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A Comparative Study Between Tapentadol Nasal Spray and Intravenous Diclofenac in Post Operative Laparoscopic Cholecystectomy

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Abstract

Background: Tapentadol having both mu-opioid receptor agonist and norepinephrine reuptake inhibitor characteristics has better GI profile and analgesic efficacy in acute and chronic including neuropathic pains. Post operative pain using tapentadol nasal spray with quicker recovery helps in minimizing the amount of time required for patient to be on bed rest, reduced hospital day, hospital expenditure and overall patient satisfaction. ***Objectives:*** We conducted this study to compare the efficacy of Tapentadol Nasal Spray and Diclofenac IV in the Post operative patients of Laparoscopic Cholecystectomy by using VAS (Visual Analogue Scale), to compare tapentadol and diclofenac in terms of safety of administration and to study the cost effectiveness. ***Methods:*** Using randomized, prospective study design, half of post-operative cases were prescribed tapentadol nasal spray and were assigned Group A. The second half of the postoperative cases received intravenous diclofenac and were assigned Group B. Scheduled dose of tapentadol nasal spray was 22.5 mg in each nostril and for intravenous diclofenac dose was 75 mg. ***Results:*** It was observed that the mean pain score in the subjects of the tapentadol nasal spray group was comparatively lower than intravenous diclofenac group by VAS ($p<0.05$). ***Conclusion:*** Tapentadol nasal spray at 22.5 mg in each nostril was found to be effective in managing the post operative pain with minimal side effects.

Keywords: Pain, Tapentadol, Diclofenac, Laparoscopic Cholecystectomy.

INTRODUCTION

The International Association (1979) described an apprehensive emotional and sensory experience as pain or a sensation like burn, ache, sting, tingle, prick. It may be sharp or dull when related to damage." It is also a significant sign of many various medical and surgical disorders' presence. Usually after surgery, it causes some discomfort to the patient thus slowing the discharge of the patient and also results to increased morbidity and reduced patient satisfaction [1]. Pain is most frequently categorized by the type of injury that originally led to its occurrence. There are two main categories of pain: Nociceptive Pain, due to tissue damage and Neuropathic Pain, due to nerve injury. The third type that is associated with psychological conditions is psychogenic pain [2]. In acute pain there is the involvement of nociceptive transmitters that occur at the time of the initial tissue damage. The autonomic nervous system, central connections and hence the nociceptors can still be further modified under the specifications of the wound site. [3]

For post operative pain relief there are various classes of analgesics, each having different mode of action. Opioids and NSAIDs are commonly administered for postoperative pain.[4]. NSAIDs inhibit formation of prostaglandins through the inhibition of the cyclooxygenase (COX) pathway that is responsible for the production of substances leading to inflammation, pain and fever [5]. Diclofenac is a NSAID which belongs to a class of COX-2 selective drugs that have pain

relieving, antipyretic and anti-inflammatory action due to the inhibition of prostaglandins synthesis. The common uses for which this particular medication is prescribed are, for example, post-surgical inflammation, rheumatoid and osteoarthritis, as well as toothaches [6]. Like other drugs in the COX-2 inhibitor group, the FDA has issued a clear warning against the use of diclofenac to patients with higher risks of heart complications including those with previous history of heart attack and stroke [7].

Clinicians should refrain from administering diclofenac or any other NSAIDs to patients with a history of gastrointestinal bleeding or ulcerations [8].

Opioids are used in the treatment of acute pain and work through opioid receptors to cause its therapeutic and toxic effects such as opioid tolerance, opioid use disorder and immune system suppression [9]. Tapentadol is a new potential pain relief drug which has dual action mechanism in CNS system exclusively. This is a unique approach wherein two mechanisms work simultaneously, namely the inhibition of reuptake of noradrenaline and activation of mu-opioid receptors within a single molecule. Compared with traditional analgesic opioids and NSAIDs, side effects of Tapentadol is less severe to the patient. This active mechanism makes tapentadol efficient in treating short term as well as chronic, mild as well as severe, and sharp as well as chronic pain conditions of neurological sources [10].

MATERIALS AND METHODS

This study was carried out using randomized, prospective study design after getting permission from the Institutional Ethics Committee (IEC) with written and informed consent from 100 post-operative patients.

The patients were randomly grouped into two groups using odd-even technique and labelled as group A and B. Patients in Group A were administered with Tapentadol NS and received a dose of 22. 5 mg in each nostril. The patients in Group B were administered with IV Diclofenac received a dose of 75 mg. They were both given three times daily on Post Operative Day (POD) 1, 2, and 3. On POD 0 drugs were given at 10:00 PM and assessment was done at 11:00 PM. On POD 1, 2, 3, at 6 AM, 2 PM, and 10 PM, the drugs were administered, and the assessment was conducted at 7 AM, 3 PM, and 11 PM. To quantify the level of pain, VAS score was used in the assessment of the patients' condition. It ranges from 0 to 10 with 0 implying that the patient is experiencing no pain, 1-4 implying mild pain, 5-7 illustrating moderate pain and above 7 implying that the patient is in severe pain. The score was evaluated on the first, second and third day of surgery, as well as on the day of the intervention. Finally, the results were computed by using SPSS Software.

STATISTICAL ANALYSIS

Data from patients were collected from Shri Mahant Indiresh Hospital, Dehradun, Uttarakhand during the study time period. Data were described in terms of range, mean ± standard deviation (± SD), frequency (n), and relative frequency (percentage). Another step of the analysis was using the Kolmogorov-Smirnov test to evaluate whether the data were of normal distribution or not. The Mann Whitney U test was employed to compare nonparametric quantitative variables where applicable between the study groups. For comparing the data in to categorical variables Chi square test (X2) was performed while fisher exact test was used in case if any expected frequency was below 5. P value <0. 05 was taken as statistically significant. All statistical analyses were conducted using the Statistical Package for the Social Science (SPSS) 21st version (SPSS Inc., Chicago, IL, USA) statistical package for Microsoft Windows.

RESULTS

In total 100 candidates were included, 50 cases in each group completed the study successfully. Both groups were comparable in terms of demographic details, duration of surgery and pre-operative pain. (Table 1).

Table 1: Comparison of demographic details and pre-operative pain among the groups.

Parameters	Group A (Mean)	Group B (Mean)	p-value
Age (years)	46.24	45.46	
Gender (Female/Male)	0.8/0.2	0.8/0.2	1.000
Duration of Surgery (minutes)	42.94	43.26	
Pre-op Pain	0.70	0.76	0.737

Table 2: p values found at different Post Operative days (POD) and time.

POD and Time	p-value
POD 0 11 PM	0.008
POD 1 7 AM, 3 PM, 11 PM	0.110, 0.212, 0.046
POD 2 7 AM, 3 PM, 11 PM	0.074, 0.006, 0.006
POD 3 7 AM, 3 PM, 11 PM	0.005, 0.004, 0.006

DISCUSSION

Alshehri FS (2023) in the study titled, Tapentadol: In A Review of Experimental Pharmacology Studies, Clinical Trials, and Recent Findings, stated that tapentadol has certain benefits that can make it an effective agent to treat pain. Tapentadol has been described as having dual mode of action being a mu opioid receptor agonist and also a noradrenaline reuptake inhibitor and this set it apart from the traditional opioids such as morphine and was effective in both the

nociceptive and neuropathic pains. Notably, tapentadol appeared to have fewer side effects than the traditional opioids making it a useful analgesic for chronic pain. In summary, tapentadol is potentially more appealing for mixed pain conditions because of its high efficacy compared with side effects [11]. Daniel *et al.,* noted a positive effect on the postoperative pain on patients who received the drug after they underwent bunionectomy surgery [12]. As also noted by Hartrick *et al.,* there was a similar reduction of the postoperative VNS scores among the patients that underwent joint replacement surgery [13].

In our study, a sample comprised of one hundred patients was reviewed with 80 percent of female and 20 percent of male patients. The distribution of study subjects was as follows: Group A – 40 females and 10 males, Group B – also 40 females and 10 males. The mean age of Group A which was administered with Tapentadol was 46.24 while that of Group B, which was administered with IV Diclofenac was 45.46. The mean duration of surgery of Group A, treated with tapentadol, was 42. 94 minutes while mean duration of surgery of Group B, treated with IV diclofenac, was 43. 26 minutes. It was concluded that females were more prone to cholelithiasis than males.

When comparing its effects on POD 0 in terms of analgesia, it was concluded that Tapentadol's efficacy was slightly more as compared to Diclofenac with p = 0. 008. The first VAS pain assessment was performed at 11 p.m. of POD 0. In the Group A, one patient reported a VAS of 4, 10 reported VAS of 3 while 21 recorded a VAS of 1. Conversely, group B included 6 patients with VAS 1, 23 patients with VAS 2, 18 subjects with VAS 3, and 3 patients with a VAS of 4.

On POD 1 we assessed the patients for pain at 7 a.m., 3 p.m., and 11 p.m. and the p-values were found to be 0.110, 0.212, and 0.046 respectively.

Similarly, on POD 2 and 3 VAS scores were evaluated for both groups at the same time and the p-values on POD 2 were found to be 0.074, 0.006, 0.006 and on POD 3 were 0.005, 0.004, 0.006.

In short, 7 out of 10 p-values were less than 0.05, indicating that the results of our study can be considered statistically significant.

The safety profile of both the drugs was also assessed and it was observed that in Group A which received Tapentadol NS, 1 out of 50 patients complained of headache and 2 patients complained of nasal irritation. In Group B which received IV Diclofenac 3 patients complained of abdominal pain.

Diclofenac is generally known to cause gastrointestinal issues and renal impairment. So, in patients with deranged RFT and gastrointestinal issues, the use of tapentadol is a good alternative as it causes relatively mild adverse effects. The cost effectiveness of both drugs was also assessed and it was observed that Diclofenac was more cost effective at 5 rupees per vial as compared to Tapentadol which is of 678 rupees.

CONCLUSION

This study suggests that tapentadol is safe and effective to use and was considered a better alternative for pain management as it provides PCA (patient-controlled analgesia). In addition to this the IV Diclofenac administration needs a trained staff and it can also present complications of IV drugs like pain at the site of injection, blood clotting, ulcers, renal impairment etc. In conclusion, for patients who can afford the higher cost and are at a risk for severe gastrointestinal side effects from NSAIDS, tapentadol may be a preferred alternative.

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