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A Comparative Study of Intravenous Nalbuphine HCl and Tramadol HCl for Post-Operative Pain Relief Following Orthopaedic Surgeries

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ABSTRACT

Background: Post-operative pain is usually nociceptive but surgical trauma also induces central and peripheral sensitization and hyperalgesia .Our aim of this study was to compare the post-operative analgesic efficacy & side effects of Nalbuphine and Tramadol in orthopaedic surgeries. **Methods:** Eighty patients of ASA grade I & II were randomly selected with forty patients in each group. All procedures were done under regional or general anaesthesia or combination of both techniques. Patients were assessed every 30 mins for pain scores on VAS in post operative period. Group N: received inj Nalbuphine HCL 0.15 mg/kg IV 8 hourly. Group T: received inj Tramadol HCL 2 mg/kg IV 8 hourly. Time of drug administration , patients VAS at drug injection , time to onset of drug effect (VAS reduced to< 4) ,VAS score , vital signs, sedation score, complications and requirement of rescue analgesia were observed thereafter **Results:** Onset of drugs effect and the duration of analgesia after first dose were comparable. Nalbuphine was proven to be having longer duration than Tramadol after third dose ($p<0.005$). There was statistically significant hemodynamic stability and higher sedation scores in Nalbuphine group ($P<0.005$). Nausea, vomiting and rescue analgesics used were significantly high in tramadol group ($P<0.005$). **Conclusion:** Nalbuphine produces better pain relief and hemodynamic stability in postoperative period in patients undergoing orthopaedic surgeries when compared to tramadol which is associated with more nausea,vomiting and rescue analgesic requirement.

Keywords: Nalbuphine, Orthopaedic surgeries, Postoperative pain, Tramadol

Introduction

Postoperatively pain is often inadequately treated leading to a number of complications, therefore the pain of surgeries must be relieved totally.[1] Effective postoperative pain relief provides mental and economic benefits and reduces the onset of chronic pain syndromes more common with orthopaedic procedures.[2]

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Many comparisons among opioid molecules have been there as a reliable pain relieving entiety in moderate to severe pain arising after massive musculoskeletal tissue handling in orthopaedic procedures.[3-5] Current study is one such attempt, using i.v. bolus doses & comparing relative efficacy & side effect profile for Nalbuphine and Tramadol.

Material and Method

This study was conducted with the permission of ethical committee of hospital after written informed consent of 80 adult patients of either sex and ASA grade I and II. Patients were posted for wide variety of

orthopaedic procedure ranging from minor wound debridement to large joint replacement surgeries. Patients with diabetes, hypertension, bleeding disorders, heart diseases, chronic lung disease, anaemia and having history of any substance abuse were excluded from the study.All patients were examined preoperatively and history noted. All the usually taken investigations were asked for. Eighty patients were randomly allocated in 2 groups, 40 patients in each Group. They were named: Group Nalbuphine and Group Tramadol. All patients were given information about the nature of study & anaesthetic technique. They were instructed to the concept of VAS to record pain. Premedication used was Tab Lorazepam 1 mg orally on previous night and Tab Diazepam 5 mg orally in the morning 3 hours prior to surgery. All the procedures were done under regional or general anaesthesia or any combination of both of these techniques. There was no any binding for the choice of anaesthetic technique. But chronological charting of analgesic administered intra operatively was done with total duration of surgery. Assessment of pain was done immediately after the completion of procedure. After completion of surgery and shifting the patient to post anaesthesia care unit, any other form of analgesia was also omitted. Patients were half hourly assessed for pain scores on VAS. Group Nalbuphine was given inj Nalbuphine HCL 0.15 mg/kg IV diluted till 10 ml volume in NS 8 hrs apart. Group Tramadol: was given inj Tramadol HCL 2 mg/kg IV diluted till 10 ml volume in NS 8 hrs apart. Time of drug administration, patient's VAS at drug injection, time to onset of drug effect. (VAS reduced to less than 4), VAS scores, pulse rate, BP, adverse effect of drugs, sedation score, and rescue analgesic requirement were observed thereafter and noted. Onset of drug action was defined as VAS reaches less than 4 after injection Pain was assessed by using VAS initially every 5 min till 30 min, every 30 min till 2 hrs, hrly till 6 hrs, then at 8 hr, 12 hr and 24 hr duration.

Visual analogue scale: 0: No pain
1-4: Mild pain
5-7: Moderate pain
8-10: Severe pain

As the VAS again reaches 7 or more rescue analgesic was administered in the form of injection Diclofenac sodium 1.5 mg/kg IV diluted till 10 ml in NS. Hemodynamic and respiratory parameters were observed post operatively. Pulse , BP , respiratory rate ,and SpO_2 were noted initially every 5 min till 30 min , then every 30 mins till 2 hrs , then hrly till 6 hrs and then at 8 hr , 12 hr and 24 hr duration.

Sedation score used was
0: alert
1: sometimes drowsy/ easily aroused
2: often drowsy / easily aroused
3: often drowsy /difficult to arouse
4: asleep or stirs to touch

Patients were monitored continuously for any side effect after administration of drug. Duration of drug effect was defined as VAS score reaching more than 7 in observation period after giving the drug. After completion of study in 24 hrs, patients were shifted to their respective wards after switching them to usual post operative analgesic regimen. During data analysis all the observations and results were calculated by applying students T Test and chi square test using SPSS version 17.0. P value less than 0.05 was considered statistically significant.

Results

The present study includes 80 adult patients of either sex : all of them were belonging to ASA grade I and II , undergoing variety of orthopaedic surgeries and were randomly assigned to two groups of 40 patients each , irrespective of surgery and anaesthesia technique. They were given post operative analgesics according to groups assigned to them; on their 1st complain of pain (VAS > 7) after the surgery, repeating the same dose 8 hrly for 24 hrs in post anaesthesia care unit.

Table 1: **Demographic data (age, sex and weight distribution) and Type of surgeries**

	Group Tramadol	**Group Nalbuphine**
Age in yrs(mean ±SD)	32.60±16.25	35.62±18.22
Weight. in kgs(mean±SD)	49.90±11.05	53.80±14.69
Sex (M:F)	20:20	22:18
Surgery type		
WE*+Reconstructions	16(40%)	13(32.5%)
WE* or Bone curettage	9(22.5%)	11(27.5%)
Local debridement/nailing	2(5%)	3(7.5%)
Limb amputations	5(12.5%)	4(10%)
Joint replacements / major joint surgery	8(20%)	9(22.5%)
Total cases	40(100%)	40(100%)

WE*-Wide Excision

This table [1] shows that the demographic data and type of surgeries were almost comparable in both the groups.

Table 2: Onset of drug effect and Duration of action

	Group Tramadol	Group Nalbuphine
Onset of effect (min)(Mean±SD)	9.37±4.55	7.95±3.94
Duration of 1st dose(hr)	5±1.55	5.05±1.23
Duration of 2nd dose(hr)	5.57±0.78	5.90±1.23
Duration of 3rd dose(hr)	6.22±0.66	7.12±0.93

Onset of drugs effect was found comparable after applying student's t-test, among both the groups. Two tailed probability was found 0.1387 with no significant difference. Table 2 explains that after 1st dose the duration of analgesia exerted by both the drugs was comparable. Later on with successive doses it became significant and Nalbuphine was proven to be having longer duration than Tramadol after 3rd dose (p-value<0.005)

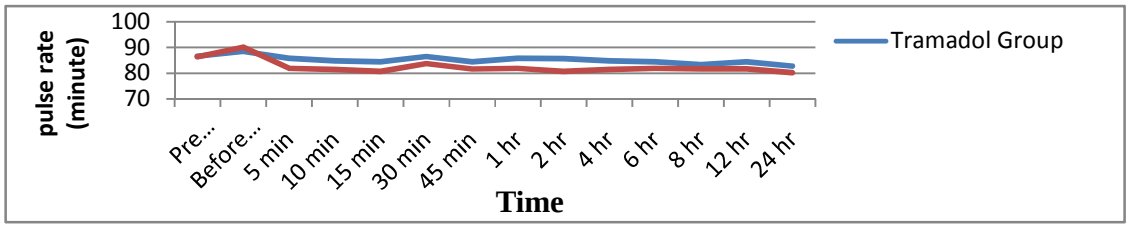

Fig 2: changes in pulse rate in both groups (BPM)

Changes in pulse rates were found statistically significant in patients receiving Nalbuphine with the mean pulse rate within 81.625±1.04 BPM in comparison to patients receiving Tramadol with the mean pulse rate within 84.694±1.25 BPM (p value <0.005) [figure-2]. None of the patient experienced profound bradycardia in both groups.

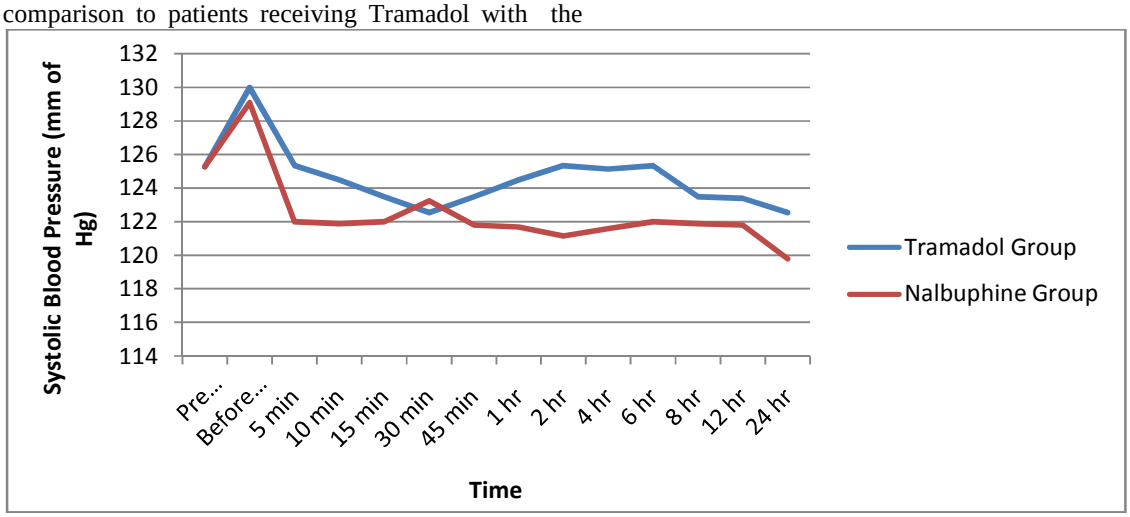

Fig 3: Changes in SBP in both groups (mmHg)

Changes in SBP were found statistically significant in patients receiving Nalbuphine with mean SBP 121.65±0.96 mmHg in comparison to patients receiving Tramadol with mean SBP 124.04±1.19 mmHg (p value <0.005)[figure-3] . None of patients in both groups had Hypotension.

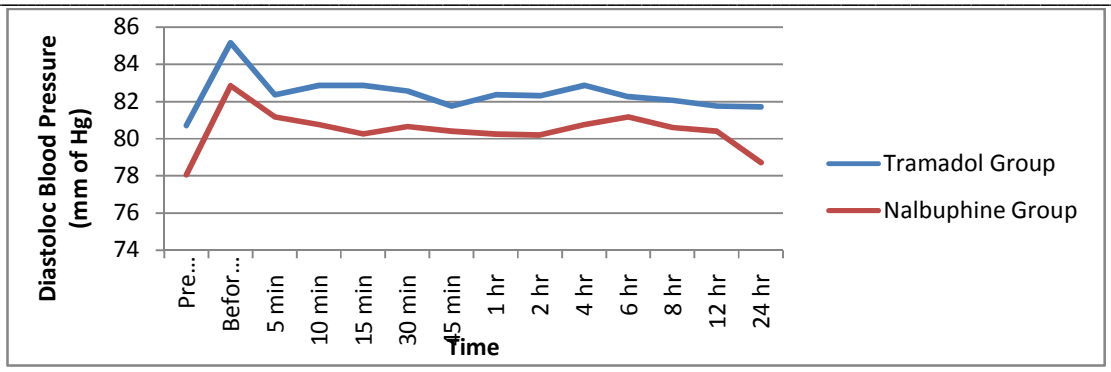

Fig 4: changes in DBP in both groups (mmHg)

Changes in DBP were found comparable in both groups [figure-4].

Table 3: sedation scores and rescue analgesic doses requirements after both the drugs

	Tramadol Group	Nalbuphine Group
Average Sedation Score(Mean ±SD)	0.125±0.335	1.025±0.577
Average number of Rescue doses (Mean±SD)	3.05±0.639	2.25±0.927

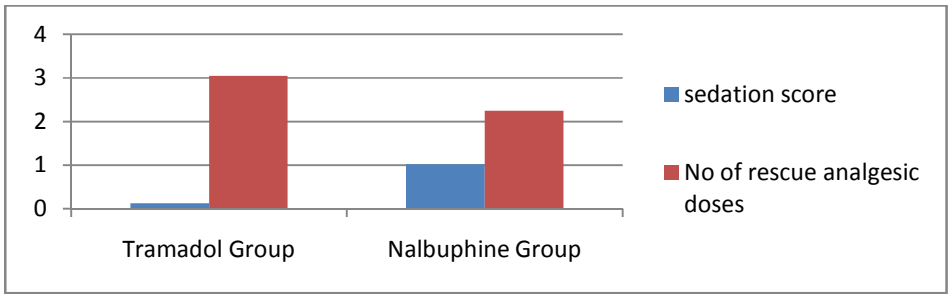

Fig 5: Average sedation score and no of rescue analgesia

Average sedation scores were significantly higher in Nalbuphine Group(P<0.0001), but none of the patient had a score higher than 2(often drowsy/easily aroused).Further rescue analgesics used were significantly high in Tramadol Group with maximum 4 doses used in 9 patients and in Nalbuphine Group maximum 4 doses were used in 3 patients(P<0.0001).[table-3]

Table 4: incidences of adverse drug reactions

	Tramadol Group	Nalbuphine Group
Nausea/vomiting	62.5%	7.5%
Resp.Depression	Nil	5%
Hypotension	Nil	Nil
Hypertension	Nil	Nil
Psycho mimetic reaction	Nil	Nil
others	Nil	Nil

Tramadol has significant propensity towards nausea and vomiting (<0.0001)while some degree of respiratory depression was observed with nalbuphine only, but it was of mild degree and SpO_2 never fell

below 95% in these two patients while respiratory rate was reduced to 12/min from the higher baseline respiratory rates[Table4].

Discussion

Under treatment of post operative pain is due to lack of knowledge regarding effective dose ranges, duration of action of opioids , unfounded fear of respiratory depression and addiction in hospitalized patients experiencing pain. This study was undertaken to compare the analgesic efficacy & safety profile of opioid agonist-antagonist Nalbuphine with one of the most common agent used in clinical practice for post operative pain relief, Tramadol Nalbuphine is a semisynthetic opioid of phenanthrene series which is related structurally to the agonist Oxymorphone & the antagonist Naloxone.[6] Nalbuphine exhibits an analgesic potency & a ceiling effect for respiratory depression.[7]Tramadol, a synthetic opioid of the aminocyclohexanol group is a centrally acting analgesic with weak opioid agonist properties and effects on noradrenergic and serotonergic neurotransmission. These opioid & nonopioid modes of action appear to act synergistically.[8]Tramadol has been shown to provide effective analgesia for post operative pain. It is generally well tolerated the most common adverse events being nausea & vomiting. [5]H. Krenna et al. have compared Nalbuphine bolus and continuous intravascular administration in post operative pain & found that both regimens were equally effective & significantly low amount of drug was used in bolus group & recommended this schedule for cost effectiveness. [10]M.Woolland et al. have proved that low dose Nalbuphine results in low adverse events but offers poor control for high proportion of patients. [11]Our study shows that Nalbuphine has mean onset of analgesia 7.95 min with Nalbuphine & 9.37 min with Tramadol with no significant difference. 9 patients in Tramadol group & 4 patients in Nalbuphine group required maximum 4 doses of rescue analgesia with an average of 3.05 & 2.25 doses required in Tramadol & Nalbuphine group respectively. Hakki Unlugane et al. have reported that Tramadol requires more cumulative analgesic consumption over 24 hours and more doses of fentanyl as a rescue analgesia in comparison with morphine & pethidine.[12]Both the drugs have almost same duration with the 1st dose and with subsequent doses duration of analgesia provided by Nalbuphine increased significantly whereas Tramadol provided equal duration with subsequent doses & needed significantly high use of rescue analgesia.F.N.Minai, F.A.Khan have observed that the time between the last intraoperative and 1st postoperative dose was significantly higher in Nalbuphine group (5.8 hrs) then Morphine group (4 hrs).[13]In our study hemodynamic parameters were also seem to be better preserved in Nalbuphine group in comparison to patients receiving tramadol. RA Green et al. reported slight fall in SBP with Nalbuphine in coronary artery disease patients.[14]Khalid Maudood et al. also reported better hemodynamic stability with Nalbuphine compared to Tramadol in perioperative settings.[15]None of the patients had significant sedation in both the groups except 7 patients of Nalbuphine group who had sedation score 2/5. But all patients were easily arousable. Average sedation score was significantly higher in Nalbuphine group (1.025) than Tramadol group (0.125).Nausea & vomiting were significantly higher in Tramadol group i.e. 62 % compared to 7.5% in Nalbuphine group.In Nalbuphine group 2 patients had respiratory depression with respiratory rate maintained at 12/min & SpO2 was >92% all the time of study, with subsequent doses also the condition remained the same.Pang ww et al. have reported more nausea & vomiting in Tramadol than Morphine (40 % vs. 11%) & (28% vs. 5%). [5]In a study done by FN Minai et al., less number of patients had nausea & vomiting in Nalbuphine group compared to Morphine. [13]

Conclusion

Nalbuphine appears to be better analgesic for the relief of moderate to severe postoperative pain in orthopaedic patients. It provides good sedation, hemodynamic stability and lower incidence of nausea & vomiting compared to Tramadol. Nalbuphine also exhibits a ceiling effect for respiratory depression.

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