IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 10 Ver. VIII (Oct. 2015), PP 80-82
www.iosrjournals.org

Sublingual piroxicam for management of postoperative pain, trismus and swelling after extraction of lower third molars: an overview

Dr. LJ Balihallimath[1], Dr. Shruti SP[2]
[1](Professor, Oral and maxillofacial surgery, KLE University, India)
[2](Postgraduate, Oral and maxillofacial surgery, KLE University, India)

Abstract: *Extraction of third molars occupies a major portion of the clinical practice in oral and maxillofacial surgery. Post surgery sequelae are a part and parcel of this branch and this applies to minor oral surgical procedure as well. It is an indispensable part of healing and also responsible for the temporary discomfort caused to the patients. These postoperative sequelae include pain, trismus and swelling. Nonsteroidal anti-inflammatory drugs have been largely used postoperatively to decrease the amount of discomfort. Piroxicam is a non-selective, oxicam derivative available in oral as well as sublingual formulations. This article reviews its use in the postoperative management of pain, trismus and swelling after third molar extraction.*
Key words*: impaction, piroxicam, sublingual and third molars*

I. Introduction:

The surgical removal of impacted third molars is one of the most common minor oral surgery procedures widely carried out in general practice and also occupies an appreciable amount of clinical time in many hospitals in oral and maxillofacial departments[1]. It is often difficult for a patient to decide whether to remove a third molar,because of its post surgery complications, which are unavoidable. Patients complain of pain, swelling and limitation of mouth opening[2].

The pain is due to release of histamine, inflammatory mediator, from the injured tissues. Histamine, being a vasodilator, causes edema from the extravasation of fluids. This sensitizes the peripheral noci-receptors resulting in hyperalgesia. These inflammatory mediators are released immediately after the surgery (trauma caused to the tissues) but the symptoms are not experienced immediately. It is a gradual and slow process. The pain is typically brief and will increase in its intensity in the early postoperative period. The facial swelling and restriction of mouth opening will reach its maximum in 48 to 72 hours after surgery. These symptoms are major disadvantages and affect the patient's quality of life temporarily.[3, 4].

Various factors contribute to determine the intensity of post-operative complications such as host defense mechanism, type of healing, duration of the procedure, [5] extent of reflection of the mucoperiosteal flap, types of flaps, bone removal, need for tooth sectioning, and experience of the surgeon.[6,7] To increase patients satisfaction after third molar surgery it is necessary to minimize the subsequent postoperative sequelae.[8,9]

The treatment for these outcomes of surgery are many and most commonly includes administration of nonsteroidal anti-inflammatory drugs (NSAIDS) [2,10-13].

Most NSAIDs function by inhibiting cyclooxygenase (COX) enzyme and thus along with other actions, eventually result in inhibition of production of prostaglandin[14]. There are three isoforms of COX.[15] COX-1 is constitutive enzyme in most cells. COX-2 normally presents in insignificant amounts, is inducible by cytokines, growth factors and other stimuli during the inflammatory response[16]. COX-3, a COX-1 derived protein, is found in abundance in cerebral cortex and heart[15]. According to their actions, they have been classified as non-selective and COX-2 preferential or COX-2 selective.

Piroxicam is a non-selective, oxicam derivative, long-acting potent NSAID. It is a reversible inhibitor of COX with good analgesic-antipyretic action. Piroxicam also inhibits synthesis of thromboxane in platelets, thus inhibiting the secondary phase of platelet aggregation. It takes more than 30 minutes to produce appreciable relief of pain when administered orally. A formulation that could increase the absorption of the active ingredient, and therefore the onset of analgesia, would benefit in the postoperative pain management[17.]

NSAIDs can be administered sublingually. Sublingual administration of the drug avoids the first passage of drug in liver, unlike oral administration. Also orally administered NSAIDs pass through the gastrointestinal tract causing disturbances whereas sublingual administration avoids that[15].

There have been very few studies on the use of sublingual piroxicam in the management of postoperative sequelae after extraction of lower third molars.

II. Mechanism Of Action:

Piroxicam is a well-established NSAID with anti-inflammatory, analgesic and antipyretic properties. It is widely used in rheumatic diseases because of its potent anti-inflammatory properties and long half-life. Its elimination half-life is 38 hours, and hepatic metabolism to inactive metabolites is the primary route of elimination. Less than 10% of a dose appears unchanged in the urine. Published studies indicate that piroxicam 20mg daily is comparable with aspirin 3 to 6g, indomethacin 75 to 150mg, phenylbutazone 400mg, naproxen 500mg, ibuprofen 1200 to 2400mg and diclofenac 75mg in rheumatoid arthritis.[18]

Piroxicam, like many other NSAIDs, inhibits the secondary phase of platelet aggregation and synthesis of prostaglandins, but unlike indomethacin and aspirin, it is a selective reversible inhibitor of the COX step of arachidonic acid metabolism. Following administration of single doses, the pharmacokinetics of piroxicam is linear. Maximum plasma concentrations are usually attained in about 2 hours, but may vary between 1 and 6 hours in different subjects. Piroxicam is eliminated largely by biotransformation, the metabolites having little or no anti-inflammatory activity. The elimination half-life is extended due to a low systemic clearance rate and often ranges from 30 to 60 hours in healthy subjects. Pharmacokinetics are not age related and renal function has a limited influence on elimination of piroxicam, but plasma concentrations are increased in patients with severe liver insufficiency.[19]

The oral mucosal lining offers a preferable route for the local and systemic administration of certain drugs and for the treatment of some diseases. This route has several distinct advantages over the enteral and parenteral routes of drug delivery due to its rich blood supply, rapid onset of action, enhanced bioavailability, avoidance of the first pass and food effects, increased patient compliance, and ease of self-medication. Over the years, a number of products taking advantage of oral mucosal drug delivery have been introduced in the market.[20]

The oral cavity has four distinct regions that can absorb drugs—the sublingual, buccal, gingival, and palatal regions. These regions differ from each other in histological structure and biochemical composition of the mucosal membrane, and their ability to retain the dosage form long enough to allow complete drug absorption. [20]

The mucosal lining consists of three distinct layers. The outermost layer is the epithelial membrane, which consists of stratified squamous epithelial cells and has a protective barrier function. The innermost layer of the epithelial membrane is called the basement membrane that replenishes the epithelium. Below the epithelium lies the lamina propria followed by the submucosa. The lamina propria is a hydrated and less dense layer of connective tissue containing collagen and elastic fibers. The oral submucosa is also richly supplied with blood vessels.

Following absorption through the mucous membrane in the sublingual region, the drug instantly diffuses into venous blood. The venous blood from the sublingual region of the oral cavity drains into a common trunk, which then drains via the internal jugular vein, the subclavian vein, and the brachiocephalic vein directly into the superior vena cava. Thus, venous return from these regions enters the systemic circulation, bypassing the pre-systemic drug elimination, unlike in oral administration. Direct drainage into systemic circulation results in immediate systemic availability of the drug and rapid onset of action. It should be noted that smoking, which causes vasoconstriction, may affect drug absorption.[20]

III. Discussion:

The use of sublingual piroxicam in oral and maxillofacial surgery when searched on Pubmed gave 3 articles.

P.A.K. Trinade , F.P. M. Giglio et al[17] have conducted a study with 53 patients receiving piroxicam either orally or sublingually after undergoing an extraction of the symmetrically positioned lower third molars. Surgical trauma on either side of the jaw was similar without significant difference. The patients were randomly given piroxicam either orally or sublingually for postoperative pain relief. Subjective postoperative pain was documented with the help of 100mm VAS. The amount and the time when rescue analgesic was noted. Mouth opening was measured before the surgery, 2nd and 7th postoperative day, and expressed as a percentage of the preoperative value. Facial swelling was measured similarly on the 2nd and 7th postoperative day. No significant differences were found in the management of pain, trismus and swelling with respect to the routes of drug delivery. Six patients had gastric discomfort when oral piroxicam was used and one patient complained of the when on administration of sublingual piroxicam.

Mohammad S, Singh V, Wadhwani P et al[21] conducted a study to assess the therapeutic effect of a single dose of 40 mg sublingual piroxicam (study group) vs 150 mg oral diclofenac (50 mg thrice a day) (control group) in patients undergoing surgical removal of impacted mandibular third molar. A total of 100 patients with asymptomatic impacted mandibular third molars were randomized into two groups. One group received two 20-mg tablets of piroxicam once daily on the first and second postoperative days, followed by one 20-mg tablet on the third post-operative day. The other group received one tablet of diclofenac 50 mg orally thrice daily on the

first, second, and third post-operative days. Repeated extra oral examinations were done for continuous assessment of swelling, trismus, and reduction in pain. In the piroxicam group there was >50% reduction in pain on all three days postoperatively. The incidence of swelling and trismus was found to be higher in the control group as compared to the study group. Adverse events, such as gastrointestinal (GI) disturbances, were significantly higher in the diclofenac group (11%) as compared to the piroxicam group (0%). They concluded that two sublingual piroxicam 20 mg tablets once daily has better efficacy and tolerability profile than diclofenac 50 mg one tablet thrice daily in the management of pain after surgical removal of impacted mandibular third molar.

A study conducted by Alpaslan C, Alpaslan G and Uğar D[22], comparing single doses of sublingually administered piroxicam and aspirin for the postoperative pain management after extraction of the lower third molars. The aim of this study was to assess and compare the efficacy of the two drug formulations and also a placebo. A total of 100 patients were included in this study. Patients received piroxicam fast dissolving dosage formulations (FDDF) (40 mg) either preoperatively or post-surgery, sublingually or aspirin (500 mg) or a placebo. Six hours postoperatively, pain was recorded every hour. Significant difference ($p<0.05$) was found with respect to piroxicam as compared to aspirin or placebo. Also amount of rescue analgesic were recorded and were found to be considerably less for piroxicam FDDF. No adverse reactions were reported with piroxicam usage. They concluded that piroxicam FDDF, administered either preoperatively or postoperatively, can be effectively used after a third molar surgery.

Thus sublingual piroxicam is effective for management of postoperative pain in oral and maxillofacial surgery but to conclude further studies with larger sample sizes are needed.

Acknowledgement:

We would like to thank Dr. Shridhar Baliga and Dr. Abhishek Motimath for extending help and support.

References

[1]. C. Mc Grahh, M. B. Comfort, E. C. M. Lo and Y.M. Luo. Changes in life quality following third molar surgery- the immediate postoperative period. British Dent Jr., March 2003; 194: 265-268.
[2]. Yakup Ustun, Ozgur Erdogan, Emin Esen and Ebru Deniz Karsli. Comparison of the effects of 2 doses of methylprednisolone on pain, swelling, and trismus after third molar surgery. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003; 96:535-9
[3]. Sinclair DC. Cutaneous sensation and the doctrine of specific energy. Brain 1955; 78(4):584-614.
[4]. Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965; 150(3699):971-9.
[5]. Micah G, Godwin T A, and A L. Assessment of Factors Associated with Surgical Difficulty in Impacted Mandibular Third Molar Extraction .Journal of oral and maxillofacial surgery2007; 65(10):1977-83
[6]. Ten Bosch JJ, Van Gool AV. The interrelation of postoperative complaints after removal of the mandibular third molar. Int J Oral Surg 1977; 6(1): 22-28.
[7]. Van Gool AV, TenBosch JJ, Boering G. Clinical consequences of complaints and complications after removal of the mandibular third molar. Int J Oral Surg 1977; 6(1): 29-37
[8]. Pedersen A. Interrelation of complaints after removal of impacted mandibular third molar. Int J Oral Surg 1985; l4(3): 241-244
[9]. Sisk AL, Hammer WB, Shelton DW, Joy ED. Complications following removal of impacted third molars: the role of the experience of the surgeon. J Oral Maxillofacial Surg 1986; 44(11) : 855-859
[10]. Paulo A. K. Trinade, Fernando P.M., Colombini-Ishikiriama et al. Sublingual ketorolac and sublingual piroxicam are equally effective for post-operative pain, trismus, and swelling management in lower third molar removal. Oral Surgery Oral Med Oral Pathol Oral Radiol 2012; 114:27-34.
[11]. Calvo AM, Sakai VT, Modena KCS, Colombini BL et al. Comparison of efficacy of etoricoxib and ibuprofen in pain and trismus contraol after lower third molar removal. Rev Odontol UNICID 2006;18:29-36
[12]. Barden J, Edwards JE, McQuay HJ, Wiffen PJ, Moore RA. Relative efficacy of oal analgesics after third molar extraction. Br Dent J 2004; 197:407-11
[13]. Urquhart E. Analgesic agents and strategies in the dental pain model. J Dent 1994;22:336-41
[14]. Lee Y, Rodiguez C, Dionne RA. The role of cox-2 in acute pain and the use of selective cox-2 inhibiors for acute pain relief. Curr Pharm Des 2005; 11:1737-1755
[15]. P. A. K. Trinade, F. P. M. Gigilio, B. L. collombini-Ishikriama et al. Comparison of oral versus sublingual piroxiam during postoperative pain management after third molar extraction. Int. J. Oral Maxillofac. Surg, 2011; 40: 292-297
[16]. Brogden RN, Heel RC, Speight TM, Avery GS. Piroxicam: a review of its pharmacological properties and therapeutic efficacy.Drugs. 1981 Sep; 22(3):165-87.
[17]. R. N. Brogden, R. C. Heel, T. M. Speight, G. S. Avery. Piroxicam A Reappraisal of its Pharmacology and Therapeutic Efficacy. Drugs.October 1984, Volume 28, Issue 4, pp 292-323
[18]. Vilayat A. Sayeed, Muhammad Ashraf .Pharmaceutical Technology,Volume 38, Issue 11. Considerations in Developing Sublingual Tablets—An Overview
[19]. Shadab Mohammad, Vibha Singh, Puneet Wadhwani, Himanshu P Tayade, Onkar K Rathod. Sublingual piroxicam in the management of postoperative pain after surgical removal of impacted mandibular third molar. Indian journal of Dental Research 2012; 6: 839-840
[20]. Alpaslan C, Alpaslan G, Uğar D. Postoperative pain control by single doses of piroxicam administered sublingually and aspirin. J Marmara Univ Dent Fac. 1997 Sep; 2(4):658-64.