Original Article

Indian Journal of Anaesthesia and Analgesia
2017, 4 (3, Part-I), 629-634
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4317.13

Preventive Analgesic Efficacy of Intravenous Tramadol Versus Intravenous Nalbuphine for Elective Inguinal Hernia Repair Surgeries :Randomised Controlled Trial

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Abstract

Background Information: One of the challenges in postoperative care in a developing country is the non-availability of narcotics. Morphine and fentanyl have excellent analgesic action but they are difficult procure as they are under Narcotics act. Besides this, they have undesirable side effects like vomiting and respiratory depression. So alternatives for pain relief in the postoperative care are under constant search. *Aim*: Our aim was to primarily assess and compare the efficacy and safety of nalbuphine and tramadol as a preventive analgesic in patients undergoing elective inguinal hernia repair surgeries. *Methods*: This was a prospective, randomized, double-blind where sixty male patients undergoing elective inguinal hernia repair surgeries under spinal anaesthesia were randomly allocated to receive i.v nalbuphine (N) or tramadol (T) when the sensory level regressed to T10. Time to first rescue analgesic (duration of analgesia), rescue analgesic consumption in 24 hours, sedation, respiratory depression, postoperative nausea and vomiting were studied. *Results*: VAS values for group N at 4^{th} and 6^{th} hour were significantly lower than group T ($p< 0.001$)($p< 0.000$). Mean VAS score remained less than 4 throughout the study in group N .Time to first rescue analgesia in group N (320.87±18.46) was statistically significant than group T (P=0.00) Requirement of total rescue analgesic in term of total number of doses in Group N (50) and Group T (72) (P=0.00). *Conclusion*: Our study concludes that pre-emptive administration of nalbuphine has a better analgesic profile than tramadol.

Keywords: Nalbuphine; Tramadol Inguinal-Hernia Central Sensitization.

Introduction

Preventive analgesia, encompasses any analgesic regimen in the perioperative period given to control sensitization induced by pain [1]. The concept of pre-emptive analgesia has now been refined and evolved to a broader concept that surgical incision alone is not the trigger for central sensitization. Factors, such as preoperative pain, noxious intraoperative inputs such as retraction, as well as postoperative inflammatory processes, related peripheral and central neuromodulators, and ectopic neural activity can all cause an intensification of acute pain and long-term postoperative pain as a result of central sensitization. The term 'pre-emptive analgesia' has been replaced by the term 'preventive analgesia [2,3].

Nalbuphine is a synthetic opioid with μ antagonist and κ agonist properties and it has been used effectively for postoperative analgesia [4,5]. Its safety and tolerability is superior to morphine and pethidine with less postoperative nausea vomiting and better patient compliance.

Tramadol inhibits serotonin & norepinephrine reuptake enhancing inhibitory effects on pain transmission in the spinal cord [6].

Numerous studies have compared nalbuphine and tramadol for postoperative analgesia through

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Received on 07.04.2017, **Accepted on** 24.04.2017

intravenous route, as patient controlled analgesic and as an intrathecal additive. But to our knowledge no study has compared it as a preventive analgesic. This prompted us to study the preventive analgesic efficacy of intravenous tramadol and nalbuphine for elective inguinal hernia repair surgeries.

Methodology

Approval of the institutional ethical committee for a prospective randomized double blind study was obtained. After informed consent, sixty male patients undergoing inguinal hernia repair were randomly allocated by sealed envelope technique to two gropus, Group N (Nalbuphine) and Group T(Tramadol) of 30 patients each.

All patients of ASA physical status I-II , height > than 150cms aged between 20-60 yrs, posted for elective inguinal hernia surgeries under spinal anaesthesia were included in the study. Exclusion criteria were age <18yrs or >60 yrs, height < than 150cms, ASA status III or more, history of bronchial asthma, hypothyroid status, prostatic hypertrophy, hepatic, renal or cardiac failure, chronic opioid dependence, consumption of monoamine oxidase inhibitors and morbid obesity (body mass index >40 kg/m^2.)

All patients were premedicated with T.ranitidine 150mg and T.emeset 4mg orally two hours prior to surgery. All received 18 G i.v cannula and were preloaded with 10ml/kg of Ringer lactate. They were briefed about the ten point visual analogue scale (VAS). On arrival in the operating room, routine physiological monitors were applied, including electrocardiogram (ECG), non-invasive blood pressure(NIBP), heart rate (HR) and pulse oximetry (SpO2) and base line parameters were noted. With the patient in lateral position, spinal anaesthesia was given at L3-L4 using 25 gauge spinal needle and 3ml of 0.5% hyperbaric bupivacaine. The patient was turned to supine position and surgery started once adequate level was achieved. At the end of the surgery, when the sensory level regressed to T10 (tested by pinprick at the level of umbilicus bilaterally [7]. The drug nalbuphine or tramadol according to their group, was prepared and administered by an anaesthesiologist who was not a part of study. Patients in Group N received 0.2mg /kg iv nalbuphine [8] (Inj Nacphin *Neon* Laboratories)and Group T received 1.5mg /kg iv tramadol [9] (Supridol 50mg/mL, Neon Laboratories)diluted in 10 ml of normal saline and shifted to postoperative ward where they were monitored for postoperative pain and complications. The postoperative ward nurse was briefed about the visual analogue score and was blinded to the drug used.

Primary Objective

To assess postoperative analgesia in terms of VAS.

Secondary Objective

Time to first rescue analgesic (duration of analgesia), Rescue analgesic consumption (Inj.Paracetamol iv) in 24 hours, sedation, respiratory depression, postoperative nausea and vomiting.

Postoperative pain was assessed using Visual analogue score. VAS assessment was done every 30 minutes for two hours, then every 2 hrs up to twelve hours and six hourly up to 24 hrs postoperatively. Rescue analgesia in the form of Inj.paracetamol 1000 mg iv was given whenever VAS was >3 [10].

Visual Analog Scale [11]: 0(no pain), 1-3(mild), 4-6(moderate), 7-9(severe) 10 (intolerable pain)

Patients were instructed to request pain medication from the nurse if they wanted analgesia and not wait for the next scheduled VAS score assessment.

The duration of analgesia was defined as the time from the nalbuphine/tramadol injection to the time of first rescue analgesic administration.

Total rescue analgesic consumption in first 24 hrs postoperatively was recorded in terms of number of doses .

Adverse Effect

Sedation was assessed using Ramsay Scale for Scoring Sedation [12]:

1. Anxious and agitated or restless or both, 2- Cooperative, orientated, 3- Drowsy, but responds to commands, 4- Asleep, brisk response to light glabellar tap or loud auditory stimulus, 5- Asleep, sluggish response to light glabellar tap or loud auditory Stimulus 6- Asleep.

Respiratory depression was defined as respiratory rate <10 or SpO_2 <95% on room air and was treated with oxygen supplementation [13].

Occurrence of postoperative nausea and vomiting (PONV) was noted and treated with inj.ondansetron 4 mg.

Methods of Statistical Analysis

Data was calculated using epidata version 2.2.2. For categorical variables chi square test and Fischer exact test were used based on need Normally distributed data was compared using student t test or one way Anova and when parametric assumption was violated corresponding non parametric test like Mann Whitney or Kruskal Wallis were used.

Sample Size in Each Group and Method of Determination of Sample Size

As per Open Epi version 3.0, considering two sided significance level as 95%, power of the study as 80% and ratio of sample size unexposed/exposed as 1, and referring the percent of unexposed with outcome as 11% and that of exposed with outcome as 62% [14] the sample size was estimated as 14 in exposed and 14 in unexposed group, anticipating the drop outs and fitness for the eligible subjects each group with a sample size of 30 was taken for the current study.

Results

Patient demographic variables are shown in Table 1. There were no differences between two groups in patient characteristics age, weight height and duration of surgery.

The VAS values were similar in both groups for initial two hours of postoperative period. VAS values for group N at 4th and 6th hour (1.31±0.54) ,(1.33±0.63)were significantly lower than group T (1.68±0.72),(2.45±1.15) (P< 0.001) (Figure 2). The mean VAS score remained less than 4 in group N throughout the study period showing adequate postoperative analgesia . Time to first rescue analgesia in group N(320.87±18.46 min) and group T(260.0±28.52 min) was statistically significant (P=0.00) (Table 2). Requirement of total rescue analgesic in term of total number of doses was significantly less in Group N(50) as compared to Group T (72) (P=0.00) .

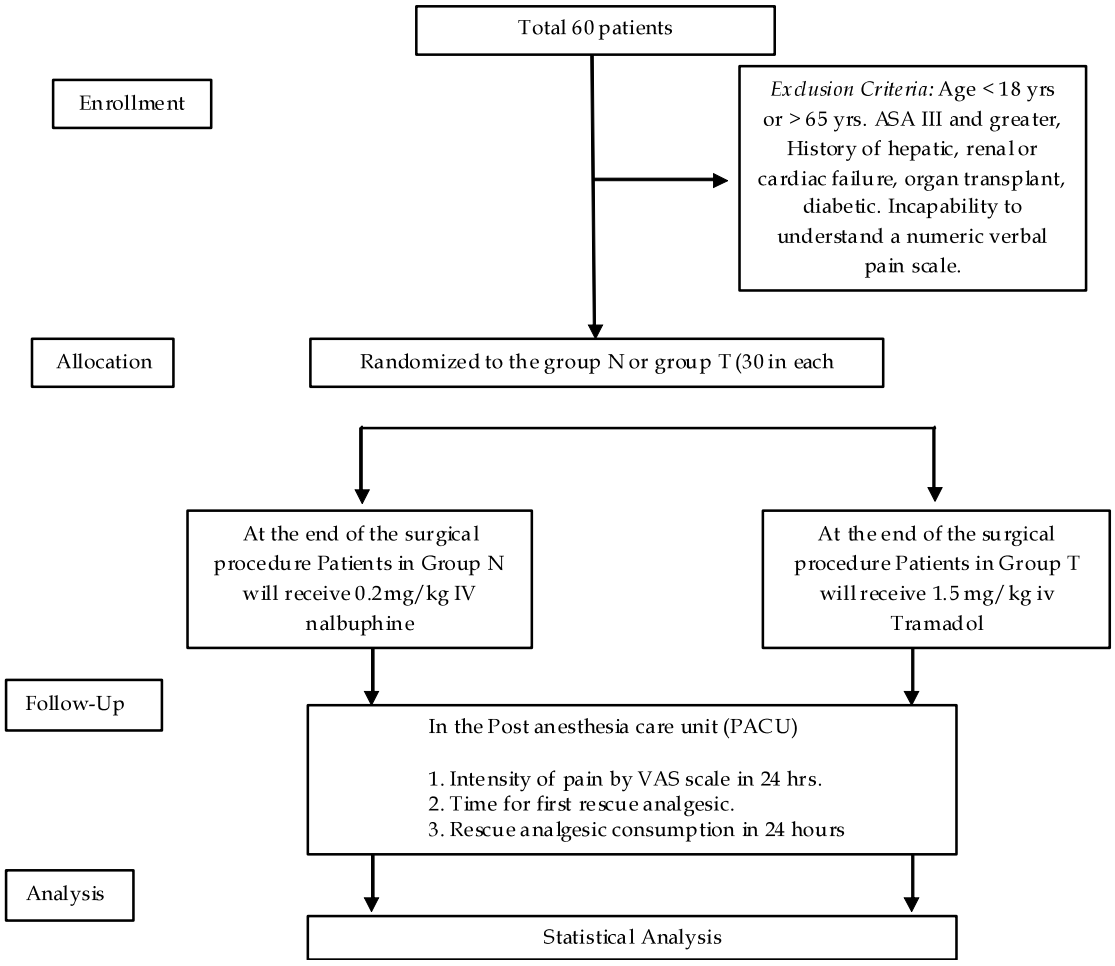

Fig. 1: Consort flow diagram

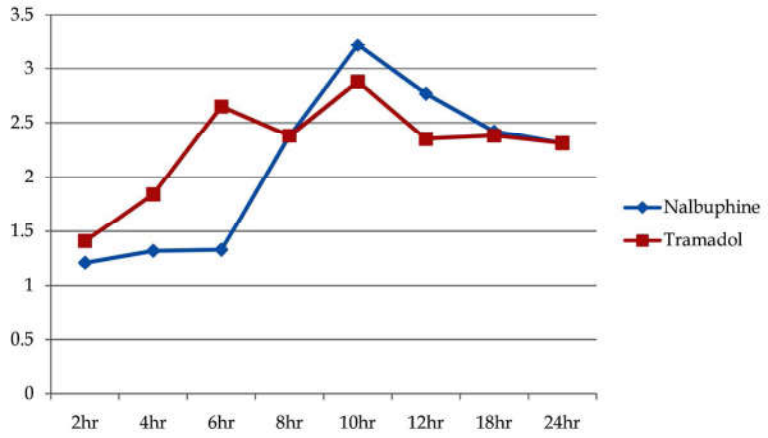

Fig. 2: Comparison of VAS between Group N and Group T.

Mean sedation score was (1.033±0.50) in Group N & Group T (1.133±0.50) which was comparable (P=0.606). It signifies negligible sedation in two groups. Respiratory depression SpO2 <94% on room air occurred in two patient of group N at two hours postoperatively which was successfully treated by supplementation of oxygen .Nausea vomiting was seen in (23%) in group T treated with injection ondensetron 8mg iv.

Discussion

Preventive analgesia is a vital component of multimodal preoperative and postoperative analgesia to alleviate postoperative pain and lessen the consumption of postoperative analgesics.

The concept of preemptive analgesia emphasizes on the pathophysiologic phenomenon of altered sensory processing rather than simply mean "before incision." An insufficient afferent blockade cannot be preemptive, even if it is administered before the incision.

Literature reviews have concluded that it is not the timing but duration and efficacy of an analgesic and antihyperalgesic intervention that are most important for treating pain and hyperalgesia after surgery [15]. Extending a multimodal analgesic treatment into the postoperative period to prevent postoperative pain may be superior compared with preemptive analgesia.

In our study the initial period of preventive analgesia was taken care by spinal anaesthesia and nalbuphine or tramadol was used as a postincisional preventive analgesic.

In a meta analysis done by Cliff K. S et al it was found that preemptive analgesia showed an overall beneficial effect in selected analgesic regimens that was most pronounced after epidural analgesia, local wound infiltrations, and systemic NSAID administration when administered preincionsonally [16].

Nalbuphine hydrochloride is a synthetic opioid analgesic with safety and tolerability superior to morphine and pethidine with a ceiling effect on respiratory depression [17].

The VAS values were similar in both groups for initial two hours of postoperative period and not statistically significant (P> 0.05). This might be because of spinal anaesthesia which had covered the initial postoperative period .The above results were congruent with the study done by Neha Chandrakar that mean VAS scores were not comparable in initial period [18].

VAS values for group N (1.31±0.54) were significantly lower than group T (1.68±0.72) at 4 h and 6 h postoperatively (P< 0.001).This is because Tramadol had slower onset of action than nalbuphine because the opioid agonist action in humans was mediated through the o-demethylated metabolite and not tramadol itself.

Although acceptable postoperative analgesia was achieved in group T, as mean VAS score was less in tramadol group more patients required supplemental analgesic to achieve lower pain scores during the first 24 h postoperatively.This observation of our study was already proven by Vardar et al [19].

The duration of analgesia or the time of first request analgesia was longer in Group N (320.87±18.46 min) compared to group T(260.0±28.52 min) and it was statistically significant (p=0.00) (Table 3). This was at concordant with with the results of Devendra

Verma et al Shehla Shakooh, Pooja Bhosle [20].

Rescue analgesic consumption in terms of total number of doses was significantly less in Group N (50) compared to Group T (72) (p value=0.00) .This observation is similar to the study of Solanki et al [21].

Mean sedation score was 1.033±0.50 in Group N and 1.133±0.50 in Group T which were comparable (p=0.606). It shows that there was negligible sedation in both the groups. Frank et al compared nalbuphine with pethidine for pain relief in labour when administered by patient- controlled analgesia (PCA) and observed that there was no significant difference between the groups in the level of sedation [22]. This result of our study was contradictory to the study of Ananda Bangera et al who had proved that nalbuphine had high sedation when compared to morphine [23].

Respiratory depression, defined as SpO2 <94% on room air, occurred in two patient of group N at 2 hours after administration of the drug and was successfully treated by supplementation of oxygen. The ceiling effect for respiratory depression by nalbuphine provides a unique safety factor among potent opioids [24].

Krishnan et al compared iv nalbuphine and morphine for post tonsillectomy pain in children and concluded nalbuphine to be an effective alternative to morphine, producing similar analgesia and no apparent respiratory depression or other undesirable side effects [25].

Nausea and vomiting were seen in (23%) in group T and were treated with inj ondansetron 8mg iv (in the method section 4 mg was mentioned). (how many patients had nausea in group N)This observation is contrary to the finding of vanderbegh et al who concluded that tramadol, nalbuphine and pethidine have similar emetic effect in the doses and manner used [26].

The limitations of this study are the limited number of patients, exclusion of female patients More studies with large numbers of samples and a balance between the sexes are necessary for further support of the study.

Conclusion

Our study concludes that Nalbuphine Hydrochloride as a preventive analgesic provided adequate analgesia in early postoperative compared to tramadol with minimum requirement of analgesic in postoperative period and less side effects.

References

1. Pogatzki-Zahn EM, Zahn PK. From preemptive to preventive analgesia. Curr Opin Anaesthesiol [Internet]. 2006;19(5):551–5.
2. Katz J. Preventive Analgesia/ : Quo Vadimus/ 2011;113 (5):1242–53.
3. Dahl JB, Kehlet H. Preventive analgesia. Curr Opin Anaesthesiol. 2011;24(3):331–8.
4. Schmidt WK, Tam SW, Shotzberger GS, Smith Jr. DH, Clark R, Vernier VG. Nalbuphine. Drug Alcohol Depend. 1985;14(3–4):339–62.
5. Schmidt WK, Tam SW, Shotzberger GS, Smith DH, Clark R, Vernier VG. Nalbuphine. Drug Alcohol Depend [Internet]. 1985;14(3–4):339–62. Available from: http:// www. sciencedirect.com.
6. Dos Santos TOD, Estrela TG, de Azevedo VLF, de Oliveira OEC, Oliveira G, Figueiredo GDS. Intravenous and subcutaneous tramadol for inguinal herniorrhaphy: comparative study. Rev Bras Anestesiol [Internet]. 2010;60(5):522–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20863932.
7. Moustafa MA, Saleh RS. Nalbuphine added to intrathecal morphine in total knee arthroplasty; effect on postoperative analgesic requirements and morphine related side effects. Alexandria J Med [Internet]. 2012;48(2):175–8.
8.. Condon RE. Groin pain after hernia repair. Ann Surg [Internet]. Lippincott, Williams, and Wilkins; 2001 Jan [cited 2016 Nov 16];233(1):8.
9. Chestnutt WN, Clarke RS, Dundee JW. Comparison of nalbuphine, pethidine and placebo as premedication for minor gynaecological surgery. Br J Anaesth [Internet]. 1987;59(5):576–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3555569.
10. Lee CR, McTavish D, Sorkin EM. Tramadol. A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in acute and chronic pain states. Drugs. 1993;46(2):313–40.
11. Deloach LJ, Stiff JL, Caplan AB. The Visual Analog Scale in the Immediate Postoperative Period: lntrasubject Variability and Correlation with a Numeric Scale. 1998;102–6.
12. Barr J, Zomorodi K, Bertaccini EJ, Shafer SL, Geller E. A double-blind, randomized comparison of i.v. lorazepam versus midazolam for sedation of ICU patients via a pharmacologic model. Anesthesiology [Internet]. 2001;95(2):286–98. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11506097.
13. Mostafa H, Nabil N. Egyptian Society of Anesthesiologists A comparison between post-operative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egypt J Anaesth [Internet]. Elsevier B.V.; 2014;30(4):405–10. Available from: http://dx.doi.org/10.1016/j.egja.2014.03.008.
14. Analgesic P, Of E, Tramadol I, Added N, Bupivacaine TO, Spinal IN, et al. Journal Of Evolution Of Medical And Dental Sciences Page 1 Of 6 Postoperative Analgesic

Efficacy Of Intrathecal Tramadol Versus Journal Of Evolution Of Medical And Dental Sciences. 2015;6–11.

15. Vadivelu N, Mitra S, Schermer E, Kodumudi V, Kaye AD, Urman RD. Preventive analgesia for postoperative pain control: A broader concept. Local Reg Anesth. 2014;7(1):17–22.
16. Ong CK-S, Lirk P, Seymour R a, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. Anesth Analg. 2005;100(3): 757–773.
17. Romagnoli A, Keats AS. Ceiling effect for respiratory depression by nalbuphine. Clin Pharmacol Ther [Internet]. 1980;27(4):478–85.
18. Errick JK, Heel RC. Nalbuphine. A preliminary review of its pharmacological properties and therapeutic efficacy. Drugs. 1983;26(3):191–211.
19. Chandrakar N, Lalwani J, Sahare KK, Bandhu S. Use of Patient Controlled Analgesia Using I.V. Tramadol and I.V. Nalbuphine for Postoperative Pain Management after Major Abdominal Surgery -A Comparative Study. Int J Res Rev Int J Res Rev. 2016;433(5).
20. Vardar MA, Tetiker S. Tramadol for Postoperative Pain Management After. 2008;106(1):309–12.
21. Shakooh S. Intrathecal Nalbuphine/: An Effective Adjuvant For Post Operative. 2014;79–82.
22. Solanki RN, Gosai ND, Joshi GM, Patel BM, Modi H V, Jain R. A Comparative Study of Intravenous Nalbuphine HCl and Tramadol HCl for Post- Operative Pain Relief Following Orthopaedic Surgeries. Asian Pac J Heal Sci ASIAN PACIFIC J Heal Sci [Internet]. 2015 [cited 2016 Nov 24];2(21):155–60. Available from: www.apjhs.com.
23. Frank M, McAteer EJ, Cattermole R, Loughnan B, Stafford LB, Hitchcock AM. Nalbuphine for obstetric analgesia. A comparison of nalbuphine with pethidine for pain relief in labour when administered by patient-controlled analgesia (PCA). Anaesthesia [Internet]. 1987;42(7):697–703.
24 Bangera A, Prasad KP. Nalbuphine as an Alternate Analgesic to Morphine in Total Abdominal Hysterectomy: A Prospective, Randomized, Comparative, Double-Blind Study. Sch J Appl Med Sci Sch J App Med Sci [Internet]. 2015 [cited 2016 Nov 24];3(2E).
25. Sprigge JS, Otton PE. Nalbuphine versus meperidine for post-operative analgesia: a double-blind comparison using the patient controlled analgesic technique. Can Anaesth Soc J [Internet]. 1983;30(5):517–21.
26. Controlled comparison of nalbuphine and morphine for post- tonsillectomy pain. 1985;40.
27. van den Berg a a, Halliday E, Lule EK, Baloch MS. The effects of tramadol on postoperative nausea, vomiting and headache after ENT surgery. A placebo-controlled comparison with equipotent doses of nalbuphine and pethidine. Acta Anaesthesiol Scand [Internet]. 1999;43 (1):28–33.