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Tapentadol Nasal Spray is an Effective Way of Pain Management after Tooth Extraction: A Randomized Control Clinical Trial

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Tapentadol nasal spray (Tapease NS) 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 oral administration of Diclofenac (50mg tablet).
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 hourly. The second extraction was done after 7

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days on the left side and administered Diclofenac tablet at eight hourly intervals. Both groups received the therapy drugs for 3 days and 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 the Diclofenac tablet experienced pain and were administered with rescue analgesics.

Conclusion: Tapentadol nasal spray demonstrated a favorable outcome compared to the Diclofenac tablet 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.

1. INTRODUCTION

Pain management after surgery has 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 neuropathic pain [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].

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 to date 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.

2. 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 and June 2022.

Patients who were allergic to drugs Tapentadol nasal spray (Tapease NS) and Diclofenac tablet 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 Fig. 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.

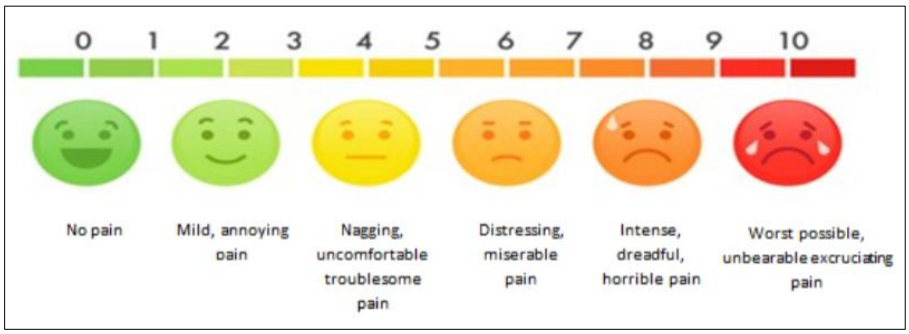

Fig. 1. A detailed questionnaire drafted with visual pain analog scale to indicate an intensity range categorized into six levels for Tapentadol nasal spray administered on the right side of extraction and Tab. Diclofenac was given on the left side

3. RESULTS

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

Mean and standard deviation was 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 from 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.

4. 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 [8]. 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 [9].

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 an existing drug’s clinical application (or disadvantages) are distinguished, target-specific compounds can be manufactured, furthermore even tested [10].

By such an iterative course of action, the biological targets can be 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 [11,12]. 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 [13]. While nausea, drowsiness, vomiting and dizziness are some of the common side effects of this medicine which do not require any medical attention.

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 [14]. 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 IR50 mg and 75 mg compared with oxycodone10 mg in the treatment of acute pain [15-20]. 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 the parenteral route of drug administration.

5. CONCLUSION

Tapentadol is observed to have great efficacy in numerous pain situations. Tapentadol nasal spray 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 postoperative 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.

6. LIMITATIONS

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

CONSENT AND ETHICAL APPROVAL

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 (CTRI trial registration number CTRI/2022/07/043654).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Abbott FV, Fraser MI. Use and abuse of over-the-counter analgesic agents." Journal of Psychiatry & Neuroscience: JPN. 1998;23(1):13-34.
2. Eissa A, Tarau E, Beuter C, Radic T, Watson E, Sohns M, Lefeber C, Hammer GB. Tapentadol for the Treatment of Moderate-to-Severe Acute Pain in Children Under the Age of Two Years. J Pain Res. 2021;14:229-248.
DOI: 10.2147/JPR.S269530. PMID: 33542653; PMCID: PMC7853441.
3. Hale M, Upmalis D, Okamoto A, Lange C, Rauschkolb C. Tolerability of Tapentadol immediate release in patients with lower back pain or osteoarthritis of the hip or knee over 90 days: a randomized, double-blind study. Curr Med Res Opin. 2009;25:1095–1104.
DOI:10.1185/ 03007990902816970
4. Raffa RB, Buschmann H, Christoph T, Eichenbaum G, Englberger W, Flores CM, Hertrampf T, Kögel B, Schiene K, Straßburger W, Terlinden R, Tzschentke TM. Mechanistic and functional differentiation of tapentadol and tramadol. Expert Opinion on Pharmacotherapy. 2012;13(10):1437–1449.
Available:https://doi.org/10.1517/14656566.2012.696097
5. Singh, Dewan Roshan et al. Tapentadol hydrochloride: A novel analgesic. Saudi Journal of Anaesthesia. 2013;7(3):322-6.
DOI:10.4103/1658-354X.115319
6. Mangold B, Oh C, Jaeger D, Terlinden R, Upmalis D. The pharmacokinetics of Tapentadol are not affected by omeprazole: results of a 2-way crossover drug-interaction study in healthy subjects. Pain Pract. 2007;7:55.
7. Daniels S, Casson E, Stegmann JU, Oh C, Okamoto A, Rauschkolb C, Upmalis D. A randomized, double-blind, placebo-controlled phase 3 study of the relative efficacy and tolerability of tapentadol IR and oxycodone IR for acute pain. Current Medical Research and Opinion. 2009;25(6):1551–1561.
Available:https://doi.org/10.1185/03007990902952825
8. Tzschentke TM, Christoph T, Schröder W, Englberger W, De Vry J, Jahnel U, Kögel BY. Tapentadol: mitzwei Mechanismen in einem Molekül Wirksam Gegen Nozizeptive und neuropathische Schmerzen. Präklinischer Überblick [Tapentadol: with two mechanisms of action in one molecule effective against nociceptive and neuropathic pain. Preclinical overview]. Schmerz. German. 2011;25(1):19-25.

DOI: 10.1007/s00482-010-1004-1. PMID: 21258822.

9. Javia, Ankit; Thakkar, Hetal. Intranasal delivery of Tapentadol Hydrochloride loaded chitosan nanoparticles: Formulation, characterization and its in-vivo evaluation. Journal of Microencapsulation. 2017;1–34. DOI:10.1080/02652048.2017.1375038
10. Hartrick CT. Tapentadol immediate release for the relief of moderate-to-severe acute pain. Expert OpinPharmacother. 2009;10(16):2687-96. DOI: 10.1517/14656560903313734. Erratum in: Expert OpinPharmacother. 2010;11(1):167. PMID: 19795998.
11. Terlinden R, Kogel BY, Englberger W, Tzschentke TM. In vitro and in vivo characterization of Tapentadol metabolites. Methods Find Exp Clin Pharmacol. 2010;32:31–38. DOI:10.1358/mf.2010.32.1. 1434165
12. Kneip C, Terlinden R, Beier H, Chen G. Investigations into the drug-drug interaction potential of Tapentadol in human liver microsomes and fresh human hepatocytes. Drug Metab Lett. 2008;2: 67–75.
13. Freo U, Romualdi P, Kress HG. Tapentadol for neuropathic pain: a review of clinical studies. J Pain Res. 2019; 12:1537-1551. DOI: 10.2147/JPR.S190162. PMID: 31190965; PMCID: PMC6529607.
14. Wade WE, Spruill WJ. Tapentadol hydrochloride: a centrally acting oral analgesic. Clin Ther. 2009;31(12):2804-18. DOI: 10.1016/j.clinthera.2009.12.003. PMID: 20110020.
15. Daniels, Stephen; Casson, Ed; Stegmann, Jens-Ulrich; Oh, Charles; Okamoto, Akiko; Rauschkolb, Christine; Upmalis, David. A randomized, double-blind, placebo-controlled phase 3 study of the relative efficacy and tolerability of Tapentadol IR and oxycodone IR for acute pain. Current Medical Research and Opinion. 2009; 25(6):1551–1561. DOI:10.1185/03007990902952825
16. Chang EJ, Choi EJ, Kim KH. Tapentadol: Can It Kill Two Birds with One Stone without Breaking Windows? Korean J Pain. 2016;29(3):153-7. DOI: 10.3344/kjp.2016.29.3.153. Epub 2016 Jul 1. PMID: 27413479; PMCID: PMC4942642.
17. Tzschentke TM, Jahnel U, Kogel B, Christoph T, Englberger W, De Vry J, Schiene K, Okamoto A, Upmalis D, Weber H, Lange C, Stegmann JU, Kleinert R. Tapentadol hydrochloride: a next-generation, centrally acting analgesic with two mechanisms of action in a single molecule. Drugs Today (Barc). 2009;45(7): 483-96. DOI:10.1358/dot.2009.45.7.1395291. Erratum in: Drugs Today (Barc). 2009;45(9):711. PMID: 19834626.
18. Muse D, Tarau E, Lefeber C, Sohns M, Brett M, Goldberg J, Rosenburg R. Pharmacokinetics, safety, and efficacy of Tapentadol oral solution for treating moderate to severe pain in pediatric patients. J Pain Res. 2019;12:1777-1790. DOI: 10.2147/JPR.S197039. PMID: 31213888; PMCID:PMC6549717.
19. Smit J, Oh C, Lannie C, Naessens I, Rengelshausen J, Upmalis D. Effects of probenecid on Tapentadol pharmacokinetics: results of an open-label, crossover, drug-drug interaction study. J Clin Pharmacol. 2009;49:1104.
20. Roulet L, Rollason V, Desmeules J, Piguet V. Tapentadol Versus Tramadol: A Narrative and Comparative Review of Their Pharmacological, Efficacy and Safety Profiles in Adult Patients. Drugs. 2021; 81(11):1257-1272. DOI: 10.1007/s40265-021-01515-z. Epub 2021 Jul 1. PMID: 34196947; PMCID: PMC8318929.

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