Journal section: Oral Surgery *doi:10.4317/jced.i.e469*
Publication Types: Review

Corticosteroids use in controlling pain, swelling and trismus after lower third molar surgery.

J. Ata-Ali [1], F. Ata-Ali [2], D. Peñarrocha-Oltra [3], M. Peñarrocha [4]

[1] DDS. Primary care dental surgeon, Valencian Health Agency. Master in Oral Surgery and Medicine. Master in Oral Surgery and Implantology. Valencia University Medical and Dental School.
[2] DDS. Valencia University Medical and Dental School.
[3] DDS. Resident of the Master in Oral Surgery and Implantology. Valencia University Medical and Dental School.
[4] Chairman of Oral Surgery. Director of the Master in Oral Surgery and Implantology. Valencia University Medical and Dental School. Valencia (Spain)

Correspondence:
Cirugía Bucal. Clínicas Odontológicas
Gascó Oliag 1
46021- Valencia (Spain)
E-mail: javiataali@hotmail.com

Received: 22/04/2011
Accepted: 03/09/2011

Ata-Ali J, Ata-Ali F, Peñarrocha-Oltra D, Peñarrocha M. Corticosteroids use in controlling pain, swelling and trismus after lower third molar surgery. J Clin Exp Dent. 2011;3(5):e469-75.
http://www.medicinaoral.com/odo/volumenes/v3i5/jcedv3i5p469.pdf

Article Number: 50560 *http://www.medicinaoral.com/odo/indice.htm*

eMail: jced@jced.es

Abstract

Objectives: A study is made of corticosteroid use in controlling pain, swelling and trismus after lower third molar surgical removal.

Material and methods: A Medline search and review was made of all randomized and controlled clinical trials on the effects of corticosteroids upon pain, swelling and trismus after lower third molar surgery. The review was limited to those studies published in the last 10 years. Of the 20 initially considered articles, 6 were finally excluded.

Results: A total of 14 articles were included. In 5 of the studies, corticosteroid use resulted in statistically significant reductions in pain after third molar removal. In 7 of the 11 articles that analyzed the effect of corticosteroid use upon postoperative swelling, such treatment was seen to be effective. In 8 of the 11 articles that analyzed the effect of corticosteroid use upon trismus, significant benefit was observed.

Conclusion: The results of the analysis of the benefits derived from corticosteroid use in relation to pain, swelling and trismus following third molar surgical extraction, and the few side effects observed after the short-term use of such medication, point to corticosteroids as a treatment option to be taken into account in such patients.

Key words: *Corticosteroids, pain, third molar, trismus, oral surgery, swelling*

Introduction

The first published article on the use of hydrocortisone in oral surgery dates back to 1952 (1). Corticosteroids (CS) are used for a number of purposes – fundamentally as replacement therapy in patients with adrenal gland insufficiency, as immunosuppressive therapy, and as antiinflammatory treatment. The use of CS may prove life-saving in patients with anaphylactic shock, and can prolong survival in patients with autoimmune diseases (2). The most widely used CS are betamethasone, dexamethasone and methylprednisolone administered via the intravenous, oral or intramuscular route (3). In a study of rationale CS dispensation in pharmacy offices, the most widely prescribed drug was seen to be prednisone (87%), followed by dexamethasone (13%)(2).

Lower third molar removal is common in oral surgical practice, since impacted molar rates of up to 40% have been reported (4). Such conditions normally cause acute inflammation with intense discomfort as well as pain, trismus and swelling during the postoperative period (5). Pain sensation is subjective and can be influenced by different factors such as patient age, sex, anxiety and surgical difficulty (6). In this sense, longer operations are typically associated with more pain, and the pain furthermore increases with the difficulty of the operation (7).

The present study explores the effect of corticosteroid use in controlling pain, swelling and trismus after lower third molar surgical removal.

Article	Patients taking CS	Controls	Sex F/M (test/control)	Mean age(test/control)	CS used	Dose/route	Timing	Analgesic efficacy after 48 h
Üstün et al. 2003 (8)	21	21	NA	NA	Methylprednisolone	1.5 mg/kg/IV	Preop.	p>0.05
						3 mg/kg/IV	Preop.	
Dionne et al. 2003 (9)	33	28	27F/6M 19F/9M	19.9±3.6 19.6±3.6	Dexamethasone	4 mg/PO	Preop.	p>0.05
Moore et al. 2005 (10)	9	20	5F/4M 13F/7M	23.4/ 22.3	Dexamethasone	10 mg/IV	Intraop.	p>0.05
Lopez-Carriches et al. 2005 (11)	37	36	27F/10M 19F/17M	23.4/23.6	Methylprednisolone	4 mg/PO	Postop.	p=0.080
Mico-Llorens et al. 2006 (12)	31	31	16F/15M	22±2.8	Methylprednisolone	40 mg/IM	Postop.	p<0.05
Buyukkurt et al. 2006 (13)	15	15	6F/9M 5F/10M	23.53±4.17 23.22±3.62	Prednisolone	25 mg/IM	Postop.	p<0.05
Graziani et al. 2006 (14)	43	43	30F/13M	24±4	Dexamethasone	4 mg/IA	NA	p>0.05
						10 mg/IA	NA	
						4 mg/SM	NA	
Grossi et al. 2007 (15)	38	23	28F/33M	27.1/28.7	Dexamethasone	4 mg/SM	Intraop.	p>0.05
						8 mg/SM	Intraop.	
Leone et al. 2007 (16)	46	44	28F/18M 27F/17M	20±5/20±5	Methylprednisolone	1 mg/kg/IV	Preop.	p>0.05
Laureano Filho et al. 2008 (17)	30	30	NA	19.5	Dexamethasone	4 mg/NA	Preop.	p>0.05
						8 mg/NA	Preop.	
Vegas-Bustamante et al. 2008 (18)	35	35	17F/18M	25	Methylprednisolone	40 mg/IM	Postop.	p<0.05
Zandi 2008 (5)	11	11	NA	NA	Dexamethasone	8 mg/IV	Preop.	p<0.05
					Methylprednisolone	15 mg/PO	Postop. (12 h)	
Chopra et al. 2009 (19)	30	120	12F/18M 46F/74M	27.93/28.08	Betamethasone	0.5 mg/PO	Postop.	p<0.001
Kang et al. 2010 (20)	124	96	NA	NA	Prednisolone	10 mg/PO	Preop.	p>0.05
						20 mg/PO	Preop.	

CS: corticosteroids; F: female; M: male; NA: non-available; IV: intravenous; PO: oral route (per os); IA: intraalveolar; IM: intramuscular; SM: submucosal

Table 1. *Effects of corticosteroids upon pain after third molar extraction.*

Material and Methods

A Medline search and review was made of all randomized and controlled clinical trials on the effects of corticosteroids upon pain, swelling and trismus after lower third molar surgery. The review was limited to those studies published in the last 10 years. Six of the 20 initially considered studies were excluded: 5 because CS use was associated to some other type of medication, and one because only saliva cortisol levels were investigated. A total of 14 articles were thus finally included (Table 1), with documentation of the following from each of them: year of publication, number of patients in the study and control groups, sex, mean age, CS administered, dosage, administration route, timing of administration, analgesic efficacy, antiinflammatory effect and the method used to measure it, and trismus and its measurement method..

General effects of corticosteroids

Corticosteroids exert potent antiinflammatory action, and have been used in different dosing regimens and administration routes to lessen the inflammatory effects of third molar surgical removal. Methylprednisolone is usually administered via the intramuscular or intravenous route (8, 12, 16, 18), though the possibility of topical (intraalveolar) application has been described, with a reduction in morbidity and possible side effects (14). Methylprednisolone has been used in a number of studies (5, 8, 12, 16, 18, 21-24). This drug is five times more potent than cortisol, with scant associated saline retention and an intermediate duration of action (12-36 hours)(11). Table 2 shows the different types of CS according to their potency.

CS induce the synthesis of endogenous proteins, which block the enzymatic activation of phospholipase A2. Block exerted at this point in turn inhibits arachidonic acid release by the cell membrane components, with ulterior inhibition of the synthesis of prostaglandins, leukotrienes or substances related to thromboxane. These effects constitute the basis of CS use in clinical practice, though they are also responsible for some of the serious effects associated with chronic CS administration (25).

Side effects of corticosteroids

The side effects of prolonged CS use are well known, and are fundamentally dependent upon the dose employed and the duration of treatment (20). A study found up to 19% of all patients to experience adverse reactions after the postoperative administration of 0.5 mg of betamethasone via the oral route (19). These effects include peptic ulcer, immune suppression, water and electrolyte balance metabolic effects, muscle atrophy, osteoporosis, increased fatty tissue (full moon facial appearance), Cushing syndrome, avascular osteonecrosis, lessened resistance to infection, hirsutism, amenorrhea, acne, hyperglycemia or hypertension (2, 5, 20). Exogenous CS exert a negative feedback effect upon the hypothalamic-hypophyseal-adrenal gland axis, suppressing the normal secretion of endogenous cortisol. This is important when temporary suppression gives way to chronic adrenal gland suppression. Doses in excess of 20 mg of hydrocortisone (> 4 mg of methylprednisolone) or 50 mg of prednisolone (> 40 mg of methylprednisolone) in long-term administration can cause adrenal gland suppression. Such suppression can also be observed when the physiological levels are elevated for more than 5 days, or when CS are administered for over 1-2 weeks. This explains why such medication should be suspended gradually (3).

Effects of corticosteroids in combination with other drugs

Many studies (26-29) have used CS in combination with other drugs to evaluate their effect upon pain, swelling and trismus. Statistically significant findings ($p<0.05$) have been reported when CS are used in combination with drugs such as diclofenac in application to pain and swelling, but not in reference to trismus (28). Statistically significant results ($p<0.05$) have also been obtained when using Rheumazin® (combination of 10 mg piroxicam, 1 mg dexamethasone, 35 mg orphenadrine citrate and 2.5 mg cyanocobalamin)(26).

Tiigimae-saar et al. (27) recorded a statistically signifi-

Type of CS	Antiinflammatory potency	Half-life (hours)	Equivalent dose with antiinflammatory effect
Cortisol	1	8-12	20 mg
Prednisolone	3-5	12-36	5 mg
Methylprednisolone	3-5	12-36	4 mg
Triamcinolone	3-5	12-36	4 mg
Betamethasone	20-30	36-54	0.6 mg
Dexamethasone	20-30	36-54	0.75 mg

CS: corticosteroids

Table 2. *Types of corticosteroids according to their potency, half-lives and equivalent doses.*

cant relationship ($p<0.05$) in reference to pain, swelling and trismus on combining 30 mg of prednisolone with 120 mg of etoricoxib 30 minutes after surgery.

Van Eeden and Bütow (29), following the administration of Covomycin D® (combination of dexamethasone, chloramphenicol and neomycin), recorded a reduction in postoperative pain in 57.9% of their patients in the first 24 hours. This percentage increased to 84.2% on the sixth postoperative day. In turn, 73.7% of the patients showed a lessening of the swelling.

Effects of corticosteroids upon pain

The use of CS for the prevention of postoperative pain is subject to controversy, in view of the production of both beneficial and side effects. Different studies have related CS administration to a reduction in postoperative complications. CS are employed particularly after surgery to reduce the presence of inflammatory mediators and thus lessen fluid transudation and edema (9, 14). Although many studies have reported statistically significant analgesic action with CS use (5, 12, 13, 18, 19), others have found the analgesic efficacy of CS to lack statistical sig-

Article	Timing of measurement	Measurement method	p-value (day 2)	p-value (day 7)
Üstün et al. 2003 (8)	Day 2 and 7	Modification of the method of Gabka and Matsunara (34)	p=0.541	p=0.710
Mico-Llorens et al. 2006 (12)	Day 2 and 7	Method of Amin and Laskin (33)	D1 P=**0.002**	p>0.05
			D2 P=**0.003**	
			D3 P=**0.038**	
Graziani et al. 2006 (14)	Day 2 and 7	Method of Amin and Laskin (33)	**p<0.05**	p>0.05
Buyukkurt et al. 2006 (13)	Day 2 and 7	Method of Amin and Laskin (33)	**p=0.001**	p=0.001
Grossi et al. 2007 (15)	Day 2 and 7	Modification of the method of Schultze-Mosgau (23)	**p=0.001**	p>0.05
Leone et al. 2007 (16)	Postop. (4 h)	Patient questioning (0=No edema/1=Edema)	p=0.09	NA
Laureano Filho et al. 2008 (17)	Preop., day 1 and 2	Measurement chin angle and 4 facial points: tragus; external canthus of eye; lip commissure and nostril	**p<0.05**	NA
Zandi 2008 (5)	Day 2 and 7	Distance tragus-lip commissure; gonion-external canthus of eye	**p<0.05**	p<0.05
Vegas-Bustamante et al. 2008 (18)	Day 2 and 7	Method of Amin and Laskin (33)	D1 p=**0.000**	D1 p=0.001
			D2 p=**0.000**	D2 p=0.002
			D3 p=**0.018**	D3 p=0.395
Chopra et al. 2009 (19)	Day 1, 3, 5 and 7	Distance tragus-lip commissure; tragus-pogonion; gonion-external canthus of eye; tragus-gonion	p<0.001*	p>0.05
Kang et al. 2010 (20)	Day 1, 2, 3, 4, 5 and 6	NA	p>0.05	p>0.05**

*p-value on postoperative day 3
**p- value on postoperative day 6
D1= Distance from tragus to lip commissure
D2= Distance from gonion to lip commissure
D3= Distance from gonion to external canthus of the eye
NA: Non-available

Table 3. *Studies analyzing the effects of corticosteroids upon postoperative swelling.*

nificance (p>0.05), despite a lessening of postoperative pain (8-11, 14-17, 20). One study surprisingly suggests the possibility that CS treatment can increase patient reaction to pain secondary to a suppression of endorphin β levels.

The most common way to assess postoperative pain in the reviewed studies has been the use of visual analog scales (VAS) and counts of the amounts of analgesics consumed (8-10, 12). A number of authors have reported a statistically significant reduction (p<0.05) in pain after the postoperative administration of CS (12, 13, 19). These results were obtained after the administration of 40 mg of methylprednisolone (12), 25 mg of prednisolone (13) or 0.5 mg of betamethasone (19).

However, Dionne et al. (9) found the administration of 4 mg of dexamethasone via the intravenous route one hour before and of 4 mg via the oral route 12 hours after third molar surgery to exert an insufficient inhibitory effect upon prostaglandin E2 (PGE2) release to induce analgesia. Ustun et al. (8) in turn compared the effect of 1.5 and 3 mg/kg of methylprednisolone via the intravenous route – these doses being insufficient to afford significant pain reduction. Furthermore, no differences were found between the two drug doses; as a result, doses in excess of 1.5 mg/kg were not considered justified. A study involving three groups of patients (control and the administration of 10 and 20 mg of prednisolone) revealed no significant differences in terms of pain among the groups (20). Table 1 summarizes the different studies analyzing the effects of CS upon pain.

Effects of corticosteroids upon swelling

Glucocorticoids are effective in controlling acute and chronic inflammation, as they interfere with multiple

Article	Timing of measurement	Measurement method	p-value (day 2)	p-value (day 7)
Üstün et al. 2003 (8)	Day 2 and 7	Distance mesioincisal margin between upper and lower incisors	p=0.727	p=0.200
Moore et al. 2005 (10)	Postop., day 1, 2, 3 and 7	Maximum aperture between upper and lower central incisors	**p<0.05**	p>0.05
Mico-Llorens et al. 2006 (12)	Day 2 and 7	Non-forced oral aperture with calibrators	**p=0.005**	p>0.05
Graziani et al. 2006 (14)	Day 2 and 7	Distance between upper and lower incisors at maximum aperture	**p<0.05**	p<0.05
Buyukurt et al. 2006 (13)	Day 2 and 7	Maximum aperture between upper and lower incisors with calibrator	**P=0.014**	p=0.023
Grossi et al. 2007 (15)	Day 2 and 7	Distance between upper and lower central incisors	p>0.05	p>0.05
Zandi 2008 (5)	Day 2 and 7	Distance between upper and lower incisors	**P<0.05**	p<0.05
Vegas-Bustamante et al. 2008 (18)	Day 2 and 7	Non-forced oral aperture with calibrators	**p<0.000**	p<0.000
Laureano Filho et al. 2008 (17)	Preop., day 1 and 2	Measurement at maximum aperture	**p<0.05**	NA
Chopra et al. 2009 (19)	Day 3 and 5	Distance between upper and lower incisors	**p<0.001***	p<0.01**
Kang et al. 2010 (20)	Day 1, 2, 3, 4, 5 and 6	NA	p>0.05	p>0.05***

*p-value on postoperative day 3
**p- value on postoperative day 5
***p- value on postoperative day 6
NA: Non-available

Table 4. *Studies analyzing the effects of corticosteroids upon trismus.*

signaling pathways in inflammatory response phenomena (phospholipase A2, COX-2, etc.)(31, 32).

Swelling can be quantified in different ways. One of the most commonly used methods (5, 12-14, 18) is that of Amin and Laskin (33), which uses suture thread grasped with two mosquito forceps to measure distances at the following reference points: from the external palpebral angle to the gonial angle on the operated side; from the lower margin of the tragus to the external angle of the oral commissure; and from the lower margin of the tragus to the midpoint of the chin symphysis. Another approach is that developed by Grossi et al. (15), involving a modification of the technique of Schultze-Mosgau (23), measuring the distance from the external portion of the tragus to the mouth, and from the tragus to the pogonion – thereby increasing the objectivity of the measurements.

A number of studies have reported antiinflammatory actions with CS use (12, 14, 15, 19). Esen et al. found facial swelling to be up to 42% less intense 48 hours after surgery in the group administered methylprednisolone (22). Table 3 shows the different studies analyzing the effects of CS upon postoperative swelling. However, Leone et al. found that 32% of the patients in the methylprednisolone group failed to show statistically significant reductions in swelling (p=0.09)(16).

Effects of corticosteroids upon trismus

Trismus is defined as a limitation in maximum oral aperture, and constitutes an important postoperative complication caused by the edema and swelling associated to surgical trauma. Trismus is also partially associated to postoperative pain, and is more intense on the first day after surgery – with a mean reduction in oral aperture of 24.1% (10). A multicenter study found the symptoms to be more notorious during the first two days, followed by gradual improvement and resolution one week after the operation (35) – though the condition may persist for up to 10 days after surgery (11).

Different studies use measurement of the distance between the incisal margins of the upper and lower incisors at maximum aperture to quantify trismus (5, 10, 11, 13). In 8 of the 11 articles that analyzed the effect of corticosteroid use upon trismus, CS treatment was seen to afford significant benefit (Table 4).

In 5 of the 14 studies, CS use resulted in statistically significant reductions in pain after third molar removal. In 7 of the 11 articles that analyzed the effect of CS use upon postoperative swelling, such treatment was seen to be effective. In 8 of the 11 articles that analyzed the effect of CS use upon trismus, significant benefit was observed. The results of the analysis of the benefits derived from corticosteroid use in relation to pain, swelling and trismus following third molar surgical extraction, and the few side effects observed after the short-term use of such medication, point to corticosteroids as a treatment option to be taken into account in such patients.

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