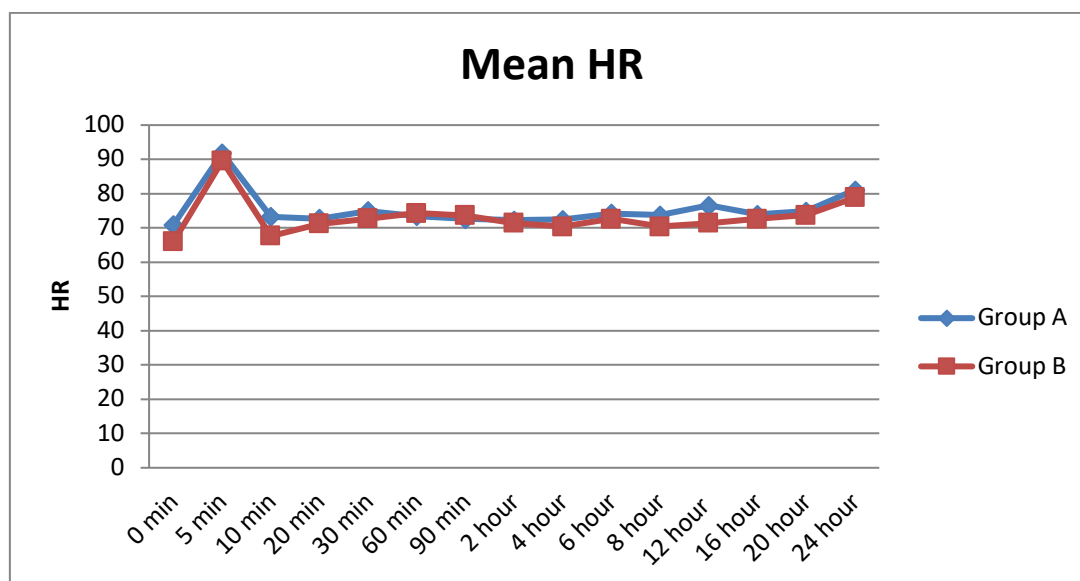


Chart 2: Comparison between the groups according to HR

Table 3: Comparison between the groups according to RR
Respiratory Rate (beats per min)

Time Interval	Group A		Group B		P value
	Mean	SD	Mean	SD	
00 Min	13.94	0.338	13.83	0.568	0.31
05 Min	14	0.686	13.77	0.808	0.2
10 Min	13.94	0.765	13.77	0.808	0.36
20 Min	14.06	0.906	13.94	0.765	0.57
30 Min	13.89	0.963	14.06	1.136	0.49
60 Min	14.46	1.379	13.83	1.485	0.07
90 Min	14.57	1.42	13.89	1.605	0.06
02 hrs	14.23	1.8	13.89	1.53	0.39
04 hrs	13.83	1.706	13.54	1.379	0.44

06 hrs	14	1.372	14.34	1.413	0.3
08 hrs	14.46	1.197	14.4	1.168	0.84
12 hrs	14.4	1.168	14.4	1.168	1
16 hrs	14.06	0.906	14.23	1.06	0.46
20 hrs	13.74	2.318	13.89	0.832	0.73
24 hrs	13.94	0.338	13.71	0.835	0.15

(p value > 0.05 statistically not significant)

Mean Respiratory Rate (RR) changes at all time intervals postoperatively from 0 min to 24 hours

were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. (Test-unpaired t test)

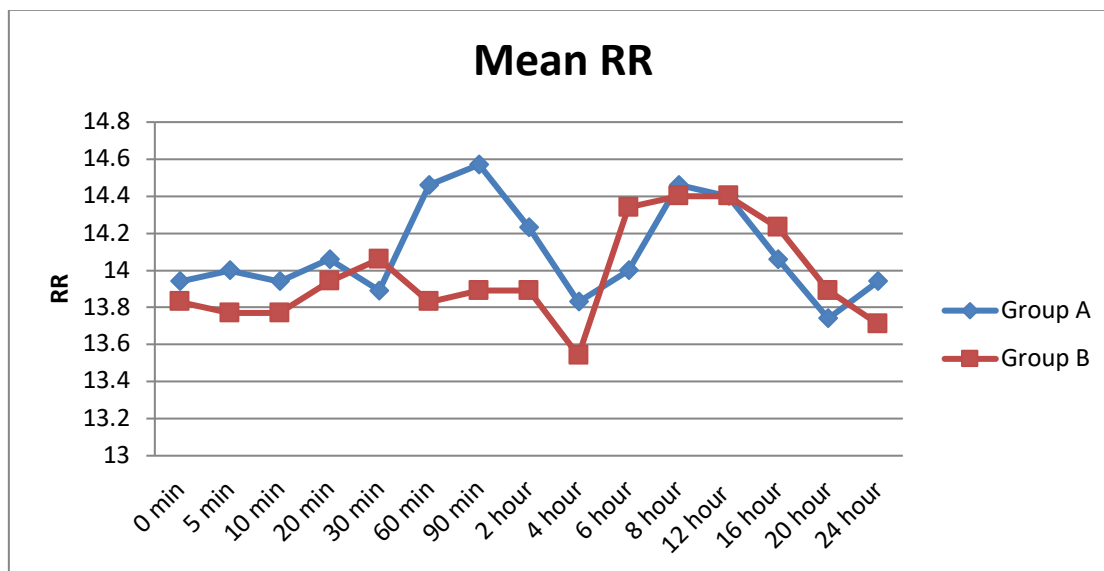


Chart 3: Comparison between the groups according to RR

Table 4: Comparison between the groups according to SPO2

SPO2 (%)					
Time Interval	Group A		Group B		P value
	Mean	SD	Mean	SD	
00 Min	98.8	0.531	98.8	0.406	1
05 Min	98.89	0.676	98.89	0.471	1
10 Min	98.83	0.618	98.97	0.747	0.38
20 Min	99.06	0.416	99.06	0.591	1
30 Min	98.66	0.482	98.74	0.95	0.63
60 Min	98.63	0.49	98.74	0.852	0.49
90 Min	99.09	0.818	98.94	0.968	0.5
02 hrs	98.46	0.701	98.63	0.942	0.39
04 hrs	98.74	0.817	98.8	0.933	0.78
06 hrs	99.09	0.818	98.94	0.968	0.5
08 hrs	98.91	0.702	99	0.874	0.65
12 hrs	99.23	0.808	99.26	0.611	0.86
16 hrs	98.66	0.482	98.74	0.95	0.63
20 hrs	98.83	0.514	98.89	0.404	0.6
24 hrs	98.77	0.547	98.86	0.43	0.46

(p value > 0.05 statistically not significant)

Mean oxygen saturation (SPO2) changes at all time intervals postoperatively from 0 min to 24 hours

were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. (Test-unpaired t test)

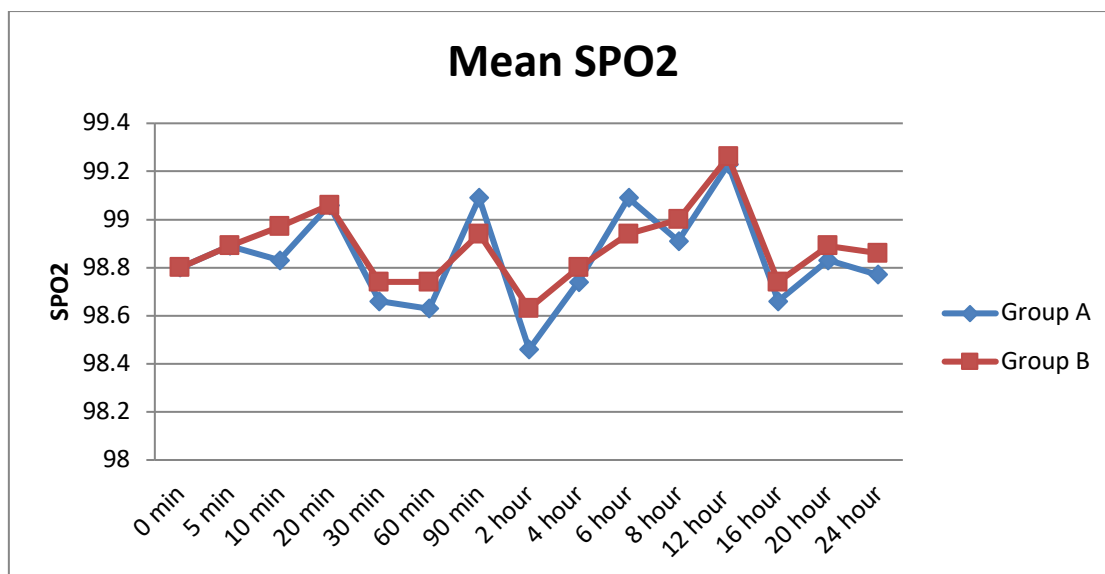


Chart 4: Comparison between the groups according to SPO2

Table 5: Comparison between the groups according to VAS Score

VAS score					
Time Interval	Group A		Group B		P value
	Mean	SD	Mean	SD	
00 Min	0	0	0	0	-
05 Min	0	0	0	0	-
10 Min	0	0	0	0	-
20 Min	0	0	0	0	-
30 Min	0	0	0	0	-
60 Min	0	0	0	0	-
90 Min	0	0	1.06	0.539	0.001
02 hrs	0.34	0.482	1.43	0.502	0.001
04 hrs	1.31	0.471	1.97	0.453	0.001
06 hrs	1.57	0.502	3.49	0.507	0.001
08 hrs	3.49	0.507	1.77	0.547	0.001
12 hrs	1.91	0.818	1.57	0.502	0.001
16 hrs	2.2	0.677	2.89	0.631	0.001
20 hrs	1.77	0.646	2.54	0.505	0.001
24 hrs	1.91	0.818	1.57	0.502	0.001

(p<0.05 statistically significant)

VAS score was used to assess pain postoperatively. When score was found more than 4, Injection Diclofenac Sodium 75mg IM was given as a rescue analgesic. Mean VAS score in 24 hours

postoperative period was less in Group A (Epidural Nalbuphine) as compared to group B (Intravenous Nalbuphine). This difference was statistically significant (p<0.05). (Test- unpaired t test)

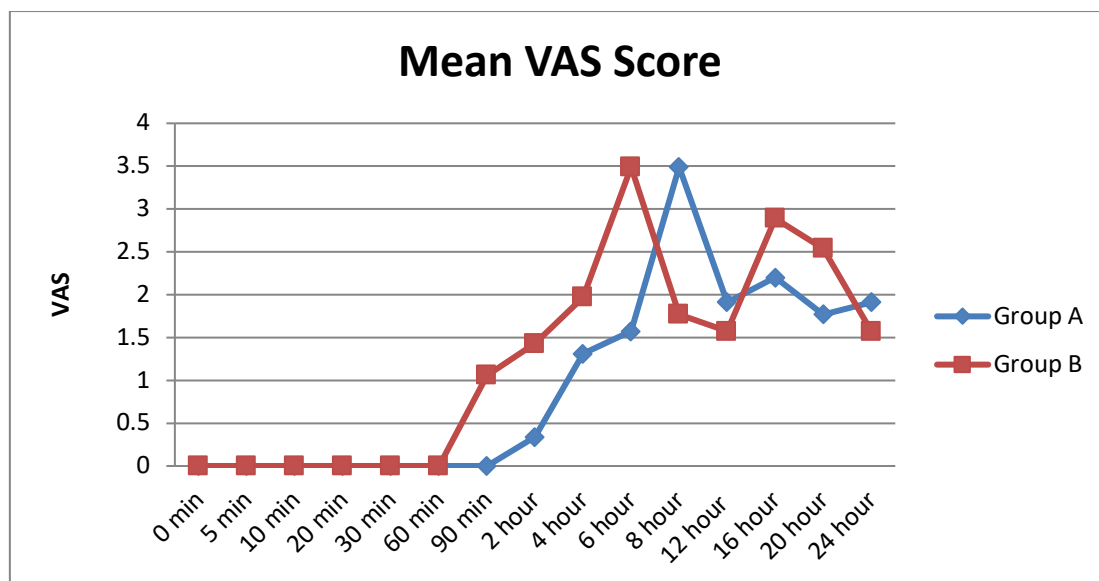


Chart 5: Comparison between the groups according to VAS Score

Table 6: Comparison between the groups according to Ramsay Sedation Scale

	Group A	Group B	P value
	Mean±SD	Mean±SD	
Ramsay Sedation Scale	1.4±0.48	2.42±0.48	0.001 Significant

Mean Ramsay Sedation Scale in Group A was 1.4 ± 0.48 and in Group B was 2.42 ± 0.48 . There was difference in Ramsay Sedation Scale when both the

groups were compared and the difference was statistically significant. ($p < 0.05$ significant)

(Test- unpaired t test)

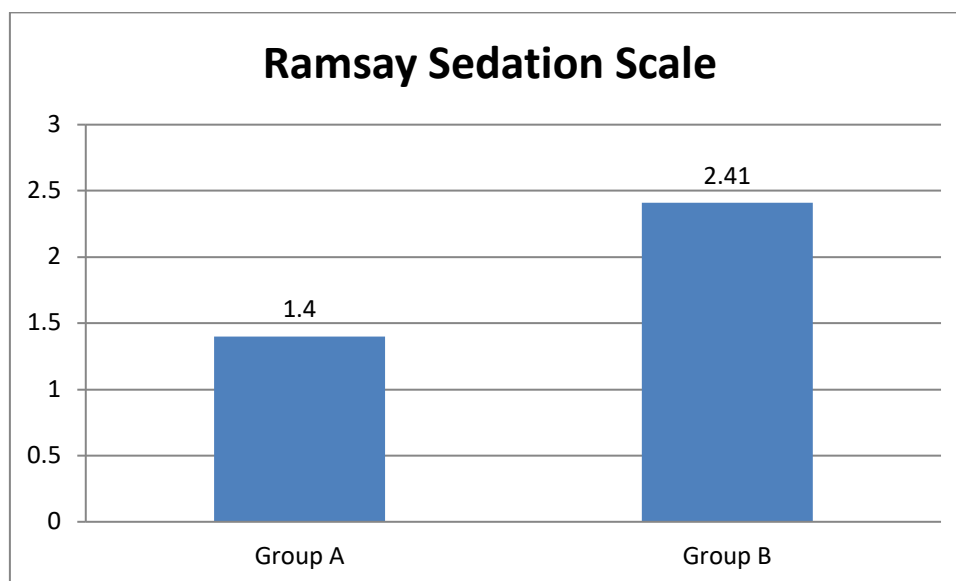


Chart 6: Comparison between the groups according to Ramsay Sedation Scale

Table 7: Comparison between the groups according to Duration of postoperative analgesia (min)

	Group A	Group B	P value
	Mean±SD	Mean±SD	
Duration of postoperative analgesia (min)	475.43±39.582	379.71±36.33	0.0001 highly significant

Duration of postoperative analgesia was compared till 24 hours postoperatively. Mean duration of postoperative analgesia in Group A was 475.43 ± 39.582 min and in Group B was

379.71 ± 36.33 min. Mean duration of postoperative analgesia was statistically highly significant ($p < 0.001$) in Group A (Epidural Nalbuphine) as

compared to Group B (Intravenous Nalbuphine).
Test- chi square test

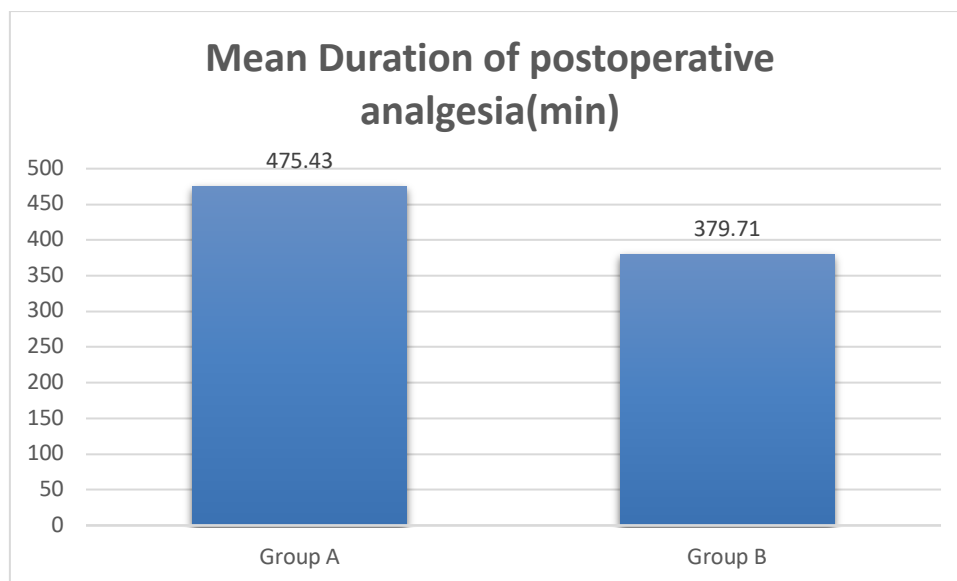


Chart 7: Comparison between the groups according to Duration of postoperative analgesia (min)

Table 8: Comparison between the groups according to total dose of Inj Diclofenac Within 24 hrs.

	Group A	Group B	P value
	Mean±SD	Mean±SD	
Number of doses of Inj Diclofenac Within 24 hrs.	1.57±0.50	2.26±0.443	0.001 significant

1-2 doses of rescue analgesia required in Group A and 2-3 doses required in Group B. More number of Inj Diclofenac (rescue analgesia) were required in Group B (Intravenous) than Group A (Epidural).

Total dose of Inj Diclofenac required within 24 hours postoperatively was compared and found to be statistically significant ($p < 0.05$). **Test- Chi square**

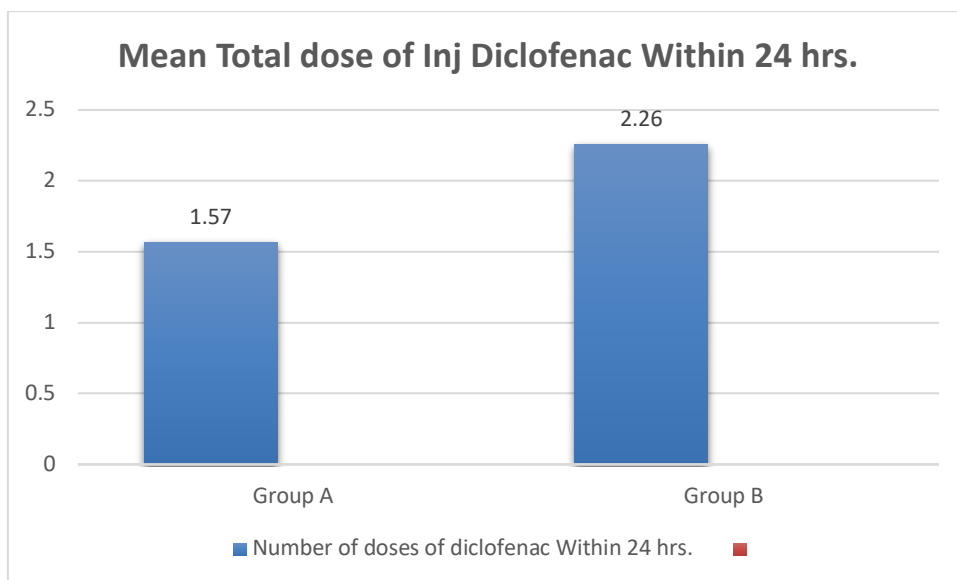


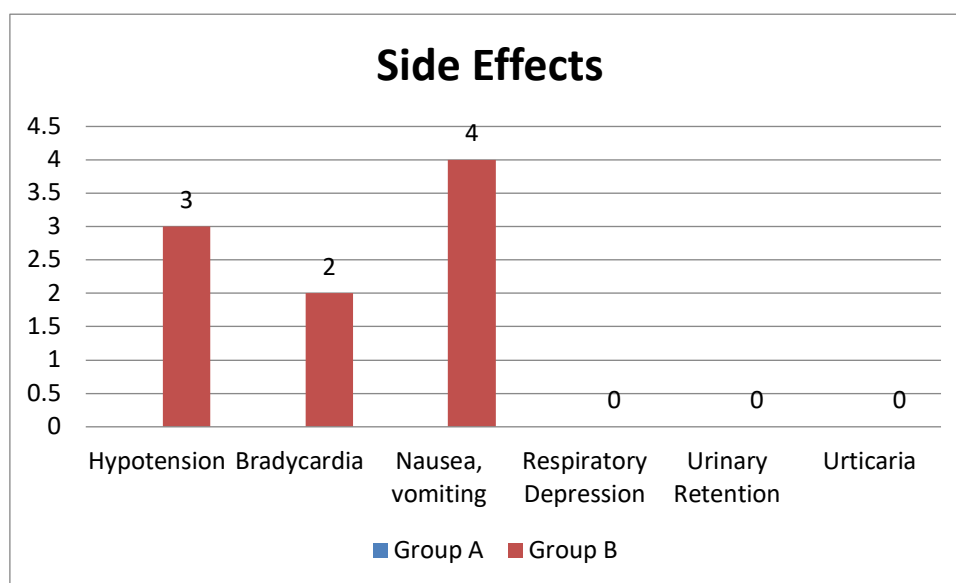
Chart 8: Comparison between the groups according to total dose of Inj Diclofenac Within 24 hrs.

Table 9: Comparison between the groups according to Side effects

Side Effects	Group A	Group B	Total
Hypotension	0	3	3
Bradycardia	0	2	2
Nausea, vomiting	0	4	4
Respiratory Depression	0	0	0
Urinary Retention	0	0	0
Urticaria	0	0	0
Total	0	9	9

Side Effects were noted till 24 hours in postoperative period. Side effect like Hypotension, Bradycardia and nausea vomiting were found to be only with Group B (Intravenous Nalbuphine) and no side

effects were noted with Group A (Epidural Nalbuphine). None of the patient in either group had respiratory depression, urinary retention, urticaria and any other side effects.

**Chart 9: Comparison between the groups according to Side effects**

Treatment was given according to the noted side effect. Total 3 patients of Group B (Intravenous) were having Hypotension which were treated with Inj Mephenteramine 6mg IV along with IV fluids. Bradycardia in 2 patients of Group B was treated with Inj Atropine 0.6 mg IV. Nausea, vomiting in 4 patients of Group B was treated with Inj Ondansetron 4 mg IV.

Discussion

Postoperative pain management is an essential component of the care of the surgical patient. Many drugs are used for postoperative pain management but opioids are mainstay of treatment amongst them. Opioids can be administered through various routes—oral, intravenous, intrathecal and epidural. Many authors have compared fentanyl through intravenous and epidural routes. Privado MS, Sakata RK, Issy AM, Garcia JB[7] (2004) conducted Comparative study of epidural and intravenous fentanyl for postoperative analgesia of orthopaedic surgeries. This was a randomized double-blind study. At postoperative pain complaint, Group 1 patients received epidural fentanyl (100 microgram) and

Group 2 patients received intravenous fentanyl (100 microgram). They concluded that effects of epidural fentanyl were better as compared to intravenous fentanyl.

Nalbuphine is recently introduced new semisynthetic opioid drug like pentazocine with less side effects and less abuse potential. It is FDA approved drug. Nalbuphine is κ receptor agonist and μ receptor antagonist. The plasma half-life of Nalbuphine is 5 hours and in clinical studies the duration of analgesic activity has been reported to range from 3 to 6 hours. There are not many studies available comparing intravenous and epidural nalbuphine. Hong Sik Lee, Jang Ho Song, Chong Kweon Chung, Young Deog Cha[8] (2000) conducted Comparison of the Plasma Concentrations of Nalbuphine after Epidural and Intravenous Administration. They concluded that the plasma concentrations of nalbuphine via epidural route and intravenous route were similar in both groups after 0.25 hour to 6 hours. At 0.25 hour and after 6 hours, the epidural administration group had a higher plasma concentration of nalbuphine than the intravenous administration group. So, the present

study was carried out to study the effect of intravenous and epidural nalbuphine.

1) Demographic Characteristics: The mean age in Group A was 46.26 ± 9.80 years and mean age in Group B was 47.46 ± 10.112 years. There was no significant difference in age distribution among two groups ($p > 0.05$). Out of 70 patients, 45 were male and 25 were female. There were 23 male and 12 females in Group A and 22 males and 13 females in Group B respectively. There was no gender difference in both the groups when compared statistically ($p > 0.05$). There were 20 ASA grade I and 15 ASA grade II patients in Group A. In Group B, 23 ASA I and 12 ASA II patients included. There was no significant statistical difference in ASA physical status distribution between two groups. ($p > 0.05$)

The mean duration of surgery in Group A was 106.28 ± 18.11 min and mean duration in Group B was 100.286 ± 10.28 min. The mean duration in both groups was comparable and statistically not significant ($p > 0.05$)

2) Haemodynamic Profile: In the present study, Mean Systolic blood pressure (SBP) changes at all time intervals postoperatively from 0 min to 24 hours were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. Mean diastolic blood pressure (DBP) changes at all time intervals postoperatively from 0 min to 24 hours were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. Mean arterial pressure (MAP) changes at all time intervals postoperatively from 0 min to 24 hours were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. Mean heart rate (HR) changes at all time intervals postoperatively from 0 min to 24 hours were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. Respiratory Rate (RR) changes at all time intervals postoperatively from 0 min to 24 hours were found to be comparable and statistically not significant ($p > 0.05$) between the two groups. Mean oxygen saturation (SPO₂) changes at all time intervals postoperatively from 0 min to 24 hours were found to be comparable and statistically not significant ($p > 0.05$) between the two groups.

Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S [9] (2015)- conducted study on epidural nalbuphine for postoperative analgesia in orthopaedic surgery. They showed that there was no significant difference in haemodynamic profile like heart rate (HR), Systolic BP(SBP), diastolic BP(DBP), respiratory rate (RR) and SPO₂.

Dr Gayatri Tadwalkar, Dr Sudarshan Chinchole[10] (2019) conducted comparison of 0.5% Bupivacaine with nalbuphine and 0.5% Bupivacaine with normal

saline for post operative epidural analgesia in lower abdominal surgery. In their study, there was no significant difference in heart rate, systolic BP, diastolic BP, respiratory rate and SpO₂ between the two groups.

3) Pain Score (VAS Score): VAS score was used to assess pain postoperatively. When score was found more than 4, Injection Diclofenac sodium 75mg IM was given as a rescue analgesic. In our study, Mean VAS score in 24 hour postoperative period was less in Group A (Epidural Nalbuphine) as compared to group B (Intravenous Nalbuphine). This difference was statistically significant ($p < 0.05$).

R L Solanki, N D Gosai, G M Joshi, B M Patel, H V Modi, R Jain[11] (2015) conducted prospective, randomized study comparing analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy. The mean Visual Analog Score was meaningfully less in Nalbuphine intervention group when compared to Tramadol intervention group by a mean difference of 0.31 points. This significant difference of 27% decrease in mean Visual Analog Score in Nalbuphine intervention group when compared to Tramadol intervention group is significant with ($p < 0.05$).

Jitesh Kumar, P.K. Sinha, B.K. Prasad, Ajay Simbha[12] (April 2017) conducted comparative study of nalbuphine and tramadol for postoperative pain relief in patients of short surgical procedures under TIVA. In their study, pain scores on VAS were significantly less in nalbuphine group after 3rd postoperative hours, means nalbuphine had better pain control than tramadol.

4) Ramsay Sedation Score: In our study, mean Ramsay Sedation Score in Group A was 1.4 ± 0.48 and in Group B was 2.42 ± 0.48 . There was difference in Ramsay Sedation Scale when both the groups were compared and the difference was statistically significant. ($p < 0.05$)

Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S[9] (2015)- conducted study on epidural nalbuphine for postoperative analgesia in orthopaedic surgery. The mean sedation score was different in two groups with the difference being statistically significant and was found to be higher in group B as compared to group A means, in tramadol group as compared to nalbuphine group due to ceiling effect of nalbuphine on sedation. Hoda Shokri and Ihab Ali [13] (2014) conducted Nalbuphine versus Morphine as part of intravenous anaesthesia post cardiac surgery. They observed that nalbuphine patients were less sedated and there was Significant difference between the 2 groups regarding Ramsay sedation score ($p \leq 0.001$).

5) Duration of postoperative analgesia: In our study, Duration of postoperative analgesia was compared till 24 hours postoperatively. Mean duration of postoperative analgesia in Group A was 475.43 ± 39.582 min and for Group B was

379.71 ± 36.33 min. Mean duration of postoperative analgesia was statistically highly significant ($p < 0.001$) in Group A (Epidural Nalbuphine) as compared to Group B (Intravenous Nalbuphine).

Epidural Nalbuphine		Intravenous Nalbuphine	
Mean Duration of Postoperative Analgesia		Mean Duration of Postoperative Analgesia	
Studies	Mean Duration	Studies	Mean Duration
1) Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S[9] (2015)- conducted study on epidural nalbuphine for postoperative analgesia in orthopaedic surgery.	The mean duration of analgesia in Group A (nalbuphine group) was 380 ± 11.49 min and in tramadol group was 380 ± 9.8 min.	1) R L Solanki, N D Gosai, G M Joshi, B M Patel, H V Modi, R Jain[11] (2015) conducted prospective, randomized study comparing analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy	The mean postoperative Rescue Analgesia Initiation Time in nalbuphine group was about 8.60 hours. In the Tramadol group, the mean Postoperative Rescue Analgesia Initiation Time was 8.27 hours. This result found to be statistically insignificant ($p > 0.05$)
2) P Sateesh kumar, B Annapurna Sarma, B V Madhusudhana Rao[14] (2015)-conducted comparison of nalbuphine with 0.5% Bupivacaine and normal saline with 0.5% Bupivacaine for postoperative epidural analgesia.	Postoperative analgesia significantly up to 449.67 ± 39.43 min in 0.5% Bupivacaine + nalbuphine group and 185.93 ± 32.43 min in 0.5% Bupivacaine + saline group.	2) VY Apte, Pradnya Bhalerao, R P Sancheti, K V Kelkar[15] (2017) conducted comparison of analgesic effects of intravenous nalbuphine and pentazocine in patients posted for short duration surgeries.	Duration of analgesia in intravenous nalbuphine group (7.43 ± 1.63 hours) was significantly prolonged as compared with intravenous pentazocine group (4.73 ± 1.62 hours). statistical significance ($p < 0.05$) was noted.
3) Atef Kalem Salama[16] (2015) conducted comparison between caudal levobupivacaine versus levobupivacaine-nalbuphine for postoperative analgesia in children undergoing hernia repair.	LN group (levobupivacaine + nalbuphine) was 384 ± 23.1 min compared to L (levobupivacaine) group 202.20 ± 23.42 min	3) Naeem Liaqat and Sajid Hamid Dar[17] (2017)- conducted comparison of single dose nalbuphine versus tramadol for postoperative pain management in children.	The mean duration of postoperative analgesia was 6.5 ± 0.5 hrs in group A (nalbuphine) and 5.3 ± 1.7 hrs in group B (tramadol) ($P = 0.06$).
4) Present study	Mean duration for Group A (Epidural nalbuphine) was 475.43 ± 39.582 min		Mean duration for Group B (intravenous nalbuphine) was 379.71 ± 36.33 min

The mean duration of post-operative analgesia in our study for epidural nalbuphine is 475.43 ± 39.582 min and for intravenous nalbuphine is 379.71 ± 36.33 min. The results are comparable with the above studies. In the epidural group, nalbuphine is administered with local anaesthetic in other studies whereas we have used epidural nalbuphine alone and got similar results. Thus, epidural nalbuphine alone is as effective as combination of nalbuphine-

bupivacaine. However, the study needs to be carried out in larger population for better evaluation of the results.

6) Requirement of rescue analgesics: In our study, a greater number of Inj Diclofenac IM (rescue analgesia) were required in Group B (Intravenous) than Group A (Epidural). In group A, the minimum number of rescue analgesics required was 1 and

maximum were 2. In group B, the minimum number of rescue analgesics required was 2 and maximum were 3. Total dose of Inj Diclofenac required within 24 hours postoperatively was compared and found to be statistically significant ($p < 0.05$).

Nama Nagarjuna Chakravarthy, A Sagar, G. Venkateshwarlu[18] (2018) conducted a comparative study of epidural 0.5% bupivacaine with nalbuphine and 0.5% bupivacaine with fentanyl in lower abdominal and lower limb surgeries. The total number of rescue analgesics required in the first 24 hours in the post-operative period was statistically significant. ($p < 0.01$). In group A (0.5% bupivacaine with nalbuphine), the minimum number of rescue analgesics required was 1 and maximum were 2 with a mean of 1.67. In group B (0.5% bupivacaine with fentanyl), the minimum number of rescue analgesics required was 2 and maximum were 3 with a mean of 2.57.

7) Incidence of Side effects: In our study, Side Effects were noted till 24 hours in postoperative period. Side effect like Hypotension (3 patients), Bradycardia (2 patients) and nausea vomiting (4 patients) were found to be only with Group B (Intravenous Nalbuphine) and no side effects were noted with Group A (Epidural Nalbuphine). None of the patient in either group had respiratory depression, urinary retention, urticarial and any other side effects.

Dr Gayatri Tadwalkar, Dr Sudarshan Chinchole[10] (2019) conducted comparison of 0.5% Bupivacaine with nalbuphine (Group A) and 0.5% Bupivacaine with normal saline (Group B) for post operative epidural analgesia in lower abdominal surgery. Hypotension was noted in 3 (10%) patients in group A and 3 (10%) patients in group B. Nausea and vomiting was noted in none of the patients in group A and 2(6.66%) patients in group B. Urinary retention was observed in 1(3.33%) patient in group A and 2(6.66%) patients in group B. None of the patients, in either group had pruritus, respiratory depression. R L Solanki, N D Gosai, G M Joshi, B M Patel, H V Modi, R Jain [11] (2015) conducted prospective, randomized study comparing analgesic effects of intravenous nalbuphine with intravenous tramadol on postoperative pain and postoperative analgesic requirement for patients undergoing percutaneous nephrolithotomy. Majority of the Nalbuphine Group patients had drowsiness as the major side effect ($n=5$, 16.67%). In the Tramadol group patients, majority had nausea and vomiting as the major side effect ($n=5$, 16.67%).

Limitations of the study: Since we have studied single dose effect of both Epidural and Intravenous Nalbuphine in postoperative period, effect of multiple doses over a period of 48-72 hours need further evaluation. Also, the studies showing use of

Epidural Nalbuphine alone without addition of local anaesthetic as used in our study are limited.

Conclusion

In our comparative study, when 10 mg nalbuphine given through Epidural route in Group A and 10 mg Nalbuphine through Intravenous route in Group B for postoperative analgesia, following conclusion were drawn the mean VAS Score over 24 hours was significantly less in Epidural Nalbuphine Group than Intravenous Nalbuphine Group and was statistically significant ($p > 0.05$). Duration of postoperative analgesia was statistically highly significant in Epidural route than Intravenous route when both routes compared. Number of rescue analgesics required in 24 hours were reduced in Epidural Nalbuphine Group than Intravenous Nalbuphine Group showing prolonged effect of Nalbuphine through Epidural route. Side effects such as hypotension, bradycardia, nausea vomiting were noted with intravenous route whereas epidural route did not have much side effects. Thus, we conclude from our study that when Nalbuphine 10mg given through epidural route provides excellent postoperative analgesia with greater duration and minimal side effects in postoperative period than intravenous route.

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