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TO ASSESS THE ROLE OF NASAL TAPENTADOL AS PRE-EMPTIVE ANALGESIA, IN BREAST SURGERY PATIENTS

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Abstract

Patients undergoes moderate to severe postoperative pain after surgery, which is troublesome during the postoperative period. Inadequately treated acute post operative pain causes prolonged morbidity to patients. Pre-emptive analgesic minimises the pain in perioperative period by central neuro sensitization. We assessed the role of Nasal Tapentadol in breast surgery patients, as a pre-emptive analgesic, in the reduction of post-operative analgesic requirement. In a double blinded prospective randomized control study, sixty breast surgery patients, received nasal spray of tapentadol (Group A) or saline Spray (Group B), 30 minutes prior to general anaesthesia. Perioperative analgesic requirement, time taken for first analgesic requirement in post operative period, post operative pain and sedation scores, we compared the following parameters in the first 24h during the postoperative period in all patients: Analgesic requirement during perioperative period, time taken for first post operative analgesic dose, pain score and sedation score in postoperative period.Data Of all sixty patients were analysed. Patients in Tapentadol Group A had significantly lower requirement of analgesics and lower Visual analog scale (VAS) than Saline group in the post operative period. However, Ramsay sedation score was more in Tapentadol group, immediately after shifting the patient to the postanaesthetic care unit. Single Pre-emptive nasal spray of tapentadol (45mg) is an effective intervention to, reduce the surgical pain and lesser requirement of analgesics, in post operative period, without added side effects.

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INTRODUCTION

Globally 70 million surgeries are performed annually, and about 80 percent of patients have moderate to severe pain following surgery [1][2]. This leads to postoperative morbidity, as inadequately managed pain in acute postoperative period can trigger central neuronal sensitization, which may lead to chronic pain. A primary challenge is our undue reliance on opioids as potent analgesics for post-surgical pain management, which has dose related adverse side effect profile [3]. Pre-emptive analgesia is a strategy to administer analgesics before the stimuli of surgical pain occurs, to diminish the

development of central neuro-sensitization, thereby mitigating postoperative pain [4][5][6]. This approach not only decreases the need for postoperative analgesics but also facilitates superior pain relief with minimal side effects.

Diverse pharmacological approaches have been explored to attain the aforementioned goals, yet the discussion regarding the identification of an "optimal preemptive analgesic" persists. Challenges related to the licensing of analgesics and the unavailability of certain drugs further complicate this issue. Tapentadol is an analgesic acting on CNS with unique pharmacodynamics: potentiates μ-opioid receptors, inhibits the reuptake of norepinephrine r, and activates alpha-2 adrenoceptors. It has a noteworthy advantage of improved tolerance and satisfaction among patients who received the drug. The effectiveness of tapentadol to reduce both acute and chronic pain of moderate to severe in nature, through oral and intravenous administration has been demonstrated by multiple trials[7][8]. Consequently, our aim was to evaluate the pre-emptive analgesia potential of Tapentadol, administered preoperatively as a Nasal spray, in breast surgery patients, to reduce postoperative requirement of analgesics.

MATERIALS AND METHODS:

Patient were selected with prior approval of IEC and written/informed consent on following criteria: all American Society of Anaesthesiologists (ASA) grade I or II patients, more than18 years of age, body mass index of 20-30, and scheduled for elective breast surgery, in between July 2022 and June 2023. Patients with current history of psychiatric disorder or intake of psychotropic drugs, any patients with disability to communicate, drug intake history of Alpha2 agonists or opioid drugs within four weeks preceding the scheduled surgery, pregnancy, and allergy to opioid, were excluded.

The patients were assigned to two equal groups, Group A and Group B, from a lot of sealed opaque envelope with random computer-generated number sequence, by a trained Anesthesiologist, who administers the Nasal spray to the patients 30 minutes prior to surgery: Group A received nasal spray of tapentadol (45mg) and Group B received nasal spray of normal saline. The study Investigator who is blinded to group allocation provides further Anesthesia care and monitoring, thereby ensuring double blinding.

Preoperatively, all the study participants received instruction on the use of the Visual analog scale (VAS) and Ramsay sedation score (RSS) for proper pain and sedation assessment. No pre-medications were administered in both the groups. In operating room, patients were attached to standard monitoring equipment and baseline parameters recorded. General anesthesia was induced with propofol (2 mg/kg IV), and fentanyl (2 μg/kg IV). Endotracheal tube was inserted after neuromuscular blockade with injection vecuronium (0.1 mg/kg IV). General Anesthesia was maintained with Sevoflurane, Nitrous oxide/Oxygen mixture (60/40%) administered to maintain a MAC of 1. During intraoperative period, we tried to achieve the mean arterial pressure (MAP) within 20 percent of the baseline value. We used fentanyl boluses of 1 μg/kg to treat a rise of MAP more than 20 percent and by increasing the concentration of inspiratory sevoflurane in steps of 0.2 percent. Any decrease in mean arterial pressure (MAP) exceeding 20% from the baseline was addressed by incrementally lowering the inspiratory concentration of Sevoflurane in 0.2% steps. In intraoperative period, vecuronium (0.02 mg/kg IV) was used for maintenance of neuromuscular blockade. Neostigmine (0.05 mg/kg IV) and glycopyrrolate (0.01 mg/ kg IV) was injected at then end of surgical procedure to reverse the neuromuscular blockade. After successful extubation, at reference time point for 0 h, Patient was shifted to the post anesthesia care room. The time duration for first postoperative analgesia requirement from 0 hr, during the first 24 h of postoperative period is the primary outcome. The 11-point VAS scale ranging from “0” indicating “no pain” to “10” indicating “maximal unbearable pain” was used for assessing acute pain post operatively. The six point RSS scale with 1 representing ‘anxious or restless’ to 6 for ‘no response to stimulus’ was used to assess sedation [9]. In the post operative period, the pain and sedation score at 0h,1/2h,1h,2h,4h,6h,8h,12h,16h,20h,24h, were noted and recorded. For any complaints of acute pain (VAS ≥4) was treated with IV infusion of 1g Paracetamol, with a least interval of 6 hour between two doses. For any breakthrough pain Intramuscular diclofenac injection (75 mg, IM) was

administered. During the first 24 hr in post operative period, following data were collected: Time to first postoperative analgesia, the number of patients requiring rescue analgesia, and any possible side effects.

The collected data was analysed using IBM SPSS statistics for windows, Version 17.0, (IBM Corp, Armonk, NY). Comparison of the continuous variables were done by the one-way ANOVA and comparison of discrete variables were done by either Fisher's exact test or Chi-square test, with a significant $P < 0.05$

RESULT:

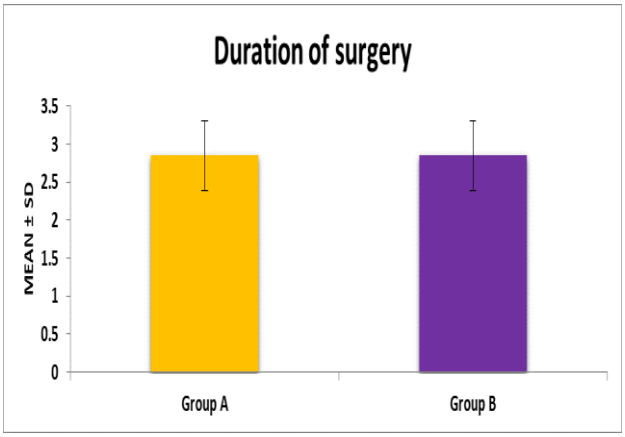

Figure 2 Comparison of duration of surgery between the groups

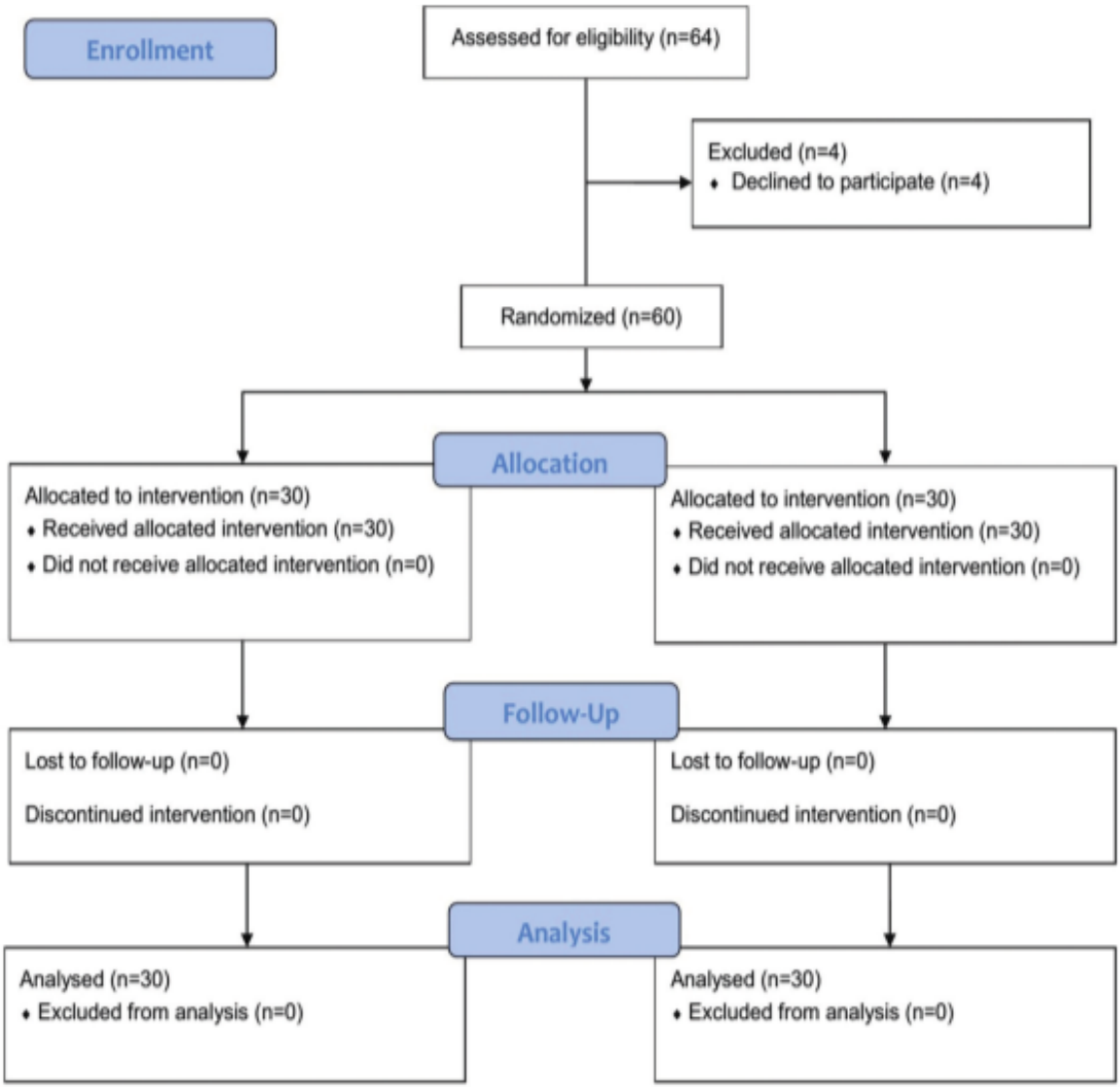

Figure 1

Data expressed as mean ± standard deviation $P < 0.05$ considered significant (*$P < 0.05$, **$P < 0.001$). Group A = Tapentadol group, Group B = Control group,

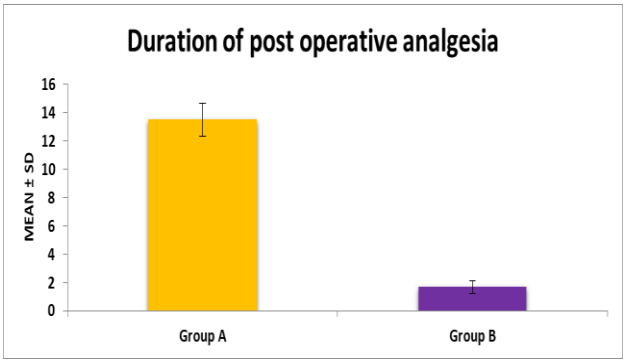

Figure 3 Comparison of duration of post-operative analgesia between the groups

Data expressed as mean ± standard deviation $P < 0.05$ considered significant (*$P < 0.05$, **$P < 0.001$). Group A = Tapentadol group, Group B = Control group,

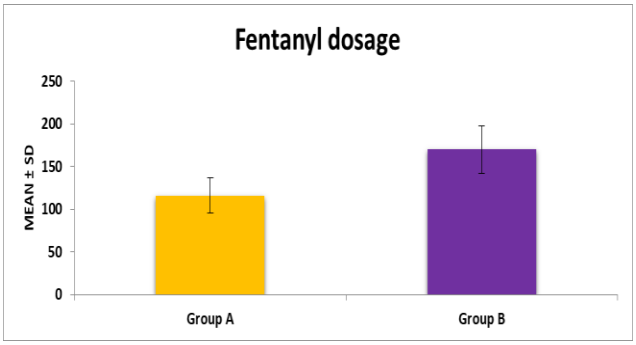

Figure 4 Comparison of fentanyl dosage between the groups

Data expressed as mean ± standard deviation $P < 0.05$ considered significant (*$P < 0.05$, **$P < 0.001$). Group A = Tapentadol group, Group B = Control group,

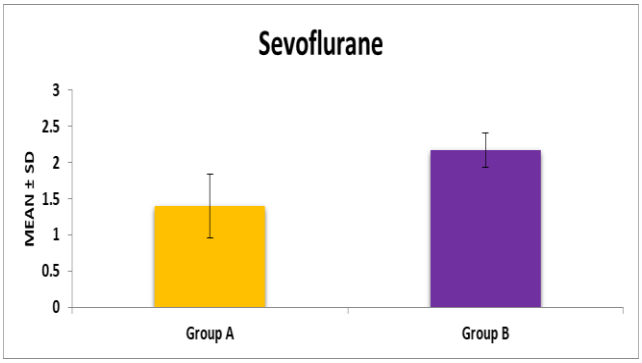

Figure 5 Comparison of sevoflurane usage between the groups

Data expressed as mean ± standard deviation $P < 0.05$ considered significant (*$P < 0.05$, **$P < 0.001$). Group A = Tapentadol group, Group B = Control group,

Table 1 Comparison of demographic and intra-operative parameters among the groups

Parameters	Group A (n=30)	Group B (n=30)	p value
Age (years)	38.10± 9.965	37.10± 8.965	1.000
Duration of anesthesia	3.850± .5577	2.850±. 4577	1.000
Fentanyl dosage	116.00± 20.443	170.00± 27.668	.000
Sevoflurane usage	1.400±. 4433	2.167± .2397	.000

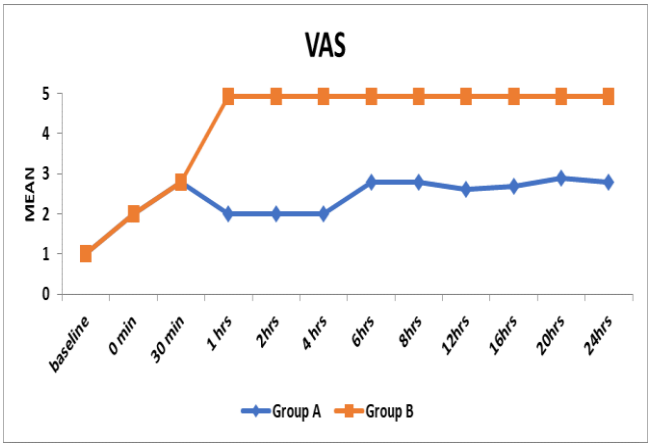

Figure 6 Comparison of postoperative pain scores between the groups.

Data expressed as mean ± standard deviation $P < 0.05$ considered significant (*$P < 0.05$, **$P < 0.001$). Group A = Tapentadol group, Group B = Control group, VAS = Visual analogue score

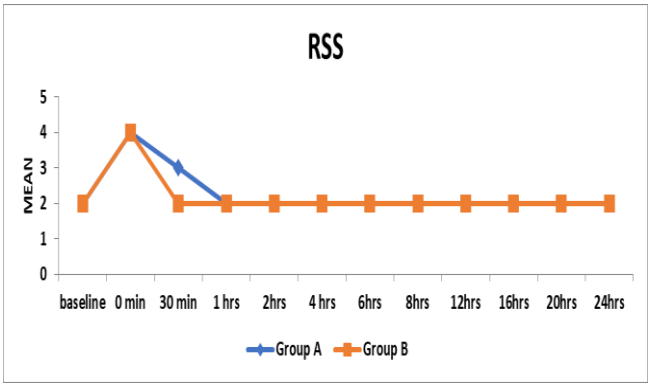

Figure 7 Comparison of postoperative sedation scores between the groups

Data expressed as mean ± standard deviation. Group A = Tapentadol group, Group B = Control group, RSS = Ramsay sedation score

Table 2 Comparison of postoperative parameters among the group

Parameters	Group A (n=30)	Group B (n=30)	p Value
Time to first analgesia	87.5± 23.5	27.9± 8.0	0.001
Patient requiring rescue analgesia	12.500± 1.1496	13.400± 2.1597	0.00
Duration of post-operative analgesia	13.500± 1.1597	1.673±. 4719	.000

Our study identified a total of 64 candidates, out of which 4 patients refused to consent, hence excluded. All 60 patients included had successfully completed the study, with 30 patients in each group with similar age profile. Intraoperative consumption of fentanyl and sevoflurane was significantly lower than Group B in Group A (P < 0.001, P = 0.05, respectively).

For first 30 min post operatively, The VAS was comparable in both groups, but after 30 min, VAS is significantly lower in Group A than Group B at all data points. (P < 0.001). RSS was found to be similar in both the groups at all data points after one hour post PACU arrival.

DISCUSSION:

This study highlights the significant role of preemptive administration of tapentadol through the nasal route to reduce the postoperative pain and also the total analgesic requirement in the first 24 hours following breast surgeries.

Tapentadol, an opioid agonist offers highly effective analgesia comparable to one-third the analgesic dosage of morphine. Tapentadol has a unique action of selective inhibition of norepinephrine reuptake thereby activating alpha-2-adrenoceptors. This receptor activation modulates pain sensation by affecting both the ascending and descending pain pathways including dorsal horn neurons and descending inhibitory fibers from periaqueductal gray matter and rostral ventromedial medulla [[10][11]. Unlike tramadol which relies on active metabolites by Cytochrome P450 system, tapentadol's advantages include its action as a single enantiomer, with inactive metabolites has time-dependent changes in opioid and monoaminergic receptor dynamics, and potent analgesic activity with minimal adverse effects.

Various researchers have explored the efficacy of tapentadol through different routes as a postoperative analgesic The effectiveness of Tapentadol as an analgesic has been explored across a dosage range of 50-200 mg. [7][8][10][11]. Kleinert et al studied the effect of tapentadol in dental patients and found that single dose of 75 mg of tapentadol given orally efficiently reduces moderate-to-severe postoperative dental pain and has better tolerability than morphine [7]. Ghanshyam et al in 2016 used 75 mg dose of tapentadol in elective laproscopic cholecystemy patients as preemptive analgesia and found to be effective to reduce perioperative analgesic requirements and lower acute postoperative pain [20].

However, there are reports of cardiovascular adverse effects after a single 100 mg dose of tapentadol to be noted which necessitates dose-response study for safety. While the typical starting dose is 50-75 mg, in patients with opioid tolerance or severe pain, higher doses should be considered [10]. Given the variable severity of postoperative pain in breast surgery patients, in our study we used 45 mg dose of tapentadol via nasal administration as a preemptive analgesic for better safety profile. Gajdhare et al 2023 [21]studied that use of preemptive tapentadol was better in laminectomy patients on comparison tramadol orally.

Nasal administration of tapentadol results in rapid and complete absorption, and attains peak plasma concentration in 25-30 minutes with an elimination half-life of approximately 3.5 hours. [16][17]

The nasal dose of tapentadol is timed 30 minutes before to concur with the timing of maximal surgical pain stimulus, evidenced by reduced requirements for perioperative analgesics in the tapentadol group.

Daniel et al. used pre-emptive tapentadol in bunionectomy patients and reported a significant better postoperative pain scores [18]. Similarly in

patients undergoing joint replacement surgery, preemptive tapentadol reduces postoperative VNS score as reported by Hartrick et al [19]. In our study, we noted a comparable decrease in postoperative VNS scores at the "0" time point with tapentadol and at other time points VNS score is similar in both the study groups which could be due to increased demand of post-operative analgesic agents in the placebo group. Conducting a dose-response study in a large group of diverse ethnic groups could offer a better understanding of the pre-emptive analgesic efficacy and potential side effects associated with tapentadol, as our study is on a small sample size.

CONCLUSION:

Our research has elucidated insights into the preemptive analgesic properties of tapentadol administered through the nasal route for addressing acute postoperative pain. Our findings suggest that nasal tapentadol serves as a suitable option for preemptive analgesia with a positive safety profile with minimal sedation.

AUTHOR CONTRIBUTION

All authors made substantial contributions to the conception, design, acquisition, analysis, or interpretation of data for the work. They were involved in drafting the manuscript or revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring its accuracy and integrity

Ethical Approval

No ethical approval was necessary for this study.

Author Contribution

All authors made substantial contributions to the conception, design, acquisition, analysis, or interpretation of data for the work. They were involved in drafting the manuscript or revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring its accuracy and integrity.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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