Review Article

Impact of Chlorhexidine Mouthrinses on the Health of Adults: A Systematic Review.

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Abstract

Aim: *This systematic review aims to systematically evaluate the impacts of using Chlorhexidine mouthwashes on adults aged from 18 to 50.*

Objectives: *To understand the frequency of using Chlorhexidine [CHX] mouthwashes, explore the long term and short term impacts on the oral health and other areas of health on adults aged 18 to 50 years by the usage of CHX, determine the impact of using CHX instead of behavioral interventions or in conjunction with behavioral interventions to aid the prevention of oral health diseases and explore the use of CHX in people who have poor oral hygiene rather than behavioral interventions like toothbrushing.*

Methods: *The review was undertaken by systematic reviews and dissemination guidelines. A range of inclusion and exclusion criteria were devised and applied to the results of the searches to exclude the irrelevant studies. The potentially relevant studies were subjected to multi-stage screening to ensure that only relevant studies were included. They were then subjected to a quality appraisal process before (followed by) data extraction and synthesis. A systematic search for studies in databases like MEDLINE, EBSCO, and Cochrane library was conducted and a total of 378 records were obtained.*

Results: *Of the total 378 studies obtained by conducting the systematic search, 23 studies were selected for final review. From the studies selected, 21 of them reported a significant reduction of plaque and gingival scores along with a reduction in probing depths when CHX is used either alone or as an adjunct to oral hygiene measures. The outcomes of 7 studies of this review entitle that the therapeutic effects of using CHX are added up when it is combined with toothbrushing. However, this review cannot explicitly state or support that the use of CHX is better than toothbrushing or the use of CHX alone is advisable for patients. No study reported the effects of CHX usage for periods more than a year.*

Conclusion: *The obtained data presented in this systematic review provides strong evidence for the anti-plaque and anti-gingivitis effects of a mouthwash containing Chlorhexidine when used alone or as an adjunct to regular oral hygiene measures in gingivitis patients.*

Keywords: *chlorhexidine, gingivitis, periodontitis.*

Introduction

Periodontal diseases are mainly characterized by inflammation which is induced due to plaque formation. Therefore, treatment interventions and maintenance recommendations must be based on the removal of plaque. Plaque control is an effective way for the treatment and prevention of gingivitis and is a critical part of treating and preventing periodontal diseases **(**1,2**)**. According to Fischman, adequate plaque control measures are essentially important for periodontal patients, because they may have active infections along with previously treated disease, and a proven susceptibility to periodontal infections. The need for additional help for controlling plaque provides the rationale for using mouthrinses with a clinically proven anti-plaque and anti-gingivitis effectiveness as adjuncts to mechanical oral hygiene regimens of the patients **(**3**)**. Hughes (2006) suggests that benefits from mouthwashes can be obtained only if the patients strictly follow the recommended regimens designed for improving gingival health, even though they provide an additional means for improved plaque and gingivitis control **(**4**)**. Therefore, for making mouth rinsing a desirable adjunctive therapy for the control of plaque and gingivitis, a clinician must select the appropriate oral rinse based on patient needs and disease severity and should also recognize the new formulations that may increase compliance **(**5**)**.

The usage of mouthwashes is currently becoming common practice for maintaining oral hygiene. The current research will determine the frequency of its usage, the impact on the health of adults who use CHX and also, the after-effects of its usage over conventional behavioral interventions like toothbrushing. This review will serve as a guide for the patients and the dental care professionals for using CHX and it also enables them to create the utmost treatment results or to produce additional benefits. Normally, the Chlorhexidine rinse is prescribed to patients after professional oral prophylaxis and also for patients having difficulty in performing conventional oral hygiene procedures like toothbrushing and flossing **(**6**)**. The current research is aimed at determining the impacts when Chlorhexidine is used instead of toothbrushing interventions or as an adjunct to them for improving the oral health of a patient.

Inclusion criteria are as follows:

1. Publications are written in English.
2. Clinical studies.
3. Prospective/retrospective design.
4. Studies were conducted in adults of the age between 18 and 50.
5. Studies conducted after the year 1976.
6. Data from Randomized controlled Trials, quasi-RCTs, cohort studies, cross-sectional studies and case-control studies.
7. Studies reporting any usage outcomes of CHX mouthrinses.
8. Reports of long term (a year or more) and short term (less than a year) health impacts of CHX.
9. Reports of usage of CHX as an adjunct to behavioral interventions.
10.

Exclusion criteria are as follows:

1. Publications that are written in other languages.
2. Studies are conducted on animals.
3. Studies and Publications before the year 1976.
4. Publications presented only in abstract form.
5. Studies are conducted only in individuals below the age of 18 years and above 65 years.
6. Studies in which formulations of CHX other than mouth rinses like gels, toothpaste, or varnishes are employed.

List of Databases Used:

1. ASSIA via ProQuest (1976 to 2013).
2. MEDLINE (R) via Ovid (1976 to present).
3. PsycINFO via Ovid (1976 to 2013).
4. CINAHL via EBSCO (1976 to present).
5. MEDLINE via EBSCO (1976 to present).
6. Cochrane Library (1976 to present

The final papers selected for the review were critically appraised using the CASP tool. Using the critical analysis summary questions, the results of the reviewed papers were collated. In the absence of a scoring system, the results have been assembled based on how many of the criteria each study met. Questions and Responses and Critical Appraisal guidelines are briefed in **Table 1** and **Table 2.**

Sl. No:	Questions	Responses		
		Yes	No	Unclear/Not given (leave blank)
1	Whether study is: RCT, quasi –RCT, Cohort study, Cross-sectional study, Case-control study			
2	Whether conducted in adults over the age of 18 years			
3	Whether the study reports any usage outcome or adverse effects of CHX			
4	Whether the study reports about use of CHX instead of a behavioral intervention or as an adjunct to any behavioral intervention			
5	Whether the study is written in English language			
6	Whether study conducted on or after the year 1976			
Final Decisions		Include	Exclude	Read full Text

Table 1: Title and Abstract Screening Questions and Responses

	Critical Appraisal Questions.	Yes	No	Can't Tell
	Study Design Questions.			
1	Have the authors stated a clear objective for the study? Hint: Have specific research questions been asked? Are there primary & secondary questions and what are they? Have any research hypotheses been presented? Does the title reflect the aims of the research?			
2	Have the authors identified and chosen an appropriate target population? Hint: Is the target population from which the sample is drawn one which is appropriate for answering the research question? Is the selected sample a biased subset of the target population? If so in what way?			
3	Was randomization achieved and comparability of groups demonstrated or differences explicitly acknowledged? Hint: Check that a truly random procedure was adopted and that intervention and control groups were compared and found to be similar, especially in small number studies and block randomization designs. Was allocation concealed?			
4	Were all intervention and control group subjects accounted for throughout the study? Hint: Was there differential drop-out, cross-over, incomplete follow-up or incomplete data?			
5	Apart from the intervention were treatment and control groups treated equally? Hint: Did they receive the same researcher involvement and were assessments conducted simultaneously and identically? In cross-over trials was the wash out period reasonable?			
6	Were subjects, measuring staff or researchers and analyzing researchers blind to intervention? Hint: Is it clear what the intervention was? Did blinding at each level occur and was it explicitly explained. If not what precautions were taken to avoid any bias likely to result from lack of blinding. What impact would this have on study results?			
7	Was the sample size chosen to ensure that the study was capable of statistically demonstrating a defined difference between the treatment and control groups? If not why? Hint: Specifically, were any power calculations employed and were the estimates of effect size and the values chosen reasonable?			

	Were these undertaken for all primary outcomes? If a formal power calculation was not used was the choice of sample size reasonable?			
	Results and analysis questions;			
8	Was analysis conducted on an 'intention-to-treat' basis? Hint: Does this apply to all the analyses conducted? If not, how was this justified? Were all subjects accounted for at the analytical stage?			
9	Are the results clearly stated or illustrated and are all the relevant results included? Hint: What are the results and are they complete? Are they presented in sufficient detail? Are adverse results and side-effects fully described?			
10	Was an appropriate statistical analysis performed and reported? Hint: Was the choice of tests justified and are confidence limits presented in addition to p values to assess precision of estimates. Are the numbers analyzed consistent with those recruited to the study and those estimated for power calculation? We're group baseline differences properly adjusted for in analysis?			
	Discussion and Conclusion Questions;			
11	Was confounding and bias considered sufficiently in accounting for the results? Hint: Check blinding, search for and control of confounders, measurement of selection, performance and attrition bias.			
12	Are the author's conclusions justified by the results? Hint: Specifically are precision estimates properly taken into consideration. Are alternative explanations for the results provided and discussed, and are limitations to the study explicitly acknowledged?			
13	Can the results be applied to a local population? Hint: Is the population in the study and the setting quite different from those you might encounter? Was subject selection so specific that the results cannot be confidently extrapolated?			
14	Should practice or policy change as a result of this study? Hint: What are the social or health benefits and costs, and the economic implications.			

Table 2: Critical appraisal guide for a Randomized controlled trial

Results

A total of 23 studies were finalized for the review of which 19 were randomized controlled trials, 3 were randomized cross-over trials and 1 was a prospective clinical study. A total of 952 patients, both males and females and aged 18 to 50 were assessed according to the inclusion criteria. Each study was conducted in a health care setting, for example, a dental hospital, dental clinic, or other medical institutions. The studies included in this review stated they were all ethically approved by their respective authorities.

Participants: The participants of 6 studies were healthy adults, 6 studies were conducted in patients with moderate to severe periodontal diseases, 7 studies were conducted in institutionalized patients, 2 studies conducted in patients who were on a ventilator inside an Intensive Care Unit and 1 study each was conducted in patients undergoing chemotherapy or radiotherapy and treatment for Acute myeloid leukemia.

Intervention: The primary aim of the studies was either to determine the efficacy of CHX or to explore the effects of its use in various situations and special types of patients. In all the studies, the fundamental intervention used was a Chlorhexidine mouthwash, either rinsed or sprayed into the mouth. In studies that were conducted to compare the efficacy of mechanical and chemical plaque control measures, at least one group in the study received CHX mouth rinse alone or as an additional measure.

Outcomes: Overall, the outcomes observed were the same and were the reduction in the amounts of plaque and severity of the gingival disease. 14 studies reported the occurrence of adverse effects like staining, increase in calculus and so on. The overall results obtained from 11 studies were significant and were supporting the use of Chlorhexidine as an effective agent for reducing plaque and maintaining good oral hygiene. On a broader aspect, the results of the studies included in this review support the use of CHX as an adjunct to toothbrushing for periods up to 1 year. The results of 11 studies suggest that when used alone, CHX can be administered for shorter periods like several weeks. Among the studies included in this review, 7 were conducted in institutionalized patients with varying degrees of disease severity. The studies conducted in them supports the use of CHX, either alone or as an adjunct to toothbrushing.

Discussion

The current review was designed to obtain information about the the use of Chlorhexidine mouthwashes in various types of adult populations, from clinical studies conducted in them. Thereby, the information gathered could be used to plan, improve and implement current and future treatments and to suggest research areas that may have been ignored, as well as to point out methodological aspects that need to be addressed when planning future activities.

Currently, Chlorhexidine is meant to be used as an additional measure for cleaning teeth and for maintaining oral hygiene **(**7**)**. It is also used in situations where the individual cannot practice toothbrushing by themselves like the physically and mentally handicapped, patients who are in Intensive Care Units and so on **(**8**)**. Due to its high potential for destruction of almost 80% of the microorganisms inside the mouth, CHX is considered as a gold standard for oral hygiene. However, the constant and continuous use of CHX creates some adverse after-effects on the people who are using it. The common adverse effects of using CHX are staining on teeth, alteration of taste sensation, increased deposition of dental calculus, enlargement of the parotid gland and hypersensitivity reactions **(**9,10**)**. Apart from the use in oral hygiene prospect, the CHX is also recommended for other medical uses like disinfection of hands, for prevention of transmission of hospital-acquired infections, for disinfection of vagina during childbirth to prevent vertical transmission of infections, for the prevention of Ventilator-Associated Pneumonia and so on **(**11,12**)**.

The effects and outcomes of using CHX in the study populations of the selected studies are measured with the help of indices. All the studies included in this review used at least one index for supporting their findings and inferences.

The results of this review show that a CHX mouth rinse is effective in controlling plaque, as established by the Plaque Index. CHX is also effective in controlling gingivitis, as established by the Gingival Index and the Papillary Bleeding Index. The effect of CHX as an adjunct to oral hygiene procedures is rather consistent throughout the selected studies. Of the 23 studies included in this review, 11 of them reported a significant reduction of plaque and gingival scores along with a reduction in probing depths when CHX is used either alone or as an adjunct to oral hygiene measures. The outcomes of 7 studies of this review entitle that the therapeutic effects of using CHX are added up when it is combined with toothbrushing. The studies favoring this view are those conducted by Asikainen et al.**(**13**)** Bergmann et al. **(**14**)** Quirynen et al. **(**15**)**. The majority of the rest of the studies of this review were dealing with the use of CHX instead of toothbrushing.

As already stated, this review entitles the fact that Chlorhexidine mouthwash is an adequate agent for controlling plaque and maintaining oral hygiene, which can be used for periods up to a year in all kinds of patients and populations like healthy adults, people with advanced periodontal diseases, people in Intensive Care Units, physically and mentally handicapped people, cancer patients undergoing treatments and so on. Among the studies considered, only two studies conducted by Stiefel et al. **(**16,17**)** had made an effort to record the behavioral outcomes of the people using CHX and the staff administering them. Their study about behavioral outcomes was favoring the use of CHX in mentally retarded individuals. They measured the behavioral outcomes of the subjects with the help of questionnaires, in addition to measuring the effects of CHX on oral health. One of the objectives of the current review was to determine the effects of CHX on the systemic or general health of the people using it. However, no studies of this review measured or assessed the effects on the general health of individuals, even though there are other studies outside this review mentioning the adverse effects on health like parotid gland enlargements and so on. This suggests the need for further researches into this relevant topic.

There is also a lack of studies in this review measuring effects of CHX for longer periods like more than 1 year for mentioning those effects in this review. However, 2 studies were conducted by Christie et al. **(**18**)**and McKenzie et al.**(**19**)** have measured the outcome of using CHX for 1 year, and reported that their use is advantageous for that period of intervention. To justify this gap, the ADA reports that the efficacy of a product for controlling the gingival diseases must be demonstrated in 6-month clinical studies. However, in practice, CHX is mostly used on a short-term basis in cases for which conventional plaque control is difficult or impossible. Therefore, the efficacy of CHX over shorter periods is also of interest **(**20**)**. Concerning adjunctive devices for controlling plaque and gingivitis, the ADA demands an evaluation period of at least 4 weeks. Consequently, for evaluating the anti-plaque and anti-gingivitis efficacy of a CHX rinse as an adjunct to regular oral hygiene, studies with an evaluation period of at least 4 weeks were also included in this review. Also, no studies of this review had conducted any assessment for determining the lengths of periods the different populations are using it which also suggests the need for further researches into the field.

Another observation obtained by conducting this review is that regarding the efficacy of CHX in reducing plaque accumulation, no studies had reported a complete absence of plaque or dental calculus as a result of CHX administration for their respective period of interventions. The studies have reported only about the significant reductions in the scores obtained for plaque and calculus, which may restrict their use as the sole measure for oral hygiene in individuals. Thus, it can be concluded that rinsing with a mouthwash containing Chlorhexidine is effective in reducing plaque and gingivitis, although it does not eliminate plaque and resolve gingivitis.

In this study, every effort was made to make the review-systematic, and adherence to the systematic review protocol was practiced as far as possible. Most of the review guidelines suggested that at least two reviewers were required for conducting a systematic review, especially for the identification of eligible studies and data extraction **(**10**)**, The reason that two reviewers are recommended as opposed to one, is to minimize the amount of bias occurring due to selection bias and human error and facilitate a full and frank discussion about any decisions that need to be made or the direction in which the review is going, and to resolve these by consensus. However, it was not always possible to adhere to the criteria stipulated by the review guidelines, because this systematic review was conducted in fulfillment of an academic submission and therefore had to be done by a single person.

Conclusion

The obtained data presented in this systematic review provides strong evidence for the anti-plaque and anti-gingivitis effects of a mouthwash containing Chlorhexidine when used alone or as an adjunct to regular oral hygiene measures in gingivitis patients. Because some of the side effects of CHX can take time to develop and the studies of this review were conducted for periods less than a year, the findings of this review are not definitive and a larger number of studies with longer intervention period that evaluate the various effects associated with usage of CHX are needed. Furthermore, since the possibility of a meta-analysis was precluded as explained earlier, more precise estimates of effects could not be computed.

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