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Chlorhexidine in the prevention of dry socket: Effectiveness of different dosage forms and regimens

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Abstract

Dry socket (DS) is a potential postoperative complication of dental extractions. It is clinically diagnosed by the presence of a denuded socket secondary to premature loss of the blood clot, and manifests as slight discomfort for the patient, followed by sudden worsening with intense or lancinating pain.

Since the underlying etiology is not clear, the best treatment is prevention. Chlorhexidine (CHX) is an antiseptic that acts upon the bacteria of the oral cavity, and is widely used in dental practice.

Objectives: A metaanalysis is made of the different CHX treatment regimens used for the prevention of DS, with the proposal of a management protocol designed to maximize the efficacy of such treatment.

Material and Methods: Literature searches were made in the PubMed Medline, Cochrane and ISI Web of Knowledge databases, crossing the terms: alveolar osteitis, dry socket and chlorhexidine. The search was limited to randomized or nonrandomized clinical trials.

Results: Twelve clinical trials using CHX in rinse or gel form at doses of 0.12% or 0.2% with different administration regimens for the prevention of DS were identified.

Conclusion: After reviewing the existing medical literature, it can be concluded that 0.2% CHX gel, applied every 12 hours for 7 days after extraction is the best available option for the prevention of DS. However, this is also the most expensive option, and since CHX is not subsidized by the Spanish public healthcare system, it occasionally may be more advisable to use the 0.12% rinse with the same dosing regimen.

Key words: Dry socket, chlorhexidine, clinical trial, metaanalysis, review.

Introduction

Dry socket (DS) is a potential postoperative complication of dental extractions. It has been defined as postoperative pain within and around the socket, which worsens at some point between the first and third postextraction day, accompanied by partial or total disintegration of the intraalveolar blood clot, with or without associated halitosis (1,2).

It clinically manifests as the presence of a denuded socket secondary to premature loss of the blood clot, with exposed bone walls and separation of the gingival margins. The condition initially manifests as slight discomfort, followed by sudden worsening with intense pain that increases upon chewing and/or suction (1).

It is widely accepted that DS is most often seen as a result of the removal of impacted third molars, with an incidence of 20-30% (2). In relation to dental extractions in general, DS is observed in 2-3% of all cases (3).

Since the underlying etiology is not clear, the best treatment is prevention. Different risk factors have been associated to the development of postextraction DS, such as the difficulty of extraction, surgeon skill, the use of oral contraceptives, deficient intraoperative cleaning of the socket, advanced age, the female sex, smoking, the excessive use of vasoconstrictors during tooth extraction, and immune suppression (1).

Chlorhexidine (CHX) is an antiseptic that acts upon the bacteria of the oral cavity, altering their cytoplasmic permeability and causing the precipitation of proteins and nucleic acids. At pH values of 5-8, CHX is bactericidal against grampositive bacteria (*Staphylococcus spp.* and *Streptococcus spp.*) and also against many gramnegative species. Its action is rapid and prolonged, but decreases in the presence of blood and organic material. In dental practice CHX is used for the treatment of infections of the oropharyngeal mucosa, aphthous ulcerations and periodontal infections. Its continuous use as an oral rinse can cause external dental staining, dysgeusia, desquamation of the oral mucosa, and favor tartar formation. As a result, the duration of treatment should be limited. Nevertheless, the risk of serious adverse reactions with CHX rinses appears to be small (4).

Material and Methods

A metaanalysis is made of the different CHX treatment regimens used for the prevention of DS, with the purpose of evaluating the efficacy of the different doses and treatment regimens, and of proposing a management protocol designed to maximize the efficacy of such treatment. To this effect, literature searches were made in December 2008 of the PubMed Medline, Cochrane and ISI Web of Knowledge databases, crossing the terms: alveolar osteitis, dry socket and chlorhexidine. The search was limited to randomized or nonrandomized clinical trials.

The studies were classified for posterior analysis according to the dosing form used (rinse or gel) and the concentration of CHX involved (0.12% or 0.2%). For the comparison of cases of DS among the different subgroups (qualitative variables), use was made of the chi-squared test (Table 1). In those studies establishing no comparisons versus placebo, the results of the placebo group of another study involving the same dosing form, dosage and regimen were used in order to allow application of the chi-squared test. In the 12 clinical trials generated by the literature search, the efficacy of CHX in the prevention of DS was examined in relation to three different dosing forms (rinses at concentrations of 0.12% and 0.2%, and bioadhesive gel at a concentration of 0.2%). With the purpose of avoiding bias in the interpretation of the results, the data from studies in which one same patient group was treated with CHX and antibiotics for the prevention of DS were excluded.

Results

The demographic data of the patients included in this metaanalysis are shown in (Table 2).

The first clinical trial evaluating CHX at a concentration of 0.12% for the prevention of DS was published by Berwick et al. in 1990 (5). The authors distributed 80 patients into three groups: the first group performed rinses with 0.12% CHX before extraction, and after tooth removal the socket was irrigated with the same rinse, while the second group performed rinses with CHX, followed by irrigation with saline solution. In turn, the third group did not perform rinses and was irrigated with saline solution. In this study, the 0.12% CHX rinse did not prove more effective than placebo in the prevention of DS.

Posteriorly, in 1991, Larsen (6) published a randomized, double-blind and placebo-controlled clinical trial involving 139 patients. The subjects were distributed into two groups: one was treated with 0.12% CHX rinse twice a day during the weeks before and after dental extraction, while the other group followed the same treatment regimen though using a solution of similar characteristics without the antiseptic. The incidence of DS was 8.3% in the treated group, versus 20.9% in the control group. For the first time in a published clinical trial, the results showed that CHX applied during the week before and after extraction is effective in reducing the risk of DS after dental extraction.

Shortly afterwards, Ragno et al. (7) published a double-blind study involving 80 patients with 160 third molars programmed for extraction (two surgical beds per patient). The patients were distributed into two balanced groups (0.12% CHX and placebo), and received intraoperative treatment, irrigations before and after extraction, and then rinses every 12 hours during 7 days. This was the first study evaluating the efficacy of CHX in

Table 1. Efficacy of chlorhexidine (CHX) in the prevention of dry socket (DS).

| AUTHOR | DOSING FORM | CHX | | PLACEBO | | p ⁴ | DOSAGE CHX |
|--|-------------|------------|-------------|------------|------------|----------------|----------------------------|
| | | DS YES | DS NO | DS YES | DS NO | | |
| Berwick and Lessin (5) | 12% rinse | 7 | 32 | 9 | 29 | 0.535 | IO rinse + irrigation |
| Berwick and Lessin (5) | 12% rinse | 9 | 31 | 9 | 29 | 0.901 | IO rinse |
| Larsen (6) | 12% rinse | 12 | 132 | 28 | 106 | 0.003 | bid 7d prophylaxis + 7d tt |
| Ragno and Szkutnik (7) | 12% rinse | 14 | 66 | 29 | 51 | 0.007 | IO + bid 7d |
| Bonine (8) | 12% rinse | 50 | 254 | 13 | 66 | 0.998 | IO rinse |
| Bonine (8) | 12% rinse | 18 | 253 | 13 | 66 | 0.007 | bid 14d tt |
| Hermesch et al. (9) | 12% rinse | 31 | 208 | 56 | 184 | 0.003 | bid 7d prophylaxis + 7d tt |
| Hita-Iglesias et al. ¹ (16) | 12% rinse | 8 | 24 | 29 | 51 | 0.253 | bid 7d |
| TOTAL | | 149 | 1000 | 157 | 531 | | |
| Field et al. (10) | rinse 0.2% | 4 | 104 | 10 | 98 | 0.097 | IO rinse + irrigation |
| Delilbasi et al. ² (11) | rinse 0.2% | 13 | 49 | 14 | 45 | 0.715 | IO + bid 7d tt |
| Metin et al. (12) | rinse 0.2% | 3 | 43 | | | | bid 7d prophylaxis + 7d tt |
| Metin et al. ³ (12) | rinse 0.2% | 6 | 53 | 14 | 45 | 0.050 | IO + bid 7d tt |
| TOTAL | | 26 | 249 | 24 | 143 | | |
| Torres-Lagares et al. (15) | 0.2% gel | 6 | 47 | 15 | 35 | 0.019 | IO |
| Hita-Iglesias et al. (16) | 0.2% gel | 3 | 37 | | | | IO + bid 7d tt |
| TOTAL | | 9 | 84 | 15 | 35 | | |

DS – Dry socket; CHX – Chlorhexidine; IO – Intraoperative; d – days; bid – twice daily; tt – treatment

- 1- The placebo group data correspond to the study of Ragno et al.
- 2- The data from this study refer to patients, not to number of extractions
- 3- The placebo group data correspond to the study of Delilbasi et al.
- 4- p < 0.05 statistically significant differences

Table 2. Demographic data and clinical trials included in the metaanalysis.

| AUTHOR | n ¹ | SEX ² | AGE ³ | SMOKERS | CONTRACEPTIVES ⁴ |
|----------------------------|----------------|------------------|------------------|---------|-----------------------------|
| Berwick and Lessin (5) | 80 | ±50.0% | 21.4 (16-40) | NF | NF |
| Larsen (6) | 139 | 43.9% | 89.2%<26 yrs | 18.70% | 30.80% |
| Ragno et al. (7) | 80 | 36.2% | 100%>18 yrs | 21.30% | 51.70% |
| Bonine (8) | 371 | 61.8% | 22.0 | 15.40% | 23.00% |
| Hermesch et al. (9) | 271 | 62.7% | 22.3 (18-52) | 17.80% | 34.70% |
| Field et al. (10) | 324 | 31.2% | NF | NF | NF |
| Delilbasi et al. (11) | 177 | 53.7% | 24.0 | 25.40% | NF |
| Metin et al. (12) | 99 | NF | 24.8 (17-46) | NF | NF |
| Fotos et al. (13) | 71 | ±66.6% | 22.0 | NF | NF |
| Torres-Lagares et al. (14) | 30 | 70.0% | 27.8 | NF | NF |
| Torres-Lagares et al. (15) | 103 | 66.6% | (18-60) | 25.20% | 14.50% |
| Hita-Iglesias et al. (16) | 73 | 74.0% | 29.0 (18-59) | 35.60% | 14.80% |

NF – Data not facilitated in the article

- 1- n = sample size
- 2- Sex refers to percentage females in each study
- 3- Age expressed as arithmetic mean and range
- 4- Contraceptives refers to percentage females using contraceptives

exclusively postoperative treatment for the prevention of DS. The results confirmed that CHX reduces the risk of DS after the extraction of third molars.

Bonine (8) presented a nonrandomized study involving 371 patients with 654 impacted third molars. The study was carried out in three successive periods. In the first period the patients were treated according to the protocol used in 1986, and which did not contemplate CHX prophylaxis. In the second period the patients were treated prophylactically with intraoperative CHX, and after surgery received 0.12% CHX rinses every 12 hours during 14 days. Finally, in the third period rinses with 0.12% CHX were provided only once before surgery. The results showed the CHX rinse before surgery to be insufficient, while the treatment during 14 days was effective in preventing DS.

In turn, Hermesch et al. (9) conducted a double-blind, comparative and controlled study involving 279 patients with at least one molar amenable to extraction. The patients were treated twice a day with 0.12% CHX or a similar rinse lacking CHX for one week before and one week after extraction. The results confirmed the efficacy of the 0.12% CHX rinse twice a day for one week before and one week after extraction in preventing DS. The first published clinical trial to demonstrate the efficacy of CHX in the prevention of DS was published by Field et al. (10) in 1988, using 0.2% CHX. The authors conducted an open-label trial in 324 patients requiring the extraction of a single tooth. The subjects were distributed into three groups: the first group did not receive socket irrigation, while the second group received saline solution in irrigation, and the third group received 0.2% CHX. The results showed a tendency towards fewer cases of DS in the group treated with CHX. There were no statistically significant differences between the group irrigated with saline and the group not subjected to irrigation.

Posteriorly, 0.2% CHX rinse was evaluated by Delilbasi et al. (11) in a randomized, parallel-group and placebo-controlled study. A total of 62 patients were treated with CHX twice a day during 7 days after dental extraction, while 59 patients were treated with saline solution using same dosing regimen and for the same period of time. The authors found no differences in the appearance of DS between the two groups of patients.

On the other hand, Metin et al. (12) conducted a randomized clinical trial involving 99 patients treated with a 0.2% CHX rinse. One group used the rinse twice a day during the week before and the week after extraction, while a second group only used the rinse in the week following extraction. The patients were evaluated 7 days after dental extraction, and the results showed no differences in the incidence of DS between the two groups on the basis of the dosing regimen used.

The efficacy of 0.2% CHX via the topical route has

been investigated in three studies seeking to demonstrate that a more local and direct effect upon the socket may substantially reduce the appearance of DS. Fotos et al. (13) carried out a double-blind, controlled study involving 70 patients programmed for bilateral extraction of the third molars. Each patient underwent one extraction with saline solution, while the second extraction comprised treatment with 0.1% or 0.2% CHX solution which after being used to irrigate the socket was impregnated in a gelatin sponge and sutured over the dental socket. Evaluation of the patients 6 days after surgery showed intraalveolar 0.2% CHX to have significantly reduced the complications and increased patient well being compared with the control group. However, the authors failed to specify the cases of DS registered in each group.

In the same line, Torres-Lagares et al. (14,15) conducted a double-blind, parallel-group placebo-controlled study in which the patients were distributed into two cohorts: the first was treated with a 0.2% CHX bioadhesive gel, while the other cohort received placebo (gel without drug substance). Preliminary results were published (14) corresponding to 17 patients in the treated group and 13 patients in the control cohort, followed by publication of the final study results (15) corresponding to 53 patients treated with CHX and 50 with placebo. The preliminary results showed a strong reduction in the incidence of DS, which nevertheless was not found to be statistically significant. However, the final results involving a larger number of patients revealed a statistically significant difference in the incidence of DS, decreasing from 30% in the control group to 11% in the treated group. The authors concluded that 0.2% CHX gel is a good alternative for the prevention of DS.

Lastly, Hita-Iglesias et al. (16) compared the efficacy of a 0.2% CHX bioadhesive gel with a 0.12% CHX rinse. The study included 41 patients in the group treated with gel and 32 patients treated with the rinse. The results revealed a statistically significant reduction in the incidence of DS in the group treated with 0.2% CHX gel.

Discussion

The daily frequency of administration of CHX for the prevention of DS has been once every 12 hours in all the consulted studies. Greater controversy has been observed as regards the duration of treatment, however.

Neither Berwick et al. (5) nor Bonine (8) were able to demonstrate the efficacy of the 0.12% CHX rinse in a single administration prior to dental extraction. Likewise, although some success was reported by Field et al. (10) using irrigations with 0.2% CHX, and by Torres-Lagares et al. (15) with the 0.2% gel, this dosing regimen seems insufficient to maximize efficacy in preventing DS (17).

We have found studies in which the duration of treatment

ranged from one week before extraction to two weeks after tooth removal, and in most cases the efficacy of CHX was confirmed. Treatment before extraction and during 7 days after removal appears to be a good option in terms of efficacy, and may prove more convenient for both the patient and dentist, who may prescribe the formulation in the office after performing the extraction. We consider that extending the treatment beyond 7 days postextraction, or starting it before extraction, does not increase the efficacy of treatment and moreover implies greater patient discomfort and unnecessary exposure to CHX—with an increased risk of adverse effects associated to prolonged use of the medication.

In relation to the different dosing forms, the 0.12% CHX rinse has firmly demonstrated its efficacy in the prevention of DS. Fewer studies are available in the case of the 0.2% rinse and gel, though some authors have also reported efficacy with this presentation.

In the prevention of DS, the rinses are usually not used until 24 hours after extraction, since premature application could favor clot detachment and thus the development of DS. An alternative in such cases could be the gel formulation of CHX, which can be used within the first 24 hours after extraction.

In the only study comparing two dosing forms of CHX for the prevention of DS (16), after applying treatment every 12 hours during the first postextraction, the 0.2% gel was seen to be superior to the 0.12% rinse. However, further studies would be needed to compare the 0.2% gel with the rinse at the same concentration and with the 0.12% rinse under different administration regimens, to determine which regimen and dosing form is most effective.

On the other hand, on selecting the dosing form for CHX, the cost factor must also be taken into account, since none of the formulations found on the Spanish market are subsidized by the public healthcare system, and the patient therefore must assume the cost of the medication. In this context, the gel dosing forms are clearly more expensive than the rinses.

Apart from the differences in dosing form and the duration of administration of CHX, the studies published to date do not apply homogeneous criteria for patient selection. In this sense, the different selection criteria used may mask the efficacy of CHX, and thus lead to wrong conclusions. Some studies included patients with several surgical beds, employed perioperative medication, or excluded subjects using oral contraceptives. Nevertheless, based on the data found in the literature to date, the 0.2% CHX gel, applied every 12 hours for 7 days postextraction, would be the best option for the prevention of DS. However this alternative also would be more expensive, and in some instances the 0.12% rinse with the same dosing regimen therefore would be more advisable.

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