Int. J. Oral Maxillofac. Surg. 2016; 45: 232–240
http://dx.doi.org/10.1016/j.ijom.2015.09.008, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Meta-analysis
Oral Surgery

Effect of submucosal injection of dexamethasone after third molar surgery: a meta-analysis of randomized controlled trials

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V. Moraschini, R. Hidalgo, E.dS. Porto Barboza: Effect of submucosal injection of dexamethasone after third molar surgery: a meta-analysis of randomized controlled trials. Int. J. Oral Maxillofac. Surg. 2016; 45: 232–240.

Abstract. The aim of this meta-analysis was to analyse the effectiveness of submucosal injection of dexamethasone to control the postoperative signs and symptoms resulting from impacted third molar surgery. An electronic search was conducted, without restriction on date or language, in the PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science databases until June 2015 . The eligibility criteria included non-randomized or randomized clinical trials in humans. After the search and selection process, eight articles were included. The fixed-effects or random-effects model, depending on heterogeneity, was built on the inverse-variance method used. The estimations of intervention were expressed as the mean difference (MD) in millimetres. The results of this meta-analysis suggest that the submucosal injection of dexamethasone presents a reduction in the postoperative signs and symptoms resulting from impacted third molar surgery, especially those associated with oedema and pain. In relation to trismus, the meta-analysis showed no statistically significant difference between dexamethasone and the placebo solution.

Keywords: third molar extraction; dexamethasone; oedema; trismus; pain; meta-analysis.

Accepted for publication 11 September 2015
Available online 14 October 2015

The surgical extraction of impacted third molars is the most frequent surgical intervention in dentistry.[1,2] This procedure is often accompanied by swelling, pain, and trismus, which are physiological events involved in the inflammatory response; if exacerbated, these can interfere with the patient's comfort and social life.[3] After injury to the tissues, a cascade of inflammatory responses is initiated, with the release of chemical mediators such as prostaglandins and leukotrienes and a consequent increase in permeability and local vascularity.[4] The intensity of the inflammatory response will vary according to each patient's physiology.

As a strategy to minimize the inflammatory response, quick and well-planned procedures performed by experienced professionals are necessary. In addition, postoperative drug therapy control of the inflammation is an effective measure. Of the numerous pharmacological options available, corticosteroids are a potent modulator of inflammation, acting by inhibiting phospholipase A_2, a chemical mediator that is responsible for the induction

of arachidonic acid. With a decrease in this enzyme, there will be less stimulation of immune cells, such as neutrophils, to release prostaglandins and leukotrienes, and consequently there will be a lower intensity of postoperative signs and symptoms.[5]

Various studies have examined the influence of systematically administered corticosteroids before or after the extraction of third molars, with good results observed.[6–8] Dexamethasone has been employed for years in oral surgery due to its powerful mechanism of action and prolonged half-life.[9] Several protocols for the administration of dexamethasone in third molar surgery have been proposed; however a consensus has yet to be reached. An interesting option that has yielded good results is the administration of dexamethasone through the submucosa.[9–12] Factors such as the low dosage, localized administration, and short-term exposure generate minimal adverse effects, for example immunosuppression.[9]

The aim of this meta-analysis was to analyse the effectiveness of submucosal injection of dexamethasone to control the postoperative signs and symptoms following impacted third molar surgery.

Materials and methods

The methodology of this review followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions[13] and the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[14] The clinical questions were broken down and organized using the PICOS strategy (Population, Intervention, Comparison, Outcome, and Study design).

Objective

The aim of this meta-analysis was to analyse the effectiveness of submucosal injection of dexamethasone to control the postoperative signs and symptoms (oedema, trismus, and pain) after impacted third molar surgery.

Search strategy

An electronic search was conducted, without restriction on date or language, in the PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science databases until June 2015. The search strategy and the PICOS framework can be viewed in Table 1. In addition, the references lists of prospective studies for inclusion were accessed to search for further articles.

Selection criteria

This review sought randomized controlled trials (RCTs) and prospective controlled studies comparing the effect of the submucosal injection of dexamethasone with that of placebo after impacted third molar surgery in humans. The exclusion criteria were animal studies, retrospective cohort studies, clinical series, case reports, and reviews. Studies involving volunteers with decompensated metabolic diseases were also excluded.

Screening process

The search and screening process was conducted by two authors/reviewers (VMF and EPB), who first analyzed the titles and abstracts. At a second stage, full articles were selected for careful reading and were analyzed according to the eligibility criteria (inclusion/exclusion) for future data extraction. Disagreements between reviewers were settled through careful discussion. The concordance between the two reviewers in relation to the search procedure was evaluated by Cohen's kappa (κ) statistical test. If necessary, the authors of the studies were contacted by e-mail to answer any questions.

Quality assessment

The quality analysis of the RCTs was conducted using the Cochrane Collaboration tool for assessing risk of bias in RCTs[15]. The analysis of each study was based on six criteria: sequence generation (Was the allocation sequence adequately generated?), allocation concealment (Was allocation adequately concealed?), blinding (Was knowledge of the allocated intervention adequately prevented during the study?), incomplete outcome data (Were incomplete outcome data adequately addressed?), selective outcome reporting (Are reports of the study free of suggestions of selective outcome reporting?), and other sources of bias (Was the study apparently free of other problems that could put it at a high risk of bias?).

Data extraction

The following data were extracted from the studies included (when available): authors, year of publication, study design, number of subjects, mean age, sex, number of smokers, jaw, impaction type (Pell and Gregory[16]), mean duration of surgery, dexamethasone dosage, use of antibiotics, use of mouth rinse, time of measurement, method of assessment of oedema, pain, and trismus, and *P*-values.

Statistical analysis

Continuous variables (oedema, pain, and trismus) from the studies included were subjected to meta-analysis when at least two studies analysed the same data type. The estimation of the intervention effect was expressed as the mean difference (MD) in millimetres with a 95% confidence interval (CI). The inverse-variance method was used for the random-effects model or the fixed-effects model. The I^2 statistic was used to express the percentage of heterogeneity of the studies. Values of up to 25% were classified as low heterogeneity, values of 50% as medium heterogeneity, and values of >70% as high heterogeneity. When a significant heterogeneity was found ($P < 0.10$), the results of the random-effects model were validated. When low heterogeneity was verified, the fixed-effects model was

Table 1. Systematic search strategy (PICOS strategy).

Search strategy		
Population	#1	(Third molar [MeSH] OR Third molars[MeSH] OR Impacted third molar*[all fields])
Intervention	#2	(Third molar surgery*[all fields] OR dexamethasone [MeSH] OR submucosal dexamethasone*[all fields] OR submucosal injection*[all fields] OR dexamethasone postoperative*[all fields])
Comparisons	#3	(Dexamethasone [MeSH] OR placebo effect [MeSH])
Outcomes	#4	Postoperative oedema*[all fields] OR postoperative pain*[all fields] OR postoperative trismus*[all fields]
Study design		Randomized controlled trials and controlled clinical trials
Search combination		#1 AND #2 AND #3 AND #4
Database search		
Language		No restriction
Electronic databases		PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science