Original Research Article

Is Tapentadol nasal spray an effective modality of pain control after extraction? A randomized control clinical trial.

Abstract-

Background:

Tapentadol nasal spray application is a novel method of pain management attributable to its action on higher centers for pain management in contrast to non-steroidal analgesics. The study aims to compare the efficacy of post-extraction pain control between Tapentadol nasal spray and Tab. Diclofenac 50 mg.

Methodology: Fifteen subjects (30 sides) between the age group of 18-50 years with bilateral extraction of teeth were randomly selected for the study. Tapentadol nasal spray [22.5mg x 2=45mg] was administered on the right side every 8 hours. The second extraction was done after 7 days on the left side and administered tablet Diclofenac 50 mg eight hourly. Both groups received their drugs for 3 days. The pain was assessed using the pain analog scale in both cases.

Results:

The subjects administered with Tapentadol nasal spray did not experience any pain and controlled group receiving Tab. Diclo-50mg experienced pain and were administered with rescue analgesics.

Conclusion: Tapentadol nasal spray demonstrated a favorable outcome compared to Tab. Diclofenac in managing post-extraction pain. Hence, the proposed Tapentadol nasal spray is an optimal choice of analgesia recommended over other forms of oral analgesia post extraction determined through thorough evaluations and approved questionnaires received from patients.

KEYWORDS: Tapentadol nasal spray, emergency analgesics, comparative analysis, bilateral extraction, pain management.

INTRODUCTION

Pain management after surgery have always turned out to be a major concern among the vast number of clinicians due to variable threshold potentials and anatomical variations and Long-term research have been conducted on effective pain management [1].

The μ-opioid receptor and its corresponding agonists have been utilized in the treatment of mild to extreme pain for a really long time. Morphine, a specialized prototypic drug in this class, has been known to be efficient for excruciating pain but lacks a similar effect in patients with persistent pain of a neuropathic or inflammatory etiology [2]. The utilization of morphine in patients with non-neuropathic or inflammatory chronic pain might also promote resilience, requiring expanded dosages over the long run, which might be related to unfavorable dose-limiting impacts (eg, nausea, emesis, constipation, mental clouding). Respiratory depression is an uncommon but serious consequence [3].may be addictive ,not indicated for inflammatory etiology

According to Wade et al., (2009) a combined mechanism of action was accomplished by utilizing μ-opioid receptor activation and norepinephrine reuptake inhibition for the therapeutic development of opioid analgesics [4]. Tapentadol hydrochloride is one such intermediary analgesic considered to be manifested for effective pain management. The latter was then approved by the US Food and Drug Administration in November of 2008 in the dosage forms of 50mg, 70mg, and 100mg respectively to be administered for mild to moderate and even severe pain [5].

The greater potency and efficacy of Tapentadol with reduced gastrointestinal adverse effects compared to classical strong opioids and multiple other unique features has promoted it to become an ideal pharmacological drug for pain management [6]. Additionally, studies carried forward till today suggest that this agent also possesses prominent efficacy over morphine or oxycodone, and profound adequacy over placebo in multiple acute and chronic pain scenarios [7].

In our study, we aimed to check the efficacy and potentiality of Tapentadol nasal spray over oral NSAIDs. Accordingly, our study has also been designed to propose Tapentadol nasal spray as a

good call by clinicians over other oral forms of analgesia in bilateral extraction cases, based on a comprehensive comparison and clinical evaluation of patient responses. This clinical experience will surely determine whether this useful class of drug best matches the physician's attempt to relieve post-operative pain in certain populations of patients.

METHODOLOGY

An invivo-prospective study was conducted on 15 medically fit 9 male and 6 female patients between the age group of 18-50 years, who reported to the Department of Oral and Maxillofacial Surgery at Yenepoya Dental College for bilateral extraction between march 2022 till June 2022. The study protocol and associated materials were approved by the Yenepoya ethics committee at each site. All participating patients provided informed written consent prior to study enrollment. The study was conducted according to the protocol and Good Clinical Practice guidelines. The CTRI trial registration number is CTRI/2022/07/043654.

Patients who were allergic to drugs (Tapentadol nasal spray(which company) and Tab. Diclofenac) and who required traumatic extraction with underlying nasal pathology viz rhinitis, polyps, and deviated nasal septum were excluded. Post extraction on the right side, the patients were administered Tapentadol nasal spray, [22.5mg x 2=45mg] every 6 hours, for 3 days. The patients were followed up after the third day of extraction, and the pain was assessed using a visual pain analog scale and a number of emergency analgesics if required. Patients were recalled after 7 days of the first extraction procedure, to undergo the second extraction on the left side, and were sufficed to tablet Diclofenac 50 mg, for a duration of 3 days, and the pain was assessed using visual pain analog scale on the third day of the second extraction. A detailed questionnaire with visual pain analog scale as shown in Figure 1 was then drafted to indicate an intensity range which was categorized into six levels: no pain (0) = 0; mild pain (1-2) = 1; annoying, uncomfortable troublesome pain (3-4) = 2; distressing miserable pain (5-6) = 3; intense dreadful pain (7-8) = 4; unbearable excruciating pain (9-10) = 5.

A simple random sampling method was utilized to collect data and the sample size was calculated by using G* power software for an independent sample -t-test. At a 10% level of significance and 80% power with a standard effect size of 0.8, the total sample size collected had 30 sides i.e. 15 patients.

RESULTS

Mean and standard deviation were calculated for the continuous variable and an Independent sample t-test or Mann-Whitney U test was used for comparing the presence of pain on both sides as shown in Table 1. The mean age group included in the study was 20.87 years with a standard deviation of 5.097 as illustrated in Table 2. The subjects administered with Tapentadol nasal spray after the first extraction did not experience any pain on the right side and no rescue analgesics were required for them as illustrated in Table 3, although 2 out of 15 patients experienced mild nasal irritation. Whereas 9 patients (60%) of the patients who were sufficed to Diclofenac suffered with mild pain, 5 patients (33.3%) had annoying pain, and 1 patient (7%) had no pain after secondary extraction as shown in Table 4. The two-tailed P value was less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant.

DISCUSSION

Chronic pain caused due to post-surgical extraction can elevate discomfort and become difficult to manage. The correct diagnosis is crucial in this regard. Recent medical research provides no evidence of the translational and meaningful approach to discovering OTC (Over counter) analgesics in the preceding years [9]. Our study illustrates one such targeted strategy that can lead to an innovative and effective new drug, Tapentadol. Tapentadol nasal spray administered in patients after the first extraction was 100 % effective when compared to Tab. Diclofenac, with mild nasal irritation, was noted in 2 patients. Therefore, it can routinely be adopted in clinical practice and hence must be further tested for its suitability by using a larger sample size and multicentric trials. Furthermore, in-vivo evaluation of intranasal delivery of Tapentadol by Javia et al,. suggested that the instillation of TAP-loaded CS-NPs delivers the drug rapidly and more effectively to the brain than the intravenous route [10].

Tapentadol was built upon comprehensive advances in the understanding of the fundamental science of pain and mechanisms of analgesia----coordinated with therapeutic medicinal chemistry modifications----to yield a new drug whose designed properties offer a differentially customized clinical (‘bench-to-bedside) profile [4]. Substantially, Tapentadol also acts as a

template for rational drug discovery and development in other therapeutic areas. Once the mechanistic targets that rationalize for an existing drug's clinical application (or disadvantages) are distinguished, target-specific compounds can be manufactured, furthermore even tested [8].

By such an iterative course of action, the biological target scan is redefined and improvements can be accomplished, resulting in new drugs that have distinctive clinical attributes that benefit patients in contrasting yet correlative ways. Tapentadol serves as an illustration of both the approach itself and the advantages that can result from such an intervention [16,17]. The pharmacological profile of Tapentadol, combining synergistically MOR agonism and NRI in one molecule, appears to be unique and it seems rational to suggest Tapentadol as the first, and so far only – drug of a new class of central-acting analgesics designated MOR-NRI.[9] While the only limitation of this study was the lack of comparative pharmacoeconomic data for Tapentadol and other commonly used analgesic agents [15]. (Habit forming ,addictive ,other side effects over conventional drugs should be mentioned)

According to a recent narrative review conducted by Roulet et al., in 2021, Tramadol and Tapentadol share the same mechanism of action, but Tapentadol is approximately two to three times more potent than tramadol but less potent than morphine [18]. The relative efficacy and tolerability of Tapentadol IR were also evaluated in a comparative analysis with oxycodone IR in moderate to severe pain management post orthopedic surgeries. Clinically meaningful and statistically significant improvements were observed with Tapentadol IR 50 mg and 75 mg compared with oxycodone 10 mg in the treatment of acute pain [20]. Tapentadol nasal spray can be used in further clinical situations like in major surgery where especially oral routes of drugs cannot be given and Tapentadol nasal spray can replace parenteral route of drug administration.

LIMITATIONS

The results are based on perception and VAS score which are subjective in nature.

Conclusion

Tapentadol is an oral analgesic observed to have great efficacy in numerous pain situations. It was generally well tolerated by all the patients included in the experimental group with no clinical significance compared to the control group. Tapentadol has effectively reduced post-

operative pain in previous studies and hence has the potential to provide imminent relief to patients. It is anticipated that Tapentadol will be an important addition to the armamentarium for the management of moderate to severe pain. Future surveys are required for the application of this potential drug in oral and maxillofacial surgery to reduce patient morbidity.

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LEGENDS

FIGURES

Fig 1: A detailed questionnaire drafted with visual pain analog scale to indicate an intensity range categorized into six levels for Tapantadol nasal spray administered on the right side of extraction and Tab. Diclofenac given on the left side.

TABLES

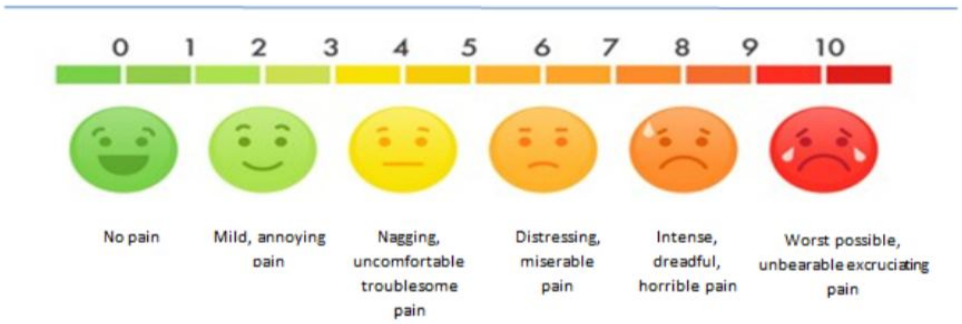
Table 1: Analysis of pain management based on visual pain analog scale:

Table 2: Mean and standard deviation of sample size.

Table 3: Frequency analysis of Tapentadol nasal spray.

Table 4: Frequency analysis of Tab. Diclofenac.

FIGURE:



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TABLES:

Table 1: Analysis of pain management based on visual pain analog scale:

SL.NO	Age	Sex	Effectiveness of Tapentadol nasal spray	Effectiveness of Tab. Diclofenac
1	18	F	0	2
2	25	F	0	2
3	21	M	0	1
4	18	F	0	2
5	19	M	0	1
6	38	M	0	2
7	18	F	0	1
8	19	M	0	1
9	20	F	0	0
10	19	F	0	1
11	20	M	0	1
12	21	M	0	2
13	18	M	0	1
14	18	M	0	1
15	21	M	0	1

Table 2: Mean and standard deviation of sample size.

Age (18-50 years)	Mean	Standard Deviation
	20.87	**5.097**

Table 3: Frequency analysis of Tapentadol nasal spray

Pain controlled with Tapentadol nasal spray	Frequency	Percentage
No pain	15	100

Table 4: Frequency analysis of Tab. Diclofenac

Pain controlled with Tab. Diclofenac	Frequency	Percentage
No pain	1	6.7
Mild	9	60
Annoying	5	33.3