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ORIGINAL ARTICLE

Comparison of Analgesic Effects of Intravenous Nalbuphine and Pentazocine in Patients posted for Short-duration Surgeries: A Prospective Randomized Double-blinded Study

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ABSTRACT

Background and objectives: Postoperative pain influences the long-term outcome of the patient in a big way. We performed a randomized prospective double-blind study to evaluate the effects of intravenous (IV) nalbuphine and compared it with IV pentazocine. The primary objective was to compare the duration of analgesia of IV nalbuphine and IV pentazocine and the secondary objective was to study the side-effect profile.

Materials and methods: Sixty American Society of Anesthesiologists (ASA) physical status I and II patients undergoing short-duration surgery under general anesthesia were randomly allocated in two groups of 30 each to receive either nalbuphine (group I) or pentazocine (group II) IV. The duration of postoperative analgesia, need for rescue analgesia, and side effects if any were monitored. Two-sample t-tests were used to investigate and model the impact of various parameters like duration of analgesia and side-effect profile.

Results: Duration of analgesia in group I (7.43 ± 1.63 hours) was significantly prolonged as compared with group II (4.73 ± 1.62 hours). Statistical significance ($p < 0.05$) was noted. Significance was not noted between the two groups when sedation score was compared.

Conclusion: Intravenous nalbuphine is superior to IV pentazocine in providing analgesia and causes less sedation.

Keywords: Nalbuphine, Pentazocine, Postoperative analgesia.

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INTRODUCTION

Postoperative pain can lead to a multitude of potentially life-threatening adverse physiological and psychological disturbances. A systemic stress response is initiated due to pain and tissue injury associated with surgery, which has neuroendocrine, immunological, and hematological effects.[1] Pentazocine is commonly used for the relief of moderate pain. This drug is a time-tested opioid agonist–antagonist of benzomorphan series with a concomitant opioid antagonist activity. It has an elimination half-life of 2 to 3 hours. Nalbuphine is generally indicated for the relief of moderate to severe pain, is a synthetic opioid agonist–antagonist analgesic with elimination half-life of 3 to 6 hours. It can also be used as a supplement to balanced anesthesia, preoperative[2] and postoperative analgesia, and obstetrical analgesia during labor and delivery. Literature studies comparing the two drugs were few. We thus decided to compare the two drugs and evaluate their effectiveness as analgesics postoperatively. Primary objective of this study was to compare the effects of intravenous (IV) nalbuphine and IV pentazocine in terms of duration of analgesia and the need for rescue analgesia, and secondary objective was to study the side-effect profile.

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MATERIALS AND METHODS

The present study was conducted in a tertiary care center between July 2015 and June 2016. Sixty patients with American Society of Anesthesiologists (ASA) grades I or II in the age group of 18 to 60 years posted for various short-duration elective surgeries requiring general anesthesia. Patients requiring surgeries like thyroidectomy, modified radical mastectomy, laparoscopic appendicectomy, and cholecystectomy were included in this study and divided into two groups of 30 subjects each by using computer-generated randomization charts. Each patient was given all information and details about the procedure and drugs used. Written informed consent was taken from all patients. Drugs were loaded by one anesthesiologist, syringes covered and were injected by another for the purpose of blinding. All patients were thoroughly assessed preoperatively including detailed case history, clinical examination, and all necessary investigations. On arrival in the operation theater, an IV line was secured and basal values of pulse, blood pressure (BP), and oxygen saturation (SpO_2) were noted. All

the patients were done under general anaesthesia. The patients were premedicated with glycopyrrolate 5 µg/kg intramuscularly (IM), ondansetron 0.08 mg/kg, and midazolam 0.03 mg/kg IV. Group I received nalbuphine 0.3 mg/kg and group II was given pentazocine 0.3 mg/kg IV. Heart rate, BP, electrocardiogram (ECG), SpO_2, and respiratory rate were noted after giving drug. Induction of anesthesia was done with injection thiopentone sodium 5 mg/kg, and injection succinylcholine was given for intubation in the dose of 2 mg/kg. Anesthesia was maintained on oxygen, nitrous oxide, and inhalational isoflurane and injection atracurium for muscle relaxation. Heart rate, BP, ECG, and SpO_2 were monitored throughout. No analgesic was given till the end of surgery. After completion of surgery, injection glycopyrrolate (10 µg/kg) and injection neostigmine (0.05 mg/kg) were used as reversal agents. After completion of surgery, patients were asked if there were any complaints. When the patient complained of pain immediately postoperatively, the visual analog score (VAS) was assessed, and if the score was more than 4, rescue analgesic was given in the form of diclofenac 1.5 mg/kg IM. If the patient had no pain, a follow-up was done for 24 hours postoperatively, every 1 hour and VAS score was assessed. A VAS score of 4 was considered as end point of duration of analgesia and if more than 4, rescue analgesic was given. Side effects like nausea, vomiting, sedation, and respiratory depression were also noted.

Statistical Analysis

Considering the power of the study as 80% and type I error of 5% (level of significance [α] = 0.05), the sample size required was calculated as 25 in each group, and to compensate for any possible dropouts and for better validation of results a sample size of 30 subjects per group was chosen. Groups I and II were compared for postoperative duration of analgesia and any side effects like nausea, vomiting, sedation, respiratory depression, and need for supplemental analgesia. Data were expressed as mean ± standard deviation. Two-sample t-test was used for various parameters like duration of surgery and duration of analgesia. A p-value <0.05 was considered statistically significant. All statistical analysis was done using Minitab 16.

RESULTS

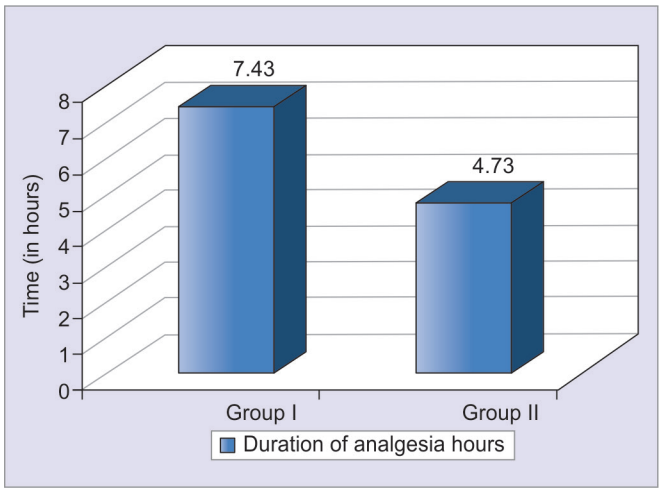
Both groups were comparable in terms of age, weight, sex, ASA grade, and duration of surgery. The average age of the patient was 38.07 ± 11.86 years in group I and 38.03 ± 12.02 years in group II (p = 0.99). The average weight of the patient was 55.5 ± 5.26 kg in group I and 55.37 ± 7.07 kg in group II (p = 0.93). Average duration of surgery was 111.67 ± 22.79 minutes in group I and 111.3 ± 22.53 minutes in group II (p = 0.95). The variety of surgeries in both the groups was comparable (Table 1). All the patients in both the groups were monitored for pulse rate, systolic and diastolic BP, SpO_2, and ECG intraoperatively at 5 minutes after giving drug and then at 15 minutes thereafter till the end of surgery. Major ECG changes were not noted in any patient intraoperatively. Mean duration of analgesia was 7.43 ± 1.63 hours in group I and 4.73 ± 1.62 hours in group II (Graph 1). The difference was statistically significant (p = 0.001: p < 0.05). Nausea, vomiting, and respiratory depression were not seen in both the groups. Sedation was assessed by Ramsay sedation score and found to be 2 in all the patients of group I, while score of more than 2 was obtained in 17 patients of group II (Table 2). In no patient was a sedation score of 4 or more noted.

Table 1: Types of surgery

	No. of patients	
Type of surgery	*Group I*	*Group II*
Thyroidectomy	8	8
Modified radical mastectomy	9	8
Laparoscopic appendicectomy	7	9
Laparoscopic cholecystectomy	6	5

DISCUSSION

Analgesia is an important aspect to be considered in preoperative, intraoperative, as well as postoperative period. Prevention of pain before surgical incision is helpful as it prevents central sensitization and thereby amplification of postoperative pain. Tissue injury as a result of surgery



Graph 1: Duration of analgesia

Table 2: Sedation score

Group	*Ramsay sedation score = 2*	*Ramsay sedation score >2*
I (n = 30)	30 (100%)	0
II (n = 30)	13 (43.33%)	17 (56.67%)

releases histamine and inflammatory mediators, such as peptides and neurotransmitters. This leads to activation of peripheral nociceptors. These stimuli ultimately reach the central nervous system causing further release of mediators leading to vasodilation and extravasation of plasma. Pain causes neuroendocrine stress response and sympathetic stimulation. Rise in level of catabolic hormones leads to sodium and water retention, hyperglycemia, increased metabolism, and oxygen consumption. Besides, hypercoagulability, immunosuppression, and poor wound healing may also result in postoperative period.[1] Poor control of acute postoperative pain can lead to chronic postsurgical pain. Opioids are an important modality of postoperative pain relief because they are said to blunt the neuroendocrine stress response to pain.[3] Morphine is the most common opioid used for postoperative analgesia. However, it often leads to several adverse effects like respiratory depression, nausea, vomiting, pruritus, constipation, urinary retention, bradycardia, and hypotension. Nalbuphine, on the contrary, is a kappa agonist, mu antagonist, and has a ceiling effect on respiratory depression.[3] Hence, it is considered to be safer than morphine. Many studies have reported that incidence of adverse effects like pruritus and postoperative nausea and vomiting is lower with nalbuphine in comparison with morphine.[4-9] Reviews on preclinical pharmacology of this drug suggest that nalbuphine moiety is approximately 10 times more pharmacologically potent than the mixed opioid agonist–antagonist butorphanol on an "antagonist index" scale, which quantitates the drug's ability to act both as an analgesic (via opioid κ-receptor agonism) and as a μ-receptor antagonist.[10] The opioid antagonist activity of nalbuphine is one-fourth as potent as nalorphine and 10 times that of pentazocine. Nalbuphine binds with high affinity to the μ-opioid receptor (Ki = 0.89 nM) and κ-opioid receptor (Ki = 2.2 nM) and has relatively low affinity for the δ-opioid receptor (Ki = 240 nM). It behaves as a moderate-efficacy partial agonist (or mixed agonist–antagonist) of the μ-opioid receptor (IA = 47%; EC50 = 14 nM) and as a high-efficacy partial agonist of the κ-opioid receptor.[11] A clinical trial, on a milligram basis, suggests that nalbuphine is about three times as potent as pentazocine in terms of analgesia.[12] The most common side effect of both the drugs is sedation. As compared with pentazocine, nalbuphine causes less dysphoria. Pentazocine by causing an increase in the plasma concentrations of catecholamines often increases the heart rate, systemic BP, pulmonary artery pressure, and left ventricular end-diastolic pressure. Thus, nalbuphine provides a safe and effective alternative to pentazocine in patients with heart disease. The advantage of nalbuphine and pentazocine in control of pain is that there is no analgesic ceiling, but ceiling to respiratory depression is present. The analgesic effects of IV nalbuphine and pentazocine in patients with postoperative pain after upper abdominal operations were studied.[12] Authors found that on a milligram basis, nalbuphine was about three times as potent as pentazocine. The duration of action seemed to be slightly longer after nalbuphine, but 2.5 hours after the injection the pain had returned to preinjection level in two out of three patients, even after the higher doses of both drugs. Except for sleepiness, there were few side effects and they were similar after both drugs.

In our study, the mean duration of analgesia was 7.43 ± 1.63 hours in the nalbuphine group and 4.73 ± 1.62 hours in the pentazocine group. Major upper abdominal surgeries were not considered in our study. The sedation score was higher in the pentazocine group in our cases. The type, duration, and expertise in performing surgery including tissue trauma have its effect on postoperative pain. In the study of comparison of nalbuphine and pentazocine in the treatment of postoperative pain by self-administration after upper abdominal surgery, the authors found that the only parameters significantly different between the two groups were systolic BP and rate pressure product, being higher in the pentazocine group. Significant difference in the side effects was not noted.[13] In a double-blind comparison between nalbuphine and pentazocine in the control of postoperative pain after orthopedic surgery,[14] authors found that onset, duration, and quality of pain relief were significantly superior for nalbuphine, with 50% of the patients having no or only moderate pain at the end of the observation period. Cardiovascular and side effects were minor in both groups. Patients in both the groups had a stable hemodynamic profile in our study. Since there was no clinically significant alteration, we did not consider this parameter as a part of our study. The nalbuphine group definitely showed a longer duration of pain relief in our study. In another study, nalbuphine and pentazocine in an opioid-benzodiazepine sedative technique, it was found that nalbuphine is a safe and effective alternative to pentazocine when used in combination with diazepam for sedation in invasive radiology.[15] Nalbuphine has been found to provide a longer duration of postoperative analgesia with less respiratory depression, chest wall rigidity, and apnea.[16] In our study, duration of analgesia was significantly prolonged in nalbuphine group (7.43 ± 1.63 hours) as compared with pentazocine group (4.73 ± 1.62 hours). Thus, the need for rescue analgesia was obviously much less in the nalbuphine group as compared with the pentazocine group. Side-effect profile was similar in both the groups except for sedation, which was less in patients receiving nalbuphine.

The limitation of our study was that major open upper abdominal surgeries were not considered. The surgeries

were all major surgeries, but the site of surgery was different. Besides, the hemodynamic profile, though not clinically significant, was not statistically considered.

CONCLUSION

In conclusion, it can be said that nalbuphine is superior to pentazocine in terms of duration of analgesia and less sedation. It can be safely used as an analgesic intraoperatively and postoperatively.

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