Antimicrobial Efficacy of Octenidine Hydrochloride, Green Tea, Sodium Hypochlorite and Chlorhexidine Gluconate as Retreatment Endodontic Irrigant Against *E. faecalis*, Candida & Mixed Culture – In-Vitro Study

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ABSTRACT

BACKGROUND

Sodium hypochlorite & chlorhexidine are usually employed as endodontic irrigants due to their antimicrobial properties, however, their cytotoxicity & allergenicity issues demand an equally effective but safer irrigant. The purpose of the study was to compare the antimicrobial efficacy of octenidine hydrochloride (OCT), green tea, sodium hypochlorite and chlorhexidine (CHX) at various concentrations against *E. faecalis*, *C. albicans* and its mixture.

METHODS

The study was conducted in Hitkarini Dental College, Jabalpur. Various concentrations of irrigants were prepared. Muller Hinton agar media plates were swabbed with the culture broth of *E faecalis* ATCC 29212, *Candida albicans* ATCC 10231 or a mixture of these. Five Whatman paper disks (6 mm), each loaded with experimental concentration of the irrigant, were placed at equal distance on to the plate. The plates were incubated at 37^0 C for 48 hours. This was done in 6 replicates. The plates were evaluated for clear zone of inhibition measured in mm.

RESULTS

The diameter readings were analysed using Kruskal Wallis and Mann Whitney U tests. There was a significant difference between the groups against *Enterococcus faecalis*; candida, & mixed culture ($P < 0.01$).

CONCLUSIONS

5 % Sodium hypochlorite is better than all others whereas 2 % CHX is better than OCT & Green tea. 0.1 % OCT is better than 3 % Green tea. OCT can be used as a contributory irrigant along with NaOCl to achieve antimicrobial advantage.

KEY WORDS

Antimicrobial Efficacy, Candida Albicans, Chlorhexidine Gluconate, E Faecalis, Green Tea, Octenidine Hydrochloride, Sodium Hypochlorite

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BACKGROUND

Decontamination and debridement play an important role in the success of endodontic treatment. Residual microorganisms are found in pulpal spaces and dentin tubules, and many of them cause recurrent intraradicular infection after root canal treatment. *E. faecalis* is frequently observed in a high percentage of root canal failures. The frequency of *E. faecalis* association in primary endodontic infection ranges from 4 - 40 % and 24 - 77 % in persistent infections.[1] *C. albicans* has been found to be present in the oral cavity in 30 to 45 % of healthy adults and 95 % of patients infected with the human immunodeficiency virus.[1] Infections of the primary root canal have been known to contain fungi occasionally. They appear to be more common in the root canals of obturated teeth that have failed treatment.[2]

Sodium hypochlorite (NaOCl) is the gold standard for the irrigation of root canal space because of the clinical efficacy & extensive research in endodontic therapy.[2] Due to toxicity concerns, it was suggested that 5.25 % NaOCl be diluted to lower concentrations. It has a foul odour and taste, bleaches clothing, has corrosive potential and when extruded into the periapical tissues, it is cytotoxic. Chlorhexidine gluconate (CHX) has been advocated as an endodontic irrigant due to its antibacterial effects, and lower cytotoxicity but greater substantivity than NaOCl and efficient clinical accomplishment.[3] Since CHX is highly cytotoxic in-vitro, caution should be exercised while using it in oral procedures.[4] It has also been linked to allergic reactions. As a result, a similarly efficient yet safer irrigant is desired.[5]

Octenidine hydrochloride (OCT), a bispyridine derivative, has been recommended as an endodontic irrigant due to its antimicrobial effects and lower cytotoxicity.[5] It tends to be more effective than chlorhexidine for bacterial antiadhesion activity that lasts longer. It is stable under different physical and chemical conditions and not prone to hydrolysis. The mode of action is bactericidal / fungicidal by interfering with cell walls and membranes.[6] Green tea polyphenols are herbal derivatives from Camellia sinensis leaves. GTPs have antioxidant, anti-inflammatory, and antimicrobial properties.[7] Despite extensive literature on the efficacy of these irrigants in primary root canal treatment, there are very few studies of antimicrobial efficacy in different concentrations of these chemicals against *E faecalis, Candida albicans* and mixed culture.

Hence this study was undertaken to compare the efficacy of various concentrations of irrigant. Purpose of the present study was to evaluate and compare the antibacterial and antifungal efficacy of octenidine hydrochloride, green tea, sodium hypochlorite and chlorhexidine gluconate at various concentrations against *E. faecalis, C. albicans* and its mixture.

METHODS

This in-vitro laboratory study was conducted at Hitkarini dental College, Jabalpur, Madhya Pradesh, India. It spanned for over a period of six months including the procurement of material and conducting the experiment.

Materials were procured and irrigating solutions were prepared as follows -

Octenidine hydrochloride (Dishman Pharmaceuticals and Chemical Ltd Ahmedabad, India), powder was dissolved in methanol to obtain 0.10 %, 0.05 % 0.025 % concentrations. Green tea (Vista Nutrition, Bangalore, India) was extracted with ethanol for 24 hours. The extract was dried to get the powdered form. 3 %, 2.5 % 2 % were prepared by dissolving it in ethanol.

Chlorhexidine gluconate (Neelkanth - Safe Plus, Jodhpur, India) 2 % was used directly from the bottle. 1 % & 0.20 % were prepared by diluting 2 % CHX with distilled water. Sodium hypochlorite (Vishal Dentocare Pvt Ltd, Ahmedabad, India), 5 % was used directly from the bottle. 2.5 % & 0.5 % were prepared by diluting with distilled water. Sterile saline solution 0.9 % W / V (Aculife Healthcare Pvt Ltd, Vasna, India) was used as control.

Fifteen ml of hot (50^0 to 60^0C), Muller Hinton agar media (HIMEDIA), was poured on the autoclaved culture plates of 100 mm diameter and was allowed to solidify under laminar air flow. Once the media was solidified, the plates were swabbed with the 6 - 8 hour old culture broth of *E faecalis* ATCC 29212, *Candida albicans* ATCC 10231 or a mixture of these. The turbidity of the broth was set to McFarland 0.5 before swabbing. The culture broth was swabbed three times on to the plate, by rotating the plate to 60^0 after each swabbing, and allowed to dry. Five Whatman paper disks (6 mm), each loaded with the experimental concentration of irrigant, were placed at equal distance on to the plate. The plate was covered with the lid and incubated at 37^0 C for 48 hours.

This was done in 6 replicates. After this, the plates were evaluated for clear zone of inhibition. The diameter of the zone was measured in mm using zone measurement scale.

Statistical Analysis

Data was entered in Microsoft excel 2013 for Windows. Mean, standard deviation (SD), median, minimum, and maximum values of zone of inhibitions against *E. faecalis*, candida and mixed culture in different concentrations in different groups were calculated.

Shapiro - Wilk test showed that zone of inhibition values in different groups did not follow normal distribution hence nonparametric test namely, Kruskal Wallis test was used for comparison between experimental groups. When Kruskal Wallis test showed significant difference, Mann Whitney U test was applied for pairwise comparison of groups (comparison of two groups). $P < 0.05$ was considered statistically significant.

RESULTS

All the experimental irrigants exhibited antibacterial and antifungal properties except saline. Kruskal Wallis test showed significant difference between the groups (Table 1) (Figure 1). Mann Whitney U test for comparison showed that, in low concentrations, CHX was significantly ($P < 0.01$) better than all other irrigants against all microbes used in the experiment.

Groups		Low			Medium			High		
		E faecalis	*Candida albicans*	Mixed	*E faecalis*	*Candida albicans*	Mixed	*E. faecalis*	*Candida albicans*	Mixed
OCT	Mean ± SD	8.18 ± 0.08	8.10 ± 0.09	7.30 ± 0.46	8.35 ± 0.19	12.20 ± 0.13	10.25 ± 0.14	13.12 ± 0.33	13.10 ± 0.31	11.13 ± 0.20
	Median	8.20	8.10	7.15	8.35	12.15	10.20	13.20	13.15	11.05
	Min - Max	8.10 - 8.30	8.00 - 8.20	7.00 - 8.20	8.10 - 8.60	12.10 - 12.40	10.10 - 10.50	12.50 - 13.50	12.60 - 13.40	11.00 - 11.50
Green tea	Mean ± SD	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	7.10 ± 0.06	8.17 ± 0.08	0.00 ± 0.00	7.90 ± 0.40	12.90 ± 0.51	8.35 ± 0.19
	Median	0.00	0.00	0.00	7.10	8.15	0.00	8.05	13.15	8.35
	Min - Max	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	7.00 - 7.20	8.10 - 8.30	0.00 - 0.00	7.10 - 8.10	12.20 - 13.40	8.10 - 8.60
NaOCl	Mean ± SD	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	13.83 ± 0.41	14.58 ± 0.49	14.10 ± 0.49	20.15 ± 0.08	16.38 ± 0.25	15.13 ± 0.12
	Median	0.00	0.00	0.00	13.75	14.75	14.30	20.10	16.35	15.15
	Min - Max	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	13.50 - 14.50	14.00 - 15.00	13.50 - 14.50	20.10 - 20.30	16.10 - 16.80	15.00 - 15.30
CHX	Mean ± SD	13.92 ± 0.55	10.63 ± 0.55	8.28 ± 0.26	15.25 ± 0.08	12.90 ± 0.46	12.28 ± 0.21	16.30 ± 0.15	14.20 ± 0.54	14.27 ± 0.18
	Median	14.05	10.65	8.30	15.20	12.70	12.20	16.30	14.15	14.20
	Min - Max	13.20 - 14.50	10.10 - 11.20	7.90 - 8.60	15.20 - 15.40	12.60 - 13.80	12.10 - 12.60	16.10 - 16.50	13.40 - 15.10	14.10 - 14.60
Saline	Mean ± SD	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	Median	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Min - Max	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00	0.00 - 0.00
Kruskal Wallis Test						p = 0.000*				
Mann Whitney U test			P = 0.002 * P = 1.000 Green tea & NaOCl, Green tea & Saline, NaOCl & Saline			P = 0.002 * Mixed culture Green tea & Saline P = 1.000			P = 0.002 * Candida OCT & CHX P = 0.004 * OCT & Green tea P = 0.589	

Table 1. Comparison of Zone of Inhibition between Different Groups in Low, Medium and High Concentrations

*significant (P < 0.05)

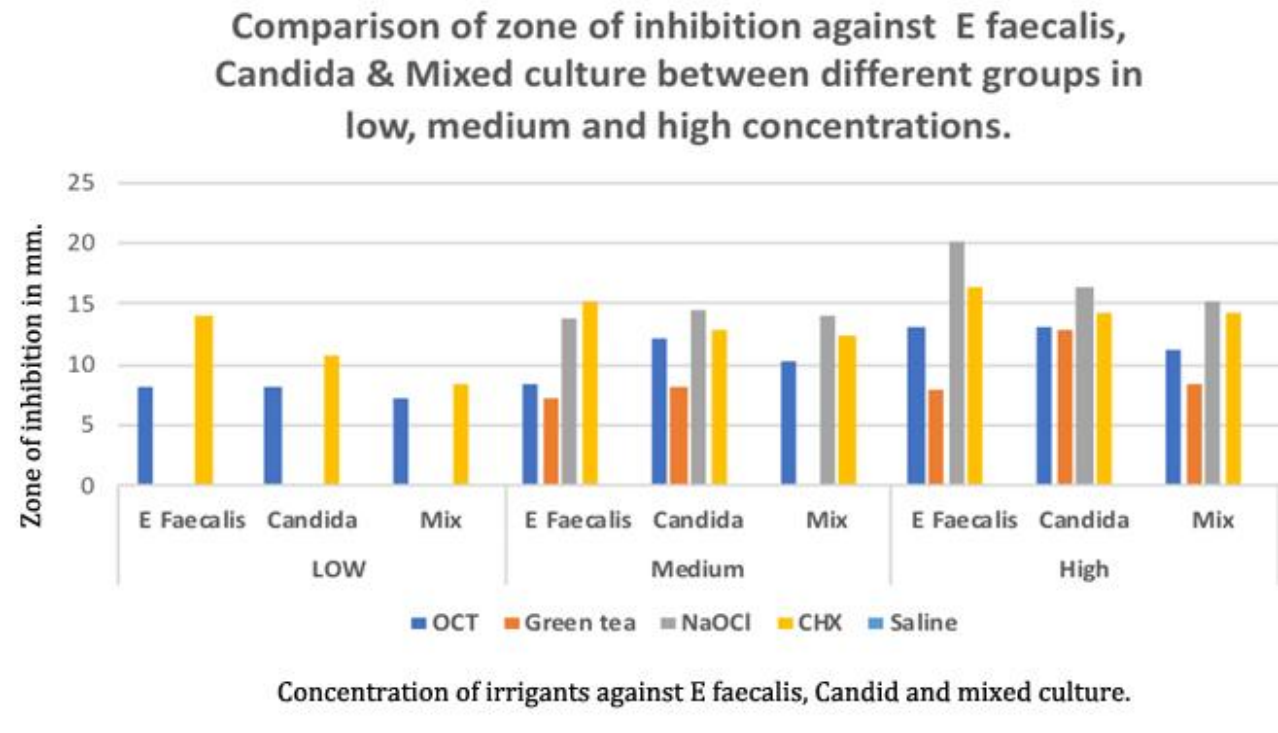

Figure 1. Zone of Inhibition against E Faecalis, Candida & Mixed Culture Observed in Low, Medium, and High Concentrations of Different Irrigants

Ranking is: 0.2 % CHX (P < 0.01) > 0.025 % OCT (P < 0.01) > 0.5 % NaOCl = 2 % Green tea = Control (P > 0.05). In medium concentration, CHX was significantly better (P< 0.01) than all other irrigants against *E. faecalis* and candida. Ranking is: 1 % CHX (P < 0.01) > 2.5 % NaOCl (P < 0.01) > 0.05 % OCT > 2.5 % Green tea > Control. However, in mixed culture, NaOCl was significantly better (P < 0.01) than all other irrigants. Ranking is: 2.5 % NaOCl (P < 0.01) > 1 % CHX (P < 0.01) > 0.05 % OCT (P < 0.01) > 2.5 % Green tea = control against mixed culture. (P > 0.05).

In high concentrations, NaOCl was significantly better (P < 0.01) than all other irrigants. Ranking against *E. faecalis* & mixed culture is: 5 % NaOCl (P < 0.01) > 2 % CHX (P < 0.01) > 0.1 % OCT (P < 0.01) > 3 % Green tea > Control (P < 0.01). However, against candida, there was no significant difference between OCT and Green tea (P > 0.05). Against candida, ranking is: 5 % NaOCl (P < 0.01) > 2 % CHX (P < 0.01) > 0.1 % OCT (P > 0.05) = 3 % Green tea > control (P<0.01).

DISCUSSION

The efficacy of endodontic irrigant is directly proportional to the concentration and the volume.[4] The antimicrobial activity of the irrigating solution should be quickly exerted against resistant microorganisms present in root canal and dentinal tubules.[5] In the present study, NaOCl showed the best antimicrobial activity at highest concentration. This finding agrees with the results of Afzal A et al.[8] Oliveira DP et al.[9] Berber VB et al.[10] The antimicrobial effect, tissue dissolution

ability, and appropriate biologic compatibility in less concentrated solutions are all important characteristics of this irrigant.

Hypochlorous acid (HOCl) is formed when NaOCl is added to water. It contains active chlorine, which is a strong oxidizer. Chlorine acts as an antibacterial agent by irreversibly oxidising the –SH groups of essential enzymes, interrupting the bacterial cell's metabolic functions. It may also form N-chloro compounds by combining with cytoplasmic components, which are toxic complexes that kill the microorganism. However, even before the formation of N chloro compounds in the cytoplasm, the first contact oxidation reactions of chlorine with bacteria can result in the rapid death of bacterial cells.[11,]

In higher concentration, it is considered to be more aggressive while in lower concentration (0.5 % - 1 %), it is biocompatible. Tissue dissolution property is concentration dependent. 5 % NaOCl dissolves pulpal tissue & necrotic debris rapidly. However, higher concentration is cytotoxic. Volume of this cytotoxic solution can be reduced by using it with an adjuvant irrigating solution.

In the existent study, 0.5 % NaOCl exhibited little antimicrobial action. This could be due to precipitation of the solution on the paper disc, during saturation procedure. According to Ayhan H et al.[11] Baumgartner & Cuenin,[12] Heling & Chandler,[13] microorganisms such as *E. faecalis* are resistant to NaOCl, particularly at low concentration. Byström A, Sundqvist G[14] showed that NaOCl was far less effective when diluted to a clinically significant level (0.5 %).

In the current study, 2.5 % NaOCl and 2 % CHX showed a better antimicrobial effect than OCT and Green tea. Kustarci A et al. also concluded that 2.5 % NaOCl and 2 % CHX have superior antimicrobial effect than OCT and propolis, against *E. faecalis, C. albicans, S. aureus* and *E. coli*. At low concentration of chlorhexidine, small molecular weight substance leaks out, leading to a bacteriostatic effect. At higher concentration, it has a bactericidal effect. It precipitates or coagulates the cytoplasm, most likely caused by protein.[15,16] Antimicrobial activity is pH dependant, with the optimal range being 5.5 – 0.741.[17]

In the existent study, green tea showed antimicrobial activity against *E. faecalis*. Pujar M et al.[18] also stated that green tea showed a better antimicrobial activity against *E. faecalis*. Martina LP et al.[19] showed that 3 % green tea extract has same antibacterial activity against *E. faecalis* as 2 % CHX. Green tea contains catechin compounds like: Catechin, epicatechin, epigallocatechin, epicatechin gallate, and epicallocatechin gallate (also known as EGCG). It binds to the lipid bilayer and causes aggregation of lipid vesicles and leaks the contents from a suspension of vesicles. It causes membrane expansion leading to membrane thickening, loss of cell structure, and finally death. It also interferes with the DNA replication process by inhibiting bacterial DNA gyrate enzyme. EGCG is found to be the most active component in green tea.

In the present study, 5 % NaOCl is more effective than 0.1 % octenidine. Tirali RE et al.[20] (2009) in their study showed that 100 % and 50 % octenidine hydrochloride are more effective than 5.25 % NaOCl against *S. aureus, E. faecalis* and *Candida albicans*. As a cation - active substance, octenidine binds readily to the negatively charged bacterial cell envelope, consequently disrupting the vital functions of the cell membrane, and killing the cell. It is relatively nontoxic. As compared to NaOCl and CHX[5], it has a faster ability to produce intratubular disinfection and is effective against endodontic pathogens, making it a better alternative for root canal irrigation than CHX.[20]

Octenidine's antiadhesive property prevents biofilm formation better than chitosan and CHX.[21] These properties, as well as OCT's ability to inactivate already formed biofilms even in the presence of serum proteins,[22] is an advantage over NaOCl, which is found to lose its efficacy in the presence of organic matter.[23] Dentin, tissue debris, blood, and their mixtures will quickly reduce NaOCl's antibacterial effectiveness. NaOCl alone cannot eradicate persistent mature biofilm communities within the root canal space.[24]

When OCT is mixed with NaOCl, phenoxyethanol (PE), which is already present in commercial OCT solution, precipitates. PE is not toxic,[25,26,27] at doses used in OCT.

PE is effective against oral bacteria and subgingival plaque, and evidence suggests that it works in conjunction with other antimicrobials.[28,29] Potential of octenidine as an individual irrigant is inadequate due to its poor tissue-dissolving properties.[30] It has good in-vivo tissue tolerance and thus could be used in regenerative endodontics, especially in teeth with a large open apex.[31] OCT can be used along with NaOCl to circumvent the problems associated with sodium hypochlorite.

CONCLUSIONS

Within the limitations of this study, it is concluded that 5 % sodium hypochlorite has better antimicrobial property than other experimental irrigants. 2.5 % NaOCl and 2 % CHX showed a better antimicrobial effect than 0.1 % OCT and 3 % Green tea. Antibacterial and antifungal properties of 0.1 % OCT is better than that of 3 % Green tea. 0.1 % OCT can be used as a contributory irrigant along with NaOCl to achieve antimicrobial advantage and reduce problems associated with usage of sodium hypochlorite, although this needs further clinical appraisal.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.
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