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ORIGINAL RESEARCH PERIOPERATIVE MEDICINE

Preemptive analgesia with tapentadol in inguinal surgery; a randomized controlled trial

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ABSTRACT

Background & Objective: Preemptive analgesia aims at minimizing the development of central sensitization thereby decreasing postoperative pain and analgesic requirements. Various drugs have been used for this purpose. Tapentadol, is a newer centrally acting analgesic which is effective in moderate to severe pain. The aim of this study was to analyze the effect of preoperative oral tapentadol upon postoperative analgesia and analgesic requirements in patients undergoing inguinal hernia surgeries.

Methodology: One hundred adult patients undergoing elective unilateral inguinal hernia repair were randomized into two groups of fifty each. Group P received placebo tablets and Group T received tapentadol (100 mg) tablets orally 30 min before anesthesia. All patients received spinal anesthesia and the duration of postoperative analgesia and analgesic consumption in the first postoperative day was recorded. Diclofenac was administered when the patients demanded analgesia.

Results: Time for first analgesic demand was significantly delayed in Group T as compared to Group P (328.00 ± 129.71 vs. 252.00 ± 101.38 min, P = 0.017) and the total analgesic consumption of diclofenac was also less than in the placebo group (73.33 ± 28.57 mg vs. 95.00 ± 31.30 mg; P = 0.006). No adverse events were observed in either group.

Conclusion: Preemptive oral tapentadol is effective for minimizing postoperative pain and analgesic requirement in patients undergoing inguinal hernia surgeries under spinal anesthesia.

Key words: Anesthesia, Spinal; Tapentadol; Hernia surgery; Analgesia, Postoperative

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1. INTRODUCTION

Postoperative analgesia is an important factor influencing surgical patients' satisfaction and early recovery. Untreated pain in the postoperative period can be deleterious. Preemptive analgesia aims to minimize central sensitization and to prevent persistent pain. Tapentadol is a newer centrally acting analgesic that acts by μ-opioid receptor agonism, norepinephrine reuptake inhibition, and alpha-2 adrenoceptor activation that is effective in several acute and chronic painful conditions.[1] The drug has a favorable profile compared to tramadol due to its negligible effect on serotonin uptake.[2] The drug has been found useful in acute pain management,[3] and a variety of postoperative pain conditions.[4] We used tapentadol as a preemptive analgesic in inguinal surgeries under spinal anesthesia, with an aim to observe the duration of postoperative analgesia of tapentadol and its effect upon analgesic consumption when compared to placebo treatment

2. METHODOLOGY

The study was designed in accordance with Equator guidelines and the Declaration of Helsinki. After obtaining approval from the Institutional Ethics Committee, the study was registered in the Clinical Trials Registry-India (CTRI/2019/03/018130).

We recruited adult patients, ages 18−60 y, of both genders, and having an ASA physical status I and II, undergoing elective unilateral inguinal hernia repair. Exclusion criteria included any contraindication to spinal anesthesia, BMI > 30 kg/m^2, history of allergy to opioids, asthma, psychiatric disorder, epilepsy, biliary disease, chronic opioid intake, patients on MAO inhibitors, and pregnancy. The participants were randomly assigned to two groups of 50 each using a computer-generated randomization table in blocks of five using sealed opaque envelopes. The patients and the investigators who administered the drugs and monitored the postoperative analgesia were blinded to the group allocation, and the study was conducted as a prospective, randomized, double-blinded controlled study.

To detect a 20% difference in the primary outcome between the groups, with a standard deviation of 27% estimated from initial pilot observations, and with 80% power and 5% alpha error (two-sided), a sample size of 50 per group was required. The sample size was calculated using the PS (Power and Sample size calculator) of the Department of Biostatistics, Vanderbilt University, USA. Taking into account a dropout rate of 5% estimated from initial pilot observations, the study selected 100 cases (50 in each group).

In the pre-anesthetic visit, assessment of each case was done by taking a history and conducting a thorough clinical examination. Investigations included hemoglobin, total and differential white cell count, bleeding time, clotting time, renal function tests, chest x-ray, ECG and serology. The nature and purpose of the study were explained to the patient. Patients were shown the visual analog scale (VAS), and they were instructed to indicate their pain on the scale. Randomization was done using computer-generated random number tables in multiples of 10. Blinding was ensured. All patients were premedicated with tablet diazepam 5 mg, tablet ranitidine 150 mg, and tablet ondansetron 4 mg on the night before surgery. All patients were randomly allocated into two groups of 50 each: Group P received placebo tablets, and Group T received tablet tapentadol extended release 100 mg, orally with sips of water 30 min before the scheduled surgery. The placebo tablets were identical to the tapentadol tablets to ensure blinding.

On arrival at the operating room, standard monitors, e.g., 3-lead ECG, NIBP, and SpO_2, were attached, and baseline parameters were recorded. Intravenous access was secured. Under full aseptic conditions, spinal anesthesia was administered to all patients using a 25G spinal needle (Quincke) at the L3−L4 intervertebral level. The dose was standardized as 0.03 mg/kg of 0.5% hyperbaric injection bupivacaine. Intraoperative hemodynamic parameters and adverse effects, if any, were noted. In the case of spinal failure, inadequate analgesia level, or inability to perform spinal technique, surgery would be conducted under general anesthesia, and the patient would be excluded from the study.

Any fall in mean arterial blood pressure (MAP) > 30% from baseline, was treated with bolus doses of ephedrine 6 mg IV. If the heart rate fell < 60 bpm for normal patients and < 55 bpm for patients on beta-blockers, bolus doses of atropine 0.6 mg were given IV. In case of vomiting, ondansetron (0.1 mg/kg) was administered.

Postoperative pain was assessed hourly for the first 6 h and every second hour for the next 6 h using the visual analog scale (VAS). Inj. diclofenac sodium 50 mg IM was given as a rescue analgesic for patients with a VAS score of ≥ 4. The dose was repeated after a minimum of 6 h if needed. The time since the administration of spinal anesthesia to the first requirement of analgesic (T1) was noted, as well as the total analgesic requirement in the first 12 h of the postoperative period. Postoperative side effects such as nausea, vomiting, fever, giddiness, shivering, and headache were recorded.

Statistical analysis

Statistical analysis was performed using SPSS software version 16.0. Descriptive statistical analysis of basic demographic data was done using a student's t-test.

Discrete variables were compared using chi-square/fisher's exact test. $P < 0.05$ was considered as a significant level.

3. RESULTS

In our study, both groups were comparable with regard to demographic data, like age, weight, height, BMI, ASA physical status and duration of surgery (Table 1).

Pain scores were significantly lower in Group T at 1, 2, 3, 4, 5, 6, 8, 10, and 12 h ($P < 0.05$) than in Group P (Figure 1).

The total postoperative analgesic consumption was also significantly lower in Group T (73.33 ± 28.57 mg) than in Group P (95.00 ± 31.30 mg). The time required for the first rescue analgesic was delayed in Group T (328.00 ± 129.71 min) compared to Group P (252.00 ± 101.38 min). Postoperative side effects were minimal and statistically non-significant.

Table 1: Comparison of demographic and procedural data in two groups

Parameter	Group Placebo	Group Tapentadol	P value
Age (y)	41.20 ± 13.31	43.67 ± 11.88	0.36
BMI (kg/m^2)	24.96 ± 4.02	25.10 ± 3.20	0.12
Duration of Surgery (h)	1.2 ± 0.56	1.44 ± 0.23	0.44
Duration of postoperative analgesia (min)	252.00 ± 101.38	328.00 ± 129.71	0.017
Total analgesic dose (mg)	95.00 ± 31.30	73.33 ± 28.57	0.006

Data presented as Mean ± SD

4. DISCUSSION

The concept of preemptive analgesia was first introduced by Crile and was later developed by Wall and Woolf.[5,6] It aims to reduce acute pain after tissue injury by preventing pain-related pathologic modulation of the central nervous system. The concept of preemptive analgesia, originally described by Wall, has evolved over the years into a more encompassing concept as preventive analgesia, which involves multifaceted perioperative pain relief strategies aimed at minimizing central sensitization. Central sensitization is an important contributor to persistent postoperative pain. The incidence of persistent pain after inguinal surgeries has been reported as 16%.[7]

Many studies have been conducted to evaluate the effect of tapentadol in chronic pain and visceral pain. Therefore, we decided to evaluate the effects of tapentadol in inguinal surgeries, which have more somatic pain components than visceral components. We used tapentadol as a preemptive analgesic to evaluate its effect on acute postoperative pain, in contrast to other studies done on chronic pain.[8]

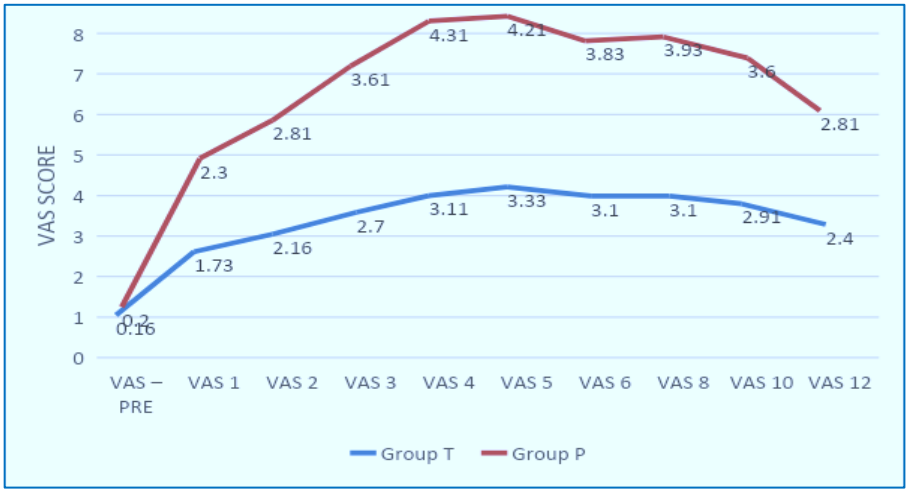

Figure 1: Mean VAS scores at various time intervals.

Opioids are considered to be more effective in dull aching visceral pain, tapentadol has been shown to be effective in laparoscopic surgeries,[9] bunionectomy and abdominal hysterectomy.[10] We used tapentadol as a preemptive analgesic for inguinal surgeries, which have moderate postoperative pain. Studies showed similar effects even in cases with severe pain, such as total hip arthroplasty, and total knee arthroplasty, when used as a preemptive analgesic.[11,12]

When used tapentadol in a dose of 100 mg, we observed that the mean time required for the first rescue analgesic was 328.00 ± 129.71 min in unilateral hernioplasty. This time was longer compared to a study that used tapentadol 75 mg as a preemptive analgesic, prolonged the mean time required for the first rescue analgesic by 96 min in laparoscopic cholecystectomy patients.[9] Therefore, we found that increasing the dose of tapentadol prolongs the duration of analgesia with a similar side effect profile. Some studies showed hyperalgesia with the use of tapentadol,[13] which was not observed in our study. This may be due to the fact that these studies used it for a prolonged period of time, whereas we used it only for a shorter duration. But still, tapentadol has been shown useful in treating acute, chronic, neuropathic and mixed pain states,[14] including pediatric population.[15]

5. LIMITATIONS

The key limitation of the study was the short follow up period which focused solely upon the immediate analgesic action of tapentadol. Whether the drug is effective in preventing chronic postoperative pain after hernia surgeries can be determined by longer follow up period. The trial was placebo controlled; hence the effect size of the intervention is not known.

6. CONCLUSION

This study demonstrates that a single tablet of tapentadol 100 mg, when given 30 min prior to surgery to patients undergoing unilateral inguinal hernioplasty under spinal anesthesia, reduces postoperative pain intensity and postoperative analgesic requirements when compared to the placebo group. It also prolongs the time required for the patients to receive the first rescue analgesic with a minimal side effect profile.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

We gratefully thank Faculty of Medicine

9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

PV – study design, data analysis, manuscript correction

IR – manuscript preparation, literature review

VK – data collection, conduction of study

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