A Comparative Study of the Effect of Prednisolone and Celecoxib on MMO (Maximum Mouth Opening) and Pain Following Removal of Impacted Mandibular Third Molars

Ali Akbar Moghaddamnia · Kamran Nosrati ·
Mohammad Mehdizadeh · Shabnam Milani ·
Maral Aghvami

Received: 11 February 2012 / Accepted: 28 May 2012 / Published online: 24 August 2012
© Association of Oral and Maxillofacial Surgeons of India 2012

Abstract

Objective The purpose of this study was to compare the effects of prednisolone and celecoxib on pain and maximum mouth opening (MMO) after surgical removal of mandibular third molars.

Methods and Materials This double-blind clinical study was conducted upon 60 subjects. These patients received 4 tablets of either 100 mg celecoxib or 5 mg prednisolone: one tablet before surgery and the rest for every 8 h post-operation. The subjects were asked to take acetaminophen codeine as rescue dose. Interincisal distance of upper and lower central teeth and pain measurements (according to Visual Analogue Scale) were taken before surgery, 24 h, 48 h and 7 days after surgery.

Results Average pain intensity in 24 h after surgery in patients receiving celecoxib was 3.6 ± 2.5 with significant difference to the other group ($p = 0.041$), but in subsequent evaluations prednisolone group reported less pain intensity, but the differences were not significant. MMO in 48 h after surgery was lower in prednisolone group ($p = 0.640$) and in further evaluations the groups were almost similar. Analyzing the data revealed no significant difference between groups in MMO.

Conclusion According to this study there is no significant difference in the effects of prednisolone or celecoxib upon

MMO, while celecoxib had better results for pain relief in 24 h after surgery in comparison to prednisolone.

Keywords Celecoxib · Prednisolone · Pain · Maximum mouth opening · Third molar surgery

Introduction

Removal of impacted third molars is a common procedure in the field of oral and maxillofacial surgery [1]. The most important step in removal of impacted mandibular third molars is achieving an appropriate mucoperiosteal flap that provides enough access to the tooth. An envelope flap with or without releasing is the common flap design [2].

Pain generated following third molar surgery has got short duration and moderate intensity that peaks in short time after the procedure and drives the patients into taking some analgesic medications [3].

Limitation of mouth opening is one of the problems which occurs following this surgery; this could be related to the inflammation of masticatory muscles. The medial pterygoid muscle is usually involved because of being inadvertently penetrated by the needle during inferior alveolar nerve block injection. This complication is not often severe and it will improve in 10–14 days [4].

Glucocorticoid agents and NSAIDs are generally used in managing some post-operation difficulties. Inhibiting the cyclooxygenase path is the mechanism of action of NSAIDs while glucocorticoids restrain production of acid arachidonic by inhibiting the phospholipase A2 enzyme [5]. COX-2 is considered as the main isoenzyme in producing pro-inflammatory prostaglandins [3]. Although some side effects such as cardiovascular risks, GI bleeding and acute renal failure should be kept in mind [6], some recent

A. A. Moghaddamnia · S. Milani (✉) · M. Aghvami
Pharmacology Department, Faculty of Medicine, Babol
University of Medical Sciences, Babol, Iran
e-mail: shabnammilani@aol.com

K. Nosrati · M. Mehdizadeh
Department of Oral and Maxillofacial Surgery, Faculty of
Dentistry, Babol University of Medical Sciences, Babol, Iran

studies showed that there is no relationship between celecoxib consumption and mentioned risks [7, 8]. The aim of this study was to compare the efficacy of prednisolone with celecoxib on maximum mouth opening (MMO) and pain relief following impacted mandibular third molar surgery.

Methods and Materials

This clinical trial, double blind study was conducted upon 60 patients aging 18–25 years who referred to Babol professional clinic of dental school and needed surgical removal of their impacted mandibular third molars.

Drugs used in this study—prednisolone (5 mg) and celecoxib (100 mg)—were separately encapsulated and encoded by the Department of Pharmacology, Babol University of Medical Sciences.

Patients having any systemic diseases were excluded and none of them had any anti-inflammatory medications in 7 days before surgery. Written consent was taken from our patients. Removal of the desired tooth was in moderately difficult group according to Fonseca classification of impacted third molars [2] and all the procedures were conducted by same surgeon. The patients were randomly distributed into two groups of 30 and received either celecoxib or prednisolone. They had their first dose 30 min before surgery and the other three capsules every 8 h after procedure. Follow up measurements for MMO and pain were done in 24 h, 48 h and 7th day after surgery. Their inter-incisal distance was measured using a Vernier caliper with accuracy of 0.02 mm. Pain measurement was conducted via VAS approach. Patients were also prescribed to have Amoxicillin (500 mg) every 8 h for 7 days after surgery. Anesthesia was made by inferior alveolar nerve block, lingual nerve block and long buccal nerve block with use of 2 % lidocaine with 1:80,000 epinephrine. Patients receiving more than three inferior alveolar nerve block injections were excluded from the investigation.

All surgical flaps were conventional ones with a releasing flap in the mesial side of second molar and they

were sutured by silk 3-0. Patients could have acetaminophen codeine as rescue dose in case of experiencing severe pain and they also reported the number of tablets they had in first 24 h. VAS data was analyzed by Mann–Whitney test and Student's *t* test for MMO and repeated measures test for both items and $p < 0.05$ was considered as statistical significant.

Results

Each group consisted of 30 patients; sex distribution in these groups was almost similar: 15 men and 15 women in celecoxib group and 13 men and 17 women in prednisolone group. Age limit was 18–25 years with the mean of 21.9 ± 2.4 in celecoxib group and 23.4 ± 1.8 in prednisolone group.

Comparing Pain Intensity Reported by Patients

Average reported pain in both groups was highest in 24 h after surgery and its minimum was on 7th day. Pain intensity was significantly lower in celecoxib group in 24 h after surgery, but in further evaluations no significant difference was observed (Table 1; Fig. 1).

Comparing Maximum Mouth Opening Measurements in Patients

Average of MMO measured in both groups was minimum in 24 h after surgery and its maximum was before the procedure. There was not any significant difference in none of the four measuring times (Table 2).

Repeated measures test showed significant differences within subjects for both VAS and MMO with $p < 0.0001$ but there were not any significant difference between subjects.

Comparing rescue dose taken by patients

No significant difference was observed in amount of rescue dose taken by patients (Table 3).

Fig. 1 VAS changes by time in patients receiving prednisolone or celecoxib after surgical removal of impacted mandibular third molars in four measuring times

Table 1 Mean $\pm$ SD for VAS in patients receiving prednisolone or celecoxib after surgical removal of impacted mandibular third molars in four measuring times

Groups	VAS			
	Before surgery	24 h	48 h	168 h
Celecoxib	0.8 $\pm$ 2.1	3.6 $\pm$ 2.5	2.2 $\pm$ 1.8	0.1 $\pm$ 0.4
Prednisolone	0.5 $\pm$ 2.0	4.9 $\pm$ 2.6	1.8 $\pm$ 2.2	0
<i>p</i> Value	NS	0.041	NS	NS

NS not significant

Table 2 Mean $\pm$ SD for MMO in patients receiving prednisolone or celecoxib after surgical removal of impacted mandibular third molars in four measuring times

Groups	MMO			
	Before surgery	24 h	48 h	168 h
Celecoxib	44.5 $\pm$ 6.9	30.4 $\pm$ 7.3	34.3 $\pm$ 7.3	42.5 $\pm$ 7.5
Prednisolone	46.6 $\pm$ 7.7	31.1 $\pm$ 10.3	33.2 $\pm$ 9.9	42.3 $\pm$ 8.9
<i>p</i> Value	NS	NS	NS	NS

MMO maximum mouth opening, NS not significant

Table 3 Mean $\pm$ SD for rescue dose taken by patients receiving prednisolone or celecoxib after surgical removal of impacted mandibular third molars in 24 h after surgery

Groups	Intake of rescue dose mean $\pm$ SD
Celecoxib	2.5 $\pm$ 1.9
Prednisolone	2.7 $\pm$ 2.0
<i>p</i> Value	NS

NS not significant

Discussion

There have been many surveys investigating the influence of administration of NSAIDs or glucocorticoid drugs on post-operative inflammation, but as a result of differences in inflammation assessment, prescriptive drugs, patterns of administration and provided dose, the comparison between the results is rather impossible.

In this study, the efficacy of prednisolone and celecoxib on MMO and pain relief after surgical removal of impacted mandibular third molars was compared.

According to the results, pain intensity in 24 h in patients receiving celecoxib was significantly lower than the other group; while in 48 h and 7th day after the procedure, the changes were in favor of the prednisolone group. This may be due to the effect of NSAIDs which is faster than Glucocorticoids. It is possible that with changing the design of this study or increasing the number of samples in each group the potential differences become more distinguishable. This fact may specially be more prominent about prednisolone rather than celecoxib.

We can probably conclude that COX-2 pathway in metabolic cascade of acid arachidonic is more efficient in production of pain and limitation in mouth opening following surgical removal of impacted mandibular third molars [9], since this route is the only one hindered by both drug types investigated in this study.

Carriches et al. compared the efficacy of methylprednisolone (glucocorticoid) versus diclofenac (NSAID) upon

inflammation and trismus after removal of impacted mandibular teeth. They also did not find any significant difference between groups [10]. Claseman et al. [11] assessed the analgesic efficacy of preemptive ketorolac and dexamethasone for third molar surgery. According to their results, the pain and the amount of having extra analgesics reported by patients receiving 8 mg IV dexamethasone did not have significant difference with patients receiving 30 mg IV Ketorolac [11]. In this study, celecoxib had better effects on pain relief in 24 h after surgery; this difference may be related to different routes of drug administration.

Moore et al. evaluated the effects of rofecoxib and dexamethasone on pain and trismus after third molar surgery. In their study, MMO of patients receiving dexamethasone had a reduction of 24.1 % from the base limit while the rofecoxib group had 43.3 %. Reported pain did not show any significant differences and both groups had moderate pain perception [12]. Mouth opening and pain conditions in Moore's study were better than ours. These differences may be contributed to the type of rescue dose given to patients which was 400 mg ibuprofen. Ibuprofen is a NSAID type of drug and can add on anti-inflammatory response and effects of rofecoxib or dexamethasone.

There are many studies for evaluating the efficacy of whether a glucocorticoid or NSAID medication on post operative complications. It has shown that there is more reduction in pain and trismus following submucosal infiltration of dexamethasone or methylprednisolone rather than control group [13]. According to Milles' study trismus and need of taking extra analgesic medications were not affected by administration of low-dose methylprednisolone [14]; whereas Baxendale et al. [15] observed the elimination of analgesic intake by administering pre-operative dexamethasone while trismus was not affected. Various results in pain and mouth opening were found by Shin et al. [16] while Bamgbose et al. [17] observed better results by administering dexamethasone and diclofenac K rather than diclofenac K alone. In another study, Buyukkurt et al. [18] found the combination of prednisolone and diclofenac more effective than the diclofenac group or the control one.

Some articles suggest having NSAIDs for post-operative pain management [18, 19] and others prefer glucocorticoids for managing post-operative edema and trismus [18, 20]. This effect can be related to the role of prostaglandins in local pain and their inhibition by NSAIDs will result in pain relief. Glucocorticoids are effective in each step of inflammation process and subsequent decrease in capillary dilation, circulating lymphocytes, fibroblast proliferation and prostaglandin and leukotriene inhibition. Most single dose glucocorticoid drugs used in oral surgeries are not effective for more than 24 h, so for maintaining their anti-inflammatory effects they should be taken for a minimum

of 3 and maximum of 5 days for gaining the maximum efficiency and minimum risk of delayed healing and suppression of HPA axis [5].

It is possible that combining the both drug types—NSAIDs and glucocorticoid drugs—will be more efficient in post-operative management of complications [12, 16–18].

Conclusion

The use of non steroidal anti-inflammatory or glucocorticoid drugs is a useful approach in reducing complications after oral surgery. In this study, we compared the efficacy of celecoxib and prednisolone on some complications following third molar surgery. According to the results of this research, prednisolone and celecoxib have the same effects on MMO; while celecoxib showed better results in acute pain relief. However, further investigations need to be carried out for obtaining a precise conclusion.

References

1. Sands T, Pynn BR, Nenniger S (1993) Third molar surgery: current concepts and controversies. Part 1. *Oral Health* 83(5):11–4, 17
2. Fonseca RJ (2000) *Oral and maxillofacial surgery*, vols 1, 2, 1st edn. Saunders, Philadelphia, pp 122, 256–260
3. Calvo AM, Sakai VT, Modena KCS, Colombini BL, Gallina MC et al (2006) Comparison of the efficacy of etoricoxib and ibuprofen in pain and trismus control after lower third molar removal. *Revista de Odontologia da Universidade Cidade de Sao Paulo* 18:29–36
4. Hupp JR, Ellis E, Tucker MR (2008) *Contemporary oral and maxillofacial surgery*, 5th edn, chap 9. Elsevier, Mosby
5. Kim K, Brar P, Jakubowski J, Kaltman S, Lopez E (2009) The use of corticosteroids and nonsteroidal anti-inflammatory medication for the management of pain and inflammation after third molar surgery: a review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 107:630–640
6. Gage T, Pickett F (2001) *Mosby's dental drug reference*, 5th edn. Elsevier Mosby, St. Louis, pp 122, 551
7. Fosbøl EL, Folke F, Jacobsen S, Rasmussen JN, Sørensen R, Schramm TK et al (2010) Cause-specific cardiovascular risk associated with nonsteroidal anti-inflammatory drugs among healthy individuals. *Circ Cardiovasc Qual Outcomes* 3:395–405
8. Wenner MM, Edwards DG, Ray CA, Rose WC, Gardner TJ, Stillabower M et al (2011) Celecoxib does not alter cardiovascular and renal function during dietary salt loading. *Clin Exp Pharmacol Physiol* 38:543–549
9. Seibert K, Zhang Y, Leahy K, Hauser S, Masferrer J, Perkins W et al (1994) Pharmacological and biochemical demonstration of the role of cyclooxygenase 2 in inflammation and pain. *Proc Natl Acad Sci USA* 91:12013–12017
10. Carriches CL, Gonzalez JM, Rodriguez MD (2006) The use of methylprednisolone versus diclofenac in the treatment of inflammation and trismus after surgical removal of lower third molars. *Med Oral Pathol Oral Cir Bucal* 11:E440–E445
11. Claseman T, Foley W, Davis R, Morrison J, Palmore C, Murchison D (1998) A clinical evaluation of the analgesic efficacy of preoperative administration of ketorolac and dexamethasone following surgical removal of third molars. *Anesth Prog* 45:110–116
12. Moore PA, Brar P, Smiga ER, Costello BJ (2005) Preemptive rofecoxib and dexamethasone for prevention of pain and trismus following third molar surgery. *J Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 99:E1–E7
13. AL-Khateeb TL, Marouf HA, Mahmoud MA (1996) Clinical evaluation of dexamethasone vs. methylprednisolone for reducing post-operative inflammatory sequelae following third molar surgery amongst preschool children in Jeddah, Saudi Arabia. *Saudi Dental J* 8:13–18
14. Milles M, Desjardins PJ (1993) Reduction of postoperative facial swelling by low dose methylprednisolone: an experimental study. *J Oral Maxillofac Surg* 51:987–991
15. Baxendale BR, Vater M, Lavery KM (1993) Dexamethasone reduces pain and swelling following extraction of third molar teeth. *Anaesthesia* 48:961–964
16. Shin Kh, Lee JK, Hwang BN (2001) The clinical study on the effect of dexamethasone and naproxen to the symptoms after removal of impacted lower third molars. *J Korean Assoc Oral Maxillofac Surg* 27:69–77
17. Bamgbose BO, Akinwande JA, Adeyemo WL, Ladeinde AL, Arotiba GT, Ogunlewe MO (2005) Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling and trismus following third molar surgery. *Head Face Med* 1:11
18. Buyukkurt MC, Gungormus M, Kaya O (2006) The effect of a single dose prednisolone with and without diclofenac on pain, trismus and swelling after removal of mandibular third molars. *J Oral Maxillofac Surg* 64:1761–1766
19. Hyrkas T, Ylipaavalniemi P, Okarinen VJ, Paakkari I (1993) A comparison of diclofenac with and without single-dose intravenous steroid to prevent postoperative pain after third molar removal. *J Oral Maxillofac Surg* 51:634
20. Gersema L, Baker K (1992) Use of corticosteroids in oral surgery. *J Oral Maxillofac Surg* 50:270–277