Clinical efficiency of Chlorhexidine:

A systematic review

Authors

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Abstract

Background: The most important aspect in Endodontic therapy is to reduce microorganisms and their by-products. This is mainly accomplished by disinfecting the root canals before obturation to ensure a healthy and functionally stable tooth. Biomechanical preparation by the use of files and irrigants plays a very important role in eliminating the bacteria and thereby preventing reinfection. In this review article, the anti-bacterial efficacy of 2% CHX was assessed by using online search engine methods such as OVID Medline, Pubmed and Cochrane library database.

Methods: Permanent mature human teeth were used and all studies had to be in vivo and all studies had to have a strong study design, such as clinical trials. We had a total of 38,454 Articles, but after excluding the articles at the title stage, abstract and full-text reading that did not meet the selection criteria, we had 7 Articles left.

Results: The patients were randomly divided into CHX & NaOCL groups and all aseptic procedures were done and the bacterial load was evaluated by counting CFU and performing real-time quantitative polymerase chain-reaction RTQ-PCR.

Conclusion: The bactericidal efficacy of 2% CHX is equal or less than that of NaOCL and more clinical studies have to be done.

***Keywords*:** Chlorhexidine percentage, Temperature, Concentration, Time in seconds or minutes, Volume, Active or passive solutions, Frequency of irrigation, Cytotoxicity, Side-effects, Complications, Tissue dissolving effect.

Introduction

One of the major objectives of root canal treatment is to eliminate or significantly decrease the population of microbes in the infected tooth as this directly translates into the successful treatment. This objective is reached by mechanical preparation accompanied by the use of chemically active irrigant solution during and after the instrumentation phase.

The gold standard for endodontic irrigation has long been sodium hypochlorite because it excellently fulfills the required antimicrobial, debridement, lubrication and dissolution of tissue properties. But one of the most distinct disadvantages is that it is highly toxic to periapical tissues. It also has a strong bleaching effect and emits unpleasant odour.

These factors have motivated researchers to look for alternative irrigants which retain the useful properties and at the same time lack the harmful effects of NaOCl.This led to the emergence of chlorhexidine as it has a potential to be used for this purpose.

There are studies which support that chlorhexidine prevents microbial activity *in vivo* (11, 9) and some studies show that chlorhexidine exhibit anti microbial effectiveness compared to sodiumhypochlorite (10) although controversy regarding this latter assertion exists (12, 7).

Materials and Methods

A systematic review of literature was used to identify, select and critically appraise relevant articles related to the search question “How efficient Chlorhexidine irrigation in endodontic treatment”.

Search Strategy

During initial search, specific keywords were applied: “Chlorhexidine percentage, temperature, concentration, time in seconds or minutes, volume, active or passive solution, frequency of irrigation, cytotoxicity, side effects, complication, tissue dissolving effect”.

The online search engines: Ovid Medline, Pub Med, Cochran library database, were used and experts in the field of endodontics at the Faculty of Dentistry, University of Toronto were consulted to obtain an additional information relevant to the search.

Inclusion criteria

Our search included the following criteria:

- strong study design such as clinical trials
- comparing diagnostic test to a gold standard
- limited to studies In vivo
- limited to studies On Humans
- studies on permanent mature teeth
- published In English

- available through the University of Toronto

Determination Of Relevance

From the initial list of 38454 articles, most were eliminated at the title stage, from 50 articles remained, an additional 42 articles were eliminated at the abstract stage according to the inclusion criteria mentioned previously, the 7 articles remaining (see table of references) were read independently by each member of the group, critical appraisal was done according to the checklist. (Please see table 1)

Results

As we mentioned earlier, the highest level of evidence that can be assigned to the studies that used NaOCL solutions as a control arm and randomization in assignment of the patients is level II-1 (7,10,12). Although the above mentioned studies showed that the bactericidal efficiency of 2%CHX is slightly less than that of NaOCL, further testing is needed to find out if this has significant impact on clinical outcome of the symptomatic and asymptomatic cases. A better design study is needed to eliminate all sorts of shortcomings present in the reviewed literature. They include but are not limited to the inclusion selection of the patients that is intrinsically biased as the asymptomatic teeth could, for example, contain microbiologic flora that had different resistance to the chemo-mechanical

canal preparation than the flora in symptomatic teeth; no control for confounding factors such as age, sex, type of teeth and the individual variations of the root canal system; samples techniques that pick up the content of the main canal only etc.

Almost all data received through conventional sampling and culturing is prone to type II error (false negative).The small sample size of all the studies did not allow for proper stratification and control of confounders. Based on the reviewed literature, it is difficult to draw any clinically valid conclusion, except for, as was noted previously that a prudent clinician would select CHX in cases where the risk of accidental exposure of the periapical tissues to the root canal irrigating solution is especially high, such as immature apex, loss of apical stop due to overinstrumentation etc.

Discussion

Microorganisms infecting the root canal system, especially those of the anaerobic type, have long been identified as the primary etiological agents for apical periodontitis (1). Resolution of apical periodontitis is considered a hallmark of endodontic success, and removal of root canal microorganisms is a necessary step in achieving such success. A variety of techniques have been used to minimize if not eliminate the bacterial population of the endodontically involved canal, and contemporary therapy often includes mechanical preparation in

conjunction with biochemical cleansing. Biochemical agents used for irrigational cleaning of the canal are considered the principal antimicrobial element of the endodontic procedure, and possess great microbicidal properties (2).

Today's standard irrigant of choice for most endodontic treatments is invariably sodium hypochlorite (NaOCl) also known as the common household bleach. NaOCl as the endodontic irrigant enjoys a multitude of advantages that make it the number one irrigant of choice: it possesses broad antimicrobial properties, excellent tissue-dissolving capabilities and low surface tension in addition to being inexpensive (3). The above benefits to the use of NaOCl have made it an optimal chemotherapeutic used in concentrations up to 5.2%. It should be noted however that the same properties that render NaOCl an effective chemical adjunct may lead to serious complications arising from its lack of biocompatibility. When in contact with live tissues beyond the root apex, the extremely caustic NaOCl solution wreaks havoc on the patient's periapical structures in an iatrogenic endodontic complication known as the "sodium hypochlorite accident".

The above disadvantage has had scientists searching for an alternative root canal irrigant that boasts tissue compatibility as well as optimal antimicrobial properties. The most qualified emerging alternative thus far has been chlorhexidine. Chlorhexidine is a potent microbicidal with great activity against a wide range of both Gram negative and positive bacteria. It is a cationic biguanide that functions by adsorbing onto microbial cell wall, leading to coagulation/precipitation of cell components and cell disruption (4). In-vitro studies suggest efficacy comparable to that of NaOCl (5); however strong in-vivo

studies comparing the two in terms of clinical success are lacking. In this systematic review we aimed to summarize the best evidence available regarding the effectiveness of chlorhexidine as a substitute irrigant for NaOCl. A systematic and explicit survey of the literature was carried out as outlined in Materials and Methods. A total of seven articles (6,7,8,9,10,11,12) were selected for further evaluation, all of which were non-randomized clinical trials (the summarized version of the papers can be found in Table 2). Among these scientific papers, data from only one article (7) was deemed the best available evidence due to the following shortcomings:

a. Of the 7 selected studies, 4 lacked the use of an endodontic irrigant as external control for chlorhexidine (6,8,9,11), thus providing no benchmark for comparison. The lack of a control irrigant significantly weakens any conclusions to be made from these articles.

b. In one of the studies (11), the authors left the canal empty between appointments, taking their post-cleaning microbiological sample 48h after completion of the preparation. This procedure has the potential of introducing possible contamination before taking the 2^{nd} microbiological specimen thus reducing chlorhexidine's apparent efficacy.

c. Six articles reported the use of culture only in quantification of the antimicrobial effect of the irrigants (7,8,910,11,12). It is well known that the vast majority of oral microbiota cannot be grown on culture (13), therefore limiting the generalizability of evidence from such reports. Polymerase chain reaction (PCR) is considered the state of the art gold standard for evaluation of microbiological

specimens and was carried out in only one study (7) as a means of quantifying the bacterial load in treated canals.

d. One study did not even quantify the data gathered, reporting *p* values as the only analytic component of their results (12).

e. In yet another report (10), microbiological assessment was restricted to the culture of only a few bacterial species, severely impacting the quality of extrapolated evidence.

f. Neutralization of the antimicrobial irrigating solution pre-sampling, deemed necessary to avoid introducing it into cultures and the laboratory samples, was not performed in two of the studies (10,11).

Considering the above shortcomings, most of which would critically impair our ability to extrapolate any of the conclusions, only one study was considered to have utilized the most desirable feasible design. The study by Vianna et al. in 2006 took advantage of three different methods of microbiological assessment: SYBRGreen PCR, TaqMan PCR and culture. The level of evidence from this article may be considered II-1 due to its non-randomized clinical trial design. The results of the above study recorded a slightly higher statistically significant efficacy of NaOCl in removing the largest quantity of bacteria as assessed by PCR. When culture was used as the microbiological tool, a 25% difference was evident in obtaining bacteria-free samples post-instrumentation with NaOCl compared with chlorhexidine. The authors concluded that even though both agents were successful in removing microorganisms from the root canal in most

cases, NaOCl still represented a superior irrigant. Despite the conclusion from the above paper, we tend to err on the side that the slight difference between NaOCl and chlorhexidine in terms of microbiological performance even though statistically significant, is unlikely to be clinically significant. There are a multitude of limitations however that every clinician should take into consideration before arriving at a conclusion:

1. The number of studies with solid design and evidence in the current English language dental literature is limited. We found only one such paper (7) and there is an obvious need for more studies before the question regarding chlorhexidine substituting NaOCl may be answered with some level of confidence.

2. Extrapolation at the clinical level from the best available current evidence would not be flawless. Even though the above studies were conducted in-vivo using samples from human subjects, the end measure was one of in-vitro nature. In other words, there are currently no articles that correlated the laboratory microbiological data with clinical success and resolution of the endodontic infection in the form of healed periapical lesions.

3. In the above studies, even the best microbiological data came from specimens taken from the main root canal only. It is clear that endodontic infections are not limited to the main canal and often spread to various aspects of the extremely complex dentiopulpal system such as dentinal tubules, accessory canals and other irregularities. Sampling from all aspects of the root canal

system although impractical at the moment, would certainly provide a much more relevant picture of procedural success in removal of microorganisms.

4. The judicious clinician may speculate further about the effectiveness of chlorhexidine as a replacement irrigant for NaOCl when considering some of its advantages compared to disadvantages. Chlorhexidine is certainly adequately microbicidal and fairly biocompatible; it also demonstrates substantivity. On the other hand, chlorhexidine unlike NaOCl is incapable of dissolving tissue, potentially leaving behind organic substance for infecting bacteria as well as dead bacterial structural remnants that can elicit inflammation. This is especially important since chlorhexidine's advantages are negatively impacted within organic matter. Its function is critically dependent on the pH of the environment with an optimal range of 5.5 – 7 (4). In teeth with necrotic canals where placement of Ca $(OH)_2$ is often necessary, chlorhexidine's microbicidal properties are significantly diminished (14).

Conclusions

In conclusion, although chlorhexidine was adequate as an irrigant, it did not demonstrate superiority to NaOCl in terms of bacterial elimination in root canals. Combined with the higher cost of using chlorhexidine in dental offices (please see Table 4, the technology assessment table), there seems to be a barrier to advocating chlorhexidine instead of NaOCl in standard endodontic therapy. In those cases where the biocompatibility of chlorhexidine is deemed crucial to the successful treatment of the patient with minimal complications, the judicious clinician may, in fact, choose to irrigate the root canals using chlorhexidine. The situations that would benefit the most from using chlorhexidine include but not limited to teeth with open apices, immature undeveloped roots, apical perforations, transportations, and patients with sensitivity to NaOCl.

References

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Appendix 1

Table 1

(Endodontic$ or root canal therapy or root canal treatment or root canal irrigation or root canal disinfection or pulpotomy or pulpectomy or root canal preparation or root canal instrument$ or root canal debridement or chemomechanical debridement or chemomechanical instrumentation or chemomechanical preparation).mp. [mp=ti, ot,ab, nm, hw, it, tx, kw, ct, sh, tn, dm, mf, ac, de,md, sd, so, rw]	38454
limit 4 to english [Limit not valid in: DARE,CCTR,CLCMR; records were retained	734
limit 5 to humans [Limit not valid in: AMED,CINAHL,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,HAPI,IPAB,Journals@Ovid; records were retained]	673
limit 6 to local holdings [Limit not valid in: CDSR,ACP Journal Club,DARE,HAPI; records were retained]	404

EXCLUDED ARTICLES TABLE

Table 3

SR.NO	CITATIONS	REASONS FOR EXCLUSION
1	Vivacqua - Gomes, N. Gurgel-Filho ED. BPFA. Sato, E. Ferraz, CCR, Teixeira, FB Zaia, A.A. Souza- Filho, FJ. *International Endodontic Journal 36(9), 604-9, 2003 September*	Excluded due to the use of CHX & calcium hydroxide
2	Zamany & Spangberg (Zamany A, Safari K, Spanberg L.S.) *Oral Surgery Oral Med Oral Pathology, Oral Radiology, Endo 2003, Nov 96 (5) 578-8-1*	Sequential use of CHX & NaOCL combined rather than separate analysis
3	Schirrmeister, Jorg F. Liebenow, Anna-Lisa. Braun, Gabriele. Wittmer, Annette. Hellwig, Elmar. Al-Ahmad, Ali. *Journal of Endodontics. 33(5):536-40, 2007 May.*	Disinfecting regimen using sodium hypochlorite (NaOCl), ethylenediaminetetraacetic acid (EDTA), chlorhexidine digluconate (CHX) irrigation, and calcium hydroxide (Ca(OH)(2)) dressing was assessed
4	Wang, Ching S. Arnold, Roland R. Trope, Martin. Teixeira, Fabricio B *Journal of Endodontics. 33(11):1283-9, 2007 Nov*.	Insufficient clinical studies on effectiveness of 2%CHX gel
5	Siqueira, Jose F Jr. Paiva, Simone S M. Rocas, Isabela N. *Journal of Endodontics. 33(5):541-7, 2007 May.*	Lack of a comparison irrigation solution, such as NaOCL as external control
6	Manzur, Aldo. Gonzalez, Ana Maria. Pozos, Amaury. Silva-Herzog, Daniel. Friedman, Shimon *Journal of Endodontics. 33(2):114-8, 2007 Feb.*	The antibacterial efficacy of intracanal medication with calcium hydroxide [Ca(OH)2], 2% chlorhexidine gel (CHX), and a combination of both [Ca(OH)2/CHX] was assessed

Appendix 2 TECHNOLOGY ASSESSMENT TABLE

Table 4

Efficacy / **Cost**	Better	Same	Worse
Less			
Same			
More		✓	