Intravenous Tramadol versus Nalbuphine in Perioperative Management of Pain and Stress - A Comparative Study

Priti Das[1], Debasish Swain[2], Roopa Parida[3], Lucy Das[4]

[1, 3] Department of Pharmacology, SCB Medical College and Hospital, Cuttack, Odisha, India. [2]Department of Anaesthesiology & Critical Care, SCB Medical College and Hospital, Cuttack, Odisha, India. [4]Department of Obstetrics and Gynaecology, SCB Medical College and Hospital, Cuttack, Odisha, India.

ABSTRACT

BACKGROUND

Managing pain and stress during and after any surgical procedure is a real challenge and a matter of concern for both surgeons and anaesthesiologists. Various analgesics like tramadol and nalbuphine have been used as adjuncts to anaesthetic agents with different efficacy. We wanted to do a comparative assessment of efficacy between intravenous (IV) administration of tramadol and nalbuphine in managing perioperative pain and stress.

METHODS

This was a single blinded randomised control trial, which included 60 female adult patients in the age group of 30 - 50 years who were posted for surgical procedures like elective vaginal hysterectomy under spinal block. Patients with comorbidities like diabetes, obesity, hypertension, impaired pulmonary function, recent history of medication with selective serotonin reuptake inhibitors were excluded from the study. Study participants were divided into two groups - group tramadol (TR) and group nalbuphine (NA) with 30 patients in each group. Group TR was given tramadol 0.5 - 0.7 mg / Kg whereas group NA was given nalbuphine 0.1 - 0.2 mg / Kg after an hour of spinal block. Both drugs were administered intravenously. Midazolam 0.01 - 0.05 mg / Kg was administered intravenously within first hour of surgery for sedation. Pain, stress and sedation score, requirement of rescue analgesics and occurrence of adverse drug reactions (ADRs) over 12 hours post-operatively were compared.

RESULTS

Significant lowering of pain and stress scores and higher sedation score was observed in group NA in comparison to group TR. The requirement of rescue analgesic and occurrence of side effects like nausea and vomiting were less in group NA.

CONCLUSIONS

Intravenous administration of nalbuphine was found to be more effective in perioperative control of pain and stress and can be a better choice than intravenous tramadol.

KEYWORDS

Efficacy, Tramadol, Nalbuphine, Rescue Analgesia

Corresponding Author:
Dr. Roopa Parida,
Room No. 93, PG Ladies Hostel,
SCB Medical College and Hospital,
Cuttack - 753007, Odisha, India.
E-mail: dr.roopa27july@gmail.com

DOI: 10.18410/jebmh/2021/103

How to Cite This Article:
Das P, Swain D, Parida R, et al. Intravenous tramadol versus nalbuphine in perioperative management of pain and stress - a comparative study. J Evid Based Med Healthc 2021;8(10):527-531. DOI: 10.18410/jebmh/2021/103

Submission 30-10-2020,
Peer Review 15-11-2020,
Acceptance 16-01-2021,
Published 08-03-2021.

BACKGROUND

Post-operative pain is the commonest morbidity in patients undergoing any surgical procedure. It causes sympathetic over activity which leads to guarded breathing, increases the chances of thrombi formation and delayed recovery. Pain leads to anxiety which enhances stress response and attenuates sleep. If the pain during and after any surgical procedure is well managed, then the patient can be mobilised early, surgical wound healing will be improved which reduces the health care costs and improves overall patient satisfaction. Prevention and treatment of pain during and after any surgical procedure continues to be a major challenge in post-operative care. It plays an important role in the early mobilisation and well-being of the surgical patients. Gynaecological surgeries like vaginal hysterectomy, total abdominal hysterectomy, ovarian tumour resection and endometrial resection are common surgeries performed in adult female population.[1] It has been reported that pain is more common in open procedures than laparoscopic procedures.[2,3]

Nowadays, a large number of drugs with analgesic action are available as a solution to these problems. Some of them are superior than others in controlling pain and controlling the stress related to surgical procedures and amongst them opioids are at the top of the list. Opioids are one of the most commonly used analgesics to manage pain and stress both during and after surgery; they blunt the neuroendocrine stress response to pain.[4] Morphine, the commonly used opioid, a very effective analgesic, is associated with many side effects including respiratory depression, nausea, vomiting, pruritus, constipation, urinary retention, bradycardia and hypotension. Tramadol is a centrally acting opioid analgesic, but different from morphine, being a weak μ-receptor agonist with additional serotonin and norepinephrine reuptake inhibitor. Though it is equipotent to Pethidine (an opioid analgesic), it does not depress respiration, but can cause an increase in blood pressure and headache via its monoaminergic actions. It is well tolerated, but nausea and dizziness are prominent.[5] Nalbuphine is a μ-receptor antagonist and kappa-receptor agonist (an agonist antagonist opioid). It is well tolerated, having less side-effects (respiratory depression, nausea and vomiting) as compared to other opioids.[6] Various studies have shown different results when the analgesic efficacy of tramadol and nalbuphine are compared in relieving postoperative pain.[7,8] Hence, the present study was carried out to compare the efficacy of these drugs in managing perioperative pain and stress

Objectives

The primary objective of the study was to compare the efficacy of intravenous tramadol and nalbuphine in controlling surgical site pain and perioperative stress in patients undergoing elective vaginal hysterectomy with spinal block. The secondary objectives were to compare the sedative effect, need for rescue medication and occurrence of any adverse effects.

METHODS

This study was carried out by the Department of Pharmacology, Department of Anaesthesiology & Critical Care and Department of Obstetrics & Gynaecology in Sriram Chandra Bhanja Medical College and Hospital, Cuttack, Odisha, India from August 2018 to November 2018. The study was approved by the institution ethics committee. All the participants provided the written informed consent.

Study Design

This was a randomised controlled single blinded study. Randomisation was done centrally by using a computer-generated random sequence. The operating theatre nurse implemented the allocation just before the surgery. Only the study participants were blinded to the treatment assignments. The control arm consisted of tramadol 0.5 – 0.7 mg / Kg administered intravenously [group TR] whereas nalbuphine 0.1 – 0.2 mg / Kg given intravenously [group NA]

Study Participants

Eligible participants were females, 30 - 50 years of age, advised to undergo an elective vaginal hysterectomy under spinal block in the Department of Obstetrics and Gynaecology. The exclusion criteria were existence of comorbid conditions like hypertension, epilepsy, impaired pulmonary function, treatment with selective serotonin reuptake inhibitors (SSRI). A thorough medication history was obtained by the investigators during the pre-operative check-up and screening.

Sample Size Calculation

Assuming the difference in the visual analogue scale (VAS) score between the test drug and the comparator to be 1.2 and a standard deviation (SD) of 1.7 for the test drug, with a type I error rate of 5 % and a power of 80 % the sample size was calculated to be 28 in each group using Masters software (free trial version). Finally, 30 participants were included in each group.

Treatment Arms and Participant Assignment

Eligible participants were randomly assigned, in a 1:1 ratio to receive either of the two treatments: intravenous tramadol 0.5 – 0.7 mg / Kg [group TR] and intravenous nalbuphine 0.1 – 0.2 mg / Kg [group NA]. Both the treatments were made identical in appearance, size and colour. All other standard protocols were followed regardless of the treatment given. The anthropometric measurements like body weight and height were also recorded. Either arm received tablet alprazolam 0.25 mg orally for premedication 15 hours before surgery. On the day of surgery, after shifting the patient to the operation theatre, ECG, pulse oximetry and non-invasive blood pressure was monitored. Spinal Block was given using 0.5 % hyperbaric bupivacaine (3 ml) prior to surgery. Intraoperative monitoring of the

haemodynamic parameters were done until the surgical procedure was over. After 1 hour of spinal anaesthesia, group TR was given IV tramadol 0.5 – 0.7 mg / Kg and group NA was given IV nalbuphine 0.1– 0.2 mg / Kg.

Outcome Assessment

The participants were scheduled for follow up at 3, 6, 9 and 12 hours after surgery. An assessment of the postoperative pain and pain score was obtained using the visual analogue scale[9,10] [VAS: It is a zero (0) to ten (10) point scale; 0 = no pain, 10 = unimaginable, unspeakable pain. The numbers in between 0 to 10 express the feeling of pain like 1 = very mild pain, 2 = discomforting, 3 = tolerable, 4 = distressing, 5 = very distressing, 6 = intense pain, 7 = very intense pain, 8 = utterly horrible pain and 9 = excruciating, unbearable pain.] at 3, 6, 9 and 12 hours after surgery. Stress assessment was done by using Spielberger State-Trait Anxiety Inventory (STAI)[11,12] where feelings like "I feel calm", "I am tensed", "I feel upset", "I am relaxed", "I feel content", and "I am worried" were noted and scoring was done as 1 (not at all), 2 (somewhat), 3 (moderately) and 4 (very much). Sedation Score was assessed using Ramsay Sedation Scale[13] where scoring was done as 1 for anxious or restlessness or both, 2 for cooperative, oriented and tranquil, 3 for responding to commands, 4 for brisk response to stimulus, 5 for sluggish response to stimulus and 6 for no response to stimulus. The need for rescue medications and occurrence of any side-effects were also noted.

Statistical Analysis

An intention to treat analysis was done that included all patients randomised to treatment. There was no loss to follow up. The scores were presented as median with interquartile range. The number of patients requiring any rescue medications and the occurrence of side effects were expressed as proportions. Mann-Whitney U test was carried out to compare the outcome in the study arms. The data was analysed using GraphPad Prism software version 7.0 (free trial version). A P-value ≤ 0.05 was considered as statistically significant.

RESULTS

The median VAS score interquartile range (IQR) was 6 (0.77), 6 (0.77), 4(1), 4 (0.78) at 3, 6, 9 and 12 hours of observation respectively in group TR and 6 (1.75), 5 (1), 3 (0.75), 2 (1) at 3, 6, 9 and 12 hours of observation respectively in group NA. Reduction in mean VAS score during 6, 9 and 12 hours of observation in group NA was statistically significant when compared with group TR during the same hours of observation (Table 1, Figure 1).

The median STAI score (IQR) was 14 (1), 14 (2), 11 (1.75), 11 (1) measured at 3, 6, 9 and 12 hours respectively in group TR and 14 (1), 13 (1), 11 (2.75), 9 (1.66) measured at 3, 6, 9 and 12 hours respectively in group NA. The mean STAI score was less in group NA during 6 and 12 hours of observation when compared with group TR and it was statistically significant (Table 2, Figure 2) The median Ramsay Sedation Score (IQR) was 4 (0), 4 (1), 3 (1), 2 (0) at 3, 6, 9 and 12 hours of observation respectively in group TR and 6 (1), 5 (1), 5 (1), 4 (0) at 3, 6, 9 and 12 hours of observation respectively in group NA. It was observed that the score was lower in group TR during all hours of observation when compared with group NA and it was statistically significant (Table 3, Figure 3).

When VAS score was > 4 at rest during 12 hours of assessment, it was an indication for need of rescue medication. Rescue medication was given in the form of injection diclofenac sodium. 18 (60 %) number of patients in group TR needed injection diclofenac sodium as rescue analgesic, whereas only 7 (23 %) patients in group NA needed injection diclofenac sodium for pain management. Mild adverse drug reactions like nausea, vomiting and dizziness were reported. Among the adverse drug reactions, nausea and vomiting were observed in 8 (27 %) patients in group TR and 1 (3 %) patient in group NA; Dizziness was found in 5 (17 %) patients in group TR and 1 (3 %) patient in group NA. Nausea and vomiting were treated by administration of ondansetron 4 mg intravenously. No treatment was given for treatment of dizziness.

Study Group	Median VAS Score (IQR) at Different Time Intervals			
	3 Hrs	6 Hrs	9 Hrs	12 Hrs
Group TR	6 (0.77)	6 (0.77)	4 (1)	4 (0.78)
Group NA	6 (1.75)	5 (1)	3 (0.75)	2 (1)
P-Value	0.26272	< 0.00001*	< 0,00001*	< 0.00001*

Table 1. Pain (VAS) Score in the Study Groups

Study Group	Median STAI Score (IQR) at Different Time Intervals			
	3 Hrs	6 Hrs	9 Hrs	12 Hrs
Group TR	14 (1)	14 (2)	11 (1.75)	11 (1)
Group NA	14 (1)	13 (1)	11.3 (2.75)	9 (1.66)
P Value	0.61708	0.00046*	0.5485	0.00188*

Table 2. Peri-Operative Stress (STAI Score) in the Study Groups

Study Group	Median Ramsay Sedation Scale(IQR) at Different Time Intervals			
	3 Hrs	6 Hrs	9 Hrs	12 Hrs
Group TR	4 (0)	4 (1)	3 (1)	2 (0)
Group NA	6 (1)	5 (1)	5 (1)	4 (0)
P-Value	< 0.00001*	< 0.00001*	< 0.00001*	< 0.00001*

Table 3. Sedation (Ramsay Sedation Scale) in the Study Groups

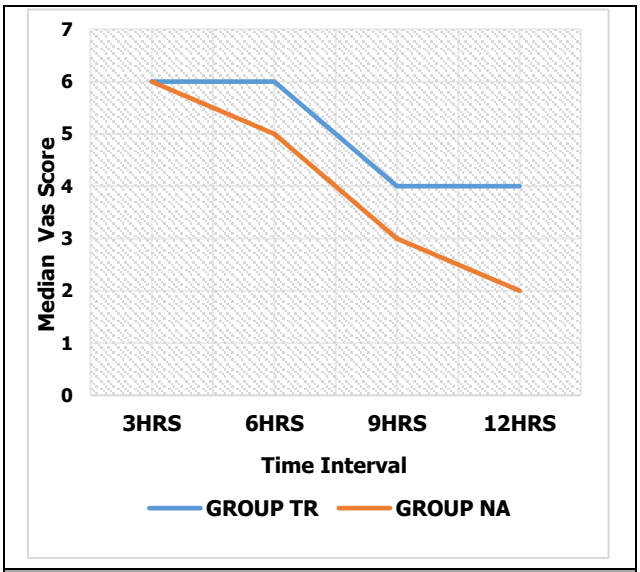

Figure 1. Comparison in VAS Score at Different Time Intervals

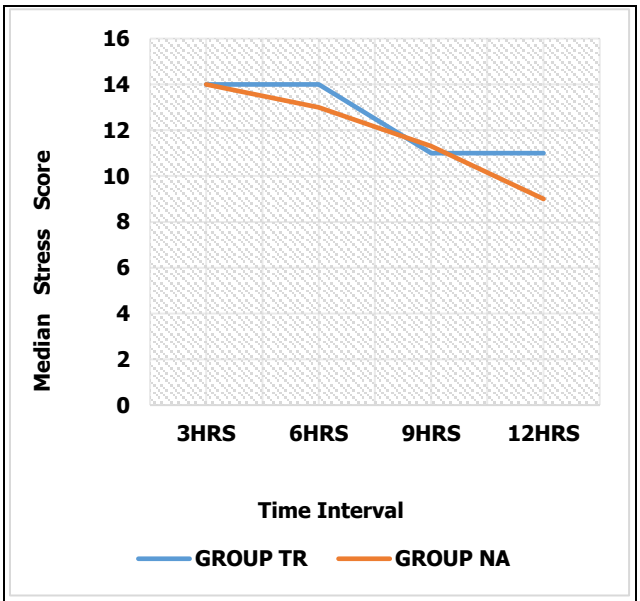

Figure 2. Comparison in Stress Score at Different Time Intervals

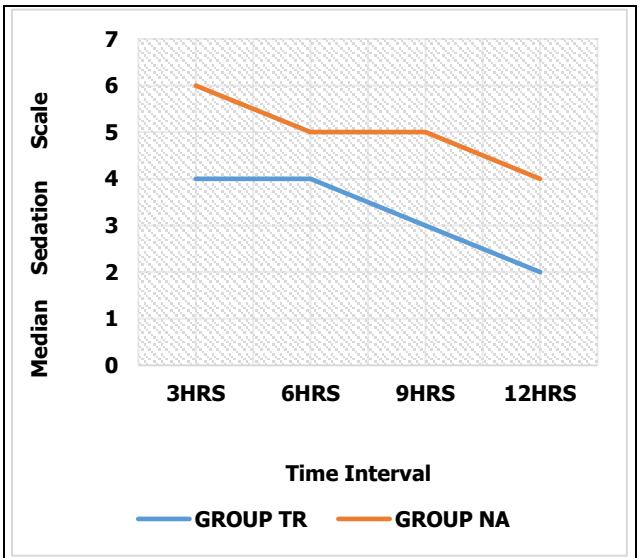

Figure 3. Comparison of Ramsay Sedation Scale at Different Time Intervals

DISCUSSION

Pain is an unpleasant condition and one of the bothersome reasons for people to remain stressed. It is a focus of fear among individuals who undergo any type of surgery whether minor or major surgical procedures. Many times, it affects the person with psychological stress and associated physiological changes in the body cannot be ruled out. It may result from disease, injury or any surgical procedure. Among various gynaecological surgeries, elective vaginal hysterectomy is one of the common surgeries carried out in females above 40 years of age. Successful management of pain during and after any surgery and the stress associated with the surgical procedures is a big challenge for both surgeons and anaesthesiologists. This study has been carried out to compare the efficacy of two drugs tramadol and nalbuphine both administered intravenously, in managing the pain and stress during and after the surgical procedure of elective vaginal hysterectomy. Pain and stress are subjective feelings sometimes difficult to explain. Various scales have been used for assessing pain and stress. We have used scales like visual analogue scale.[9,10] Spielberger State-Trait Anxiety Inventory (STAI)[11,12] and Ramsay Sedation Scale[13] for assessment of pain, stress and sedation. In our study, the VAS score, that was used for pain assessment was found to be significantly lower in the group receiving nalbuphine during 6, 9 and 12 hours of observation, when compared to tramadol group. Our observation resembles that of Solanki et al.; they have observed and reported better postoperative pain relief with nalbuphine when compared with tramadol in patients undergoing orthopaedic operative procedures, but in their study, medications were administered eight hourly unlike single dose in our study.[7] In contrast to our study, another study conducted by Kumar et al. have reported no significant difference in VAS score for pain between two groups of nalbuphine and tramadol; they have compared the VAS score for pain between nalbuphine (0.25 mg / Kg) and tramadol (2 mg / Kg), until 3hours of surgery.[8]

We found the stress score was significantly lower in nalbuphine group at 6 and 12 hours of observation than tramadol in our study. We could not find literatures either in support or against our observation.

The sedation score was found to be higher at all the time of observation in the group N than in group T . This finding is similar to that of Kumar et al.; they have reported that they observed significantly higher mean sedation scores at second and fourth postoperative hour in nalbuphine group when compared with tramadol group.[8] Also similar findings were reported by Solanki et al.; they observed higher sedation score with intravenous nalbuphine when compared with tramadol, but unlike our study, they have given the drugs eight hourly.[7]

In our study we observed a greater number of patients in the tramadol group required rescue analgesia when compared to nalbuphine group. This finding of ours is in contrast to the observation of a comparative study among patients undergoing gynaecological laparotomies where tramadol group needed lesser rescue boluses and less amount of medicine during initial 12 hr. after surgery as compared to nalbuphine group.[14] However, in another study among patients undergoing orthopaedic procedures, use of rescue medicine was higher in the tramadol group as compared to nalbuphine group when given eight hourly.[7]

Nausea, vomiting are among the most common side effects of opioids.[15,16] In our study, we noticed, the side effects like nausea, vomiting and dizziness were more in the group receiving tramadol than the group that received nalbuphine. Our findings are comparable to the study done by Khan et al., although in their study, instead of tramadol, they have compared morphine and nalbuphine.[17] The major limitations of the study included, that unlike some other studies where pain score has been evaluated 72 hr. after surgery,[1] in our study, it was evaluated up to 12 hr. after surgery. Further the single dose treatment of the study medication may not provide significant insights into safety and efficacy of the test medications.

CONCLUSIONS

Intravenous nalbuphine caused greater lowering of pain and stress than intravenous tramadol, needing less rescue medications as well. Intravenous nalbuphine was found to be more effective and may be an alternative or a better choice than intravenous tramadol for managing pain and stress during and after a surgical procedure. However, further elaborate studies are required where the pain and stress assessment can be done for a period longer than we have done in this study.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Akshat S, Ramchandran R, Rewari V, et al. Morphine versus nalbupnine for open gynaecological surgery: a randomized controlled double blinded trial. Pain Research and Treatment 2014;2014:727952. https://doi.org/10.1155/2014/727952
[2] Holzer A, Jirecek ST, Illievich UM, et al. Laproscopic versus open myomectomy: a double-blind study to evaluate postoperative pain. Anesthesia and Analgesia 2006;102(5):1480-1484.
[3] Mais V, Ajossa S, Guerriero S, et al. Laproscopic versus abdominal myomectomy: a prospective, randomized trial to evaluate benefits in early outcome. American Journal of Obstetrics and Gynaecology 1996;174(2):654-658.
[4] Mcdonald RK, Evans FT, Weise VK, et al. Effect of morphine and nalorphine on plasma hydrocortisone levels in man. Journal of Pharmacology and Experimental Therapeutics 1959;125(3):241-247.
[5] Van den Berg A, Halliday E, KisemboLule E, et al. The effects of tramadol on postoperative nausea, vomiting and headache after surgery, Acta Anaesthesiologica Scandinavia 1999;43(1):28-33.
[6] Fragen RJ, Caldwell N. Acute intravenous premedication with nalbuphine. Anesthesia and Analgesia 1977;56(6):808-812.
[7] Solanki RN, Gosai ND, Joshi GM, et al. A comparative study of intravenous nalbuphine HCl and tramadol HCl for postoperative pain relief following orthopaedic surgeries. Asian Pac J Health Sci 2015;2(1):155-160.
[8] Kumar J, Sinha PK, Prasad BK, et al. Comparative study of nalbuphine and tramadol for postoperative pain relief in patients of short surgical procedures under TIVA. Int J Contemp Med Res 2017;4(4):977-979.
[9] Huskisson EC. Measurement of pain. Lancet 1974;2(7889):1127-1131.
[10] Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain 1986;27(1):117-126.
[11] Tluczek A, Henriques JB, Brown RL. Support for the reliability and validity of a six-item state anxiety scale derived from the State-Trait Anxiety Inventory. J Nurs Meas 2009;17(1):19-28.
[12] Chlan L, Savik K, Weinert C. Development of a shortened state anxiety scale from the Spielberger State-Trait Anxiety Inventory (STAI) for patients receiving mechanical ventilatory support. J Nurs Meas 2003;11(3):283-293.
[13] Sessler CN, Grap MJ, Ramsay MAE. Evaluating and monitoring analgesia and sedation in the intensive care unit. Critical Care 2008;12(Suppl 3):S2.
[14] Hussain T, Ahmad S, Taqi A, et al. A comparison of equipotent doses of tramadol and nalbuphine in gynecological laparotomies postoperatively. Pak Armed Forces Med J 2016;66(5):738-741.
[15] Inturrisi CE. Clinical pharmacology of opioids for pain. Clin J Pain 2002;18(Suppl 4):S3-S13.
[16] Beakley BD, Kaye AM, Kaye AD. Tramadol, pharmacology, side effects and serotonin syndrome: a review. Pain Physician 2015;18(4):395-400.
[17] Minai FN, Khan FA. Comparison of morphine and nalbuphine for intraoperative and postoperative analgesia. Journal of Pakistan Medical Association 2003;53(9):391-396.