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The use of chlorhexidine in the prevention of alveolar osteitis after third molar extractions.

Abstracted from

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Does Chlorhexidine Prevent Alveolar Osteitis After Third Molar Extractions? Systematic Review and Meta-Analysis. *J Oral Maxillofac Surg* 2017; 75: 901-914. doi: 10.1016/j.joms.2017.01.002. Epub 2017 Jan 13.

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Question: Does chlorhexidine prevent alveolar osteitis (AO) after third molar extractions?

Data sources Cochrane Central Register of Controlled Trials (CENTRAL), Medline through PubMed, Scopus, Science Direct, ISI Web of Science, Evidence-Based Dentistry, ClinicalTrials.gov, the European Union Clinical Trials Register, the Spanish General University Board database of doctoral theses in Spain (TESEO), the Spanish National Research Council (CSIC) bibliographic databases, and the Spanish Medical Index (IME).

Study Selection Randomised controlled trials (RCTs)(with or without placebo) of patients of any age or gender who underwent maxillary or mandibular third molar extractions. Studies were required to have analysed the efficacy of only chlorhexidine in any concentration, formulation, or treatment regimen for preventing alveolar osteitis (AO). There was no language restriction.

Data extraction and synthesis Data extraction was carried out independently by two researchers and a third researcher was consulted in case of disagreements. When explicit data was not stated in the text, it was calculated using data from the tables where possible. In addition, authors were contacted to obtain any necessary missing information. Datasets were assessed for heterogeneity and meta-analysis was conducted on homogenous datasets. Publication bias was assessed through funnel plots. The research was conducted and is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Results Twenty-three studies published from 1979 to 2015, corresponding to 18 trials (16 parallel-group and 2 split-mouth RCTs), that reported on 2,824 third molar extractions (1,458 in experimental group and 1,366 in control group) were included. The overall relative risk (RR) was 0.53 (95% CI, 0.45-0.62; $P<.0001$). There was evidence of low heterogeneity ($I^2=9.3\%$; $P=0.336$ by χ^2 test). The number needed to treat was 8 (95% CI, 7-11). There were no differences between chlorhexidine rinse (RR=0.58; 95% CI, 0.47-0.71) and gel (RR=0.47; 95% CI, 0.37-0.60) for the prevention of AO after third molar extractions. Chlorhexidine did not cause more adverse reactions than placebo.

Conclusions The use of chlorhexidine, in any formulation (rinse or gel), concentration (0.12% or 0.20%), or regimen (before, during and/or after surgery), is efficacious and effective in preventing AO in patients who have undergone third molar extraction. The findings showed that in order to prevent one case of AO, 8 patients would have to be treated with chlorhexidine. Chlorhexidine gel was found to be moderately more efficacious than the rinse formulation.

Commentary

Alveolar osteitis (AO), commonly known as dry socket, is a self-limiting complication following tooth extraction. The exact incidence of AO is unknown, but for routine dental extractions it has been reported to be in the range of 0.5-5%.¹ The incidence of AO after extraction of mandibular third molars varies from 1-37.5%.¹ Surgical extractions and extraction of third molars; when compared to other extractions, result in about ten times higher incidence of AO.^{2,3} A patient developing AO tends to require more visits post-extraction due to the acute pain and discomfort, translating into an increased cost for either the patient (missed work) or the general dental practitioner (extra appointments).³

Several systemic reviews have previously attempted to synthesise the evidence relating to chlorhexidine and AO. In 2005 a review and meta-analysis of seven trials concluded that rinsing with chlorhexidine on the day of surgery and several days after might reduce the incidence of AO.⁴ A Cochrane review carried out in 2012 included 21 trials and concluded that chlorhexidine was the only local method assessed for which there was moderate evidence on the prevention of AO.⁵ In May 2017 a systematic review and meta-analysis of 10 trials suggested that chlorhexidine gel was superior to a placebo in reducing the incidence of AO after third molar extractions.⁶

The stated aim of this systematic review was to assess the efficacy and effectiveness of chlorhexidine in preventing AO, compared with a control group, in patients undergoing third molar extractions. Twenty-three studies corresponding to 18 trials met the authors' inclusion criteria for this systematic review and meta-analysis; the largest number of randomised control trials included in a systematic review that focused on the use of

chlorhexidine in the prevention of alveolar osteitis after third molar extractions. The review asked a focused question and the eligibility criteria was appropriate for the formulated question.

Although the systematic review seemed comprehensive in terms of data collection (multiple databases and no restriction on language) and the number of studies retrieved, there were several significant limitations that reduce confidence in the conclusions. The systematic review was not registered in advance, there is no information on whether pharma were involved in funding any of the studies and no assessment of risk of bias or quality evaluation of studies were carried out. Therefore, it was not possible to judge the quality of the evidence contributing to the meta-analysis and the review conclusions. In addition, the interventions and outcomes for the included studies varied considerably. One trial included two treatment groups with chlorhexidine and one control group, and for four other studies an artificial control group was created. The authors have synthesised the data from the studies, seemingly regardless of the comparison group heterogeneity and the differing outcomes between the studies. The forest plot was sparsely labeled, lacking some key data including the outcome being analysed, the direction of effect and the individual study data.

There is some confusion in the reporting of adverse events with three trials reported in the text as having adverse signs of symptoms including bad taste, stomatitis, glossitis, staining and stomach upset. However, only one trial has adverse events noted in the summary table with them not reported in eight trials and the remaining nine trials reporting no serious adverse effects and adequate tolerance. There was no discussion however on the potential of a chlorhexidine allergy or the possibility of anaphylaxis. In 2016 two high profile incidents of fatal anaphylaxis to chlorhexidine in dental practice were reported and it was concluded that the potential risks of using chlorhexidine as an irrigant appeared to outweigh any known benefit.⁷

The authors alluded to the requirement of future studies to evaluate the efficacies between the gel and rinse formulations as well as different chlorhexidine concentrations and regimens. Clinicians should be aware of the potential benefit of the use of chlorhexidine in the prevention of AO after third molar extractions but this systematic review is not of high enough quality to influence current practice.

Practice Points

- While there may be a benefit in the use of chlorhexidine to prevent AO before, during and/or after third molar extractions, this systematic review is not of high enough quality to provide information to alter current clinical practice.
- Future clinical trials and systematic reviews should consider the risk-benefit and cost-effectiveness of the use of chlorhexidine to prevent AO.

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