



# The Influence of Preventive Regimens Containing Different Toothpastes on Caries Risk of High-Risk Patients: A Randomized Clinical Trial

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## Abstract

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**BACKGROUND:** The main objective of conservative dentistry is maintaining the health of the dentition and restored teeth free from dental caries. The prevention of dental caries can be achieved by personal prevention programs at home, dental health care professional, and public health application programs. Based on knowledge related to the etiology and pathogenesis of dental caries, this provides a chance for application of effective prevention program for the prevention of dental caries.

**AIM:** This study aimed to evaluate the effect of different preventive regimens using different toothpastes on caries risk using cariogram and decayed, missing, and filled (DMF) scores of high caries risk patients.

**MATERIALS AND METHODS:** The study was conducted on 66 participants with high caries risk. Participants were divided into three groups, 22 participant each. According to the test regimen, where (A1) participants were exposed to a regimen including dual zinc plus arginine-based toothpaste (Colgate total), (A2) participants were exposed to a regimen including zinc-based toothpaste (Crest complete), and (A3) control group was participants that were exposed to a regimen including fluoride-based toothpaste (Signal). The study was carried for 1 year, assessment of cariogram and DMF scores was done in four intervals:  $T_0$ : baseline,  $T_3$ : after 3 months,  $T_6$ : after 6 months, and  $T_{12}$ : after 12 months.

**RESULTS:** According to cariogram, there was a statistically significant difference between Groups A1, A2, and A3, where  $p < 0.001$ . However, DMF scores of all groups showed no statistically significant difference between the three groups.

**CONCLUSIONS:** Dual zinc plus arginine-based toothpaste is a superior caries preventive regimen in high caries risk patients.

**CLINICAL SIGNIFICANCE:** The benefits of preventive regimen to the practitioner will be providing a non-invasive, and cost-efficient method to prevent dental caries. Benefits to the patient will be an improvement of oral hygiene, prevention of dental caries, and maintain healthy dental supporting structures.

## Introduction

Dental caries is a common, multifactorial, and chronic infectious disease. According to the World Health Organization (WHO), dental caries remains a significant oral health problem, affecting 60–90% of the population. By evidence, the prevention of dental caries can be achieved by following suitable preventive regimen programs that can interrupt the process of the disease and modifying caries risk assessment (CRA) [1], [2]. Accumulation of dental plaque and microorganisms is considered the main predisposing factors of dental caries and targeting these factors is the best way to manage and control dental caries. Regular and appropriate tooth brushing with toothpaste besides using antimicrobial mouthwash considered the best method to remove and control cariogenic dental plaque [3]. Toothpaste in the market is always a concern for dentists and patients. Despite the wide

spread of fluoridation programs to reduce dental problems and using fluoride-based toothpaste as a method for caries prevention, the problem of dental caries still exists and raised controversy among dental clinicians and researchers to find new strategies for caries prevention [4]. Due to the high incidence of dental caries, finding new caries prevention regimen program to prevent dental caries, should be accomplished this, through minimal side effects, besides the most potent antibacterial effect for inhibiting cariogenic bacteria, should be considered for qualifying the new treatment preventive regimen [5]. The ecological preventive method considered the most recent approach to prevent dental caries as using prebiotics like arginine.

Arginine containing oral hygiene products significantly reduce the incidence of dental caries, and it has a negative impact on the pathogenic activity and growth of cariogenic bacteria. It can counter the acid accumulation within the oral biofilm, interfering with the growth and survival of cariogenic bacteria,

and thus serves as a promising approach for caries management [6].

Zinc is important trace element provided multiple oral health benefits with improvement of antibacterial effect on oral biofilm. Zinc based dentifrices even at lower concentration have an anti caries effect through significant inhibition of cariogenic bacteria. *In vitro* studies reported, an incredible decrease in the number of cariogenic bacteria was reported by zinc-based dentifrices. Antibacterial efficacy of zinc can be achieved by tooth brushing with zinc-based toothpaste through incredible reduction of mutans streptococci count [7]. New toothpaste containing dual arginine plus zinc has been proposed protective effect against dental caries [8], [9].

Cariogram is a computer-based CRA program. It is considered an ideal and valid tool for risk assessment as easy use in daily practice besides, it is based on clinical judgment in addition to information gain from the patient. This will provide a complete image of a patient's risk for dental caries and afford proper guideline for management of dental caries [10].

This study was conducted to determine the effect of caries prevention regimen including dual zinc plus arginine-based toothpaste and regimen including zinc-based toothpaste versus regimen including fluoride-based toothpaste on the risk assessment of patients with high caries risk.

## Materials and Methods

### Materials

Materials used in this study were as follows:

1. Dual zinc plus arginine-based toothpaste (Colgate total)
2. Zinc-based toothpaste (Crest complete)
3. Fluoride-based toothpaste (Signal)
4. Chlorhexidine mouthwash (Hexitol Mouthwash)
5. Fluoride varnish (Enamelast)

### Methods

#### Study settings and ethical approval

This randomized controlled clinical study was conducted in Faculty of Dentistry, Cairo University, Egypt. This study was registered in clinical trials ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) with I.D: NCT04032210. Ethical approval was obtained before the start of the study. The study was approved by the Research Ethics Committee (CREC), Faculty of Dentistry, with approval number 19/7/52.

### Ethics approval

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee. Ethical approval number: 19/7/52. This study was registered in clinical trials ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) with I.D: NCT04032210.

### Informed consent

The procedure and the aim of the study were explained to the participants and each of them signed informed consent.

### Data availability statement

Data are available on reasonable request.

### Sample size calculation

Sample size calculation was performed using G\*Power 3.1.9.2. According to the results of Karabekiroglu and Ünlü [1], the predicted sample size (n) was a total of (54). Sample size was increased by (20%) to account for possible dropouts during follow-up intervals to be total of (66) cases, that is, (22) for each group.

### Patient recruitment, study design, and grouping

Patients were recruited from the outpatient clinic of Conservative Department, Faculty of Dentistry, Cairo University, Egypt. Only eligible patients who fulfilled the eligibility criteria were included in the study. The inclusions criteria were high caries risk patients with age range 20–50 defined according to cariogram CRA model with no orthodontic or prosthodontic appliance and systemically healthy. Exclusion criteria were patients on cariogenic diet and patient with a compromised medical history. A written consent was obtained from the patients willing to participate in the trial.

A total of 66 participants were assigned in this study, they were randomly divided into three groups according to the test regimen, where A1 represents participants exposed to regimen including dual zinc plus arginine-based toothpaste (Colgate total), A2 represents participants exposed to regimen including zinc-based toothpaste (Crest complete), and A3 represents control group, where participants exposed to regimen including fluoride-based toothpaste (Signal). The study was carried for 1 year, assessment of cariogram and decayed, missing, and filled (DMF) scores were done in four intervals:  $T_0$ : baseline,  $T_3$ : after 3 months,  $T_6$ : after 6 months, and  $T_{12}$ : after 12 months.

### Examination and diagnosis

Examination and selection of all participants were done according to inclusion and exclusion criteria. High caries risk patients were selected according to cariogram with non-cariogenic diet, and with plaque accumulations. Moreover, international caries detection and assessment system (ICDAS) score range was 0–3 to avoid any restorative intervention that would affect on the result of preventive regimen.

### Allocation sequence generation

The randomization process was made according to a checklist done by a dentist other than the researcher including the number of participants divided into three groups denoting with letter A1, A2, and A3 using computer software [www.random.org](http://www.random.org). Participants were equally randomized for three intervention regimens according to randomized numbers in a sequentially numbered opaque sealed envelope.

### Blinding

It was a double-blinded study so that data analysts and the participants were blinded. All toothpastes were sprayed

### Interventions

- Participants were provided with toothbrushes and the given dentifrice according to the tested regimen and they were instructed to brush their teeth 2 times a day for 2 min with soft-bristled toothbrush as explained by the examiner. They were instructed, no eating or drinking was permitted for a minimum of 2 h post brushing.
- Participants of the three groups were instructed to use 10 ml of 0.12% chlorhexidine rinse for 1 min/day, 30 min after tooth brushing before going to bed. Such a regimen was repeated 1 week every month to avoid bacterial resistance which can occur in long-term use [11].
- Fluoride varnish was applied onto all teeth surfaces of the three groups every 3 months at baseline then after 3, 6, 9, and 12 months intervals from the beginning of the trial.

### Outcome

#### CRA (Primary outcome)

The CRA was done using the cariogram model. It was evaluated in four visits:  $T_0$ ,  $T_3$ ,  $T_6$ , and  $T_{12}$ . The cariogram is a computer program that evaluates data collected from the patient such as diet contents and frequency, plaque amounts, fluoride program, and amount of saliva secretion, *S. mutans* count, DMF score, and buffering capacity then summarize the results in a pie chart. When entered 7 scores out of the ten parameters,

the software starts to produce a pie diagram which represents the percentages of “Bacteria” (Red), “Diet” (Dark Blue), “Circumstances” (Yellow), and “Susceptibility” (Light Blue). These four sectors provided the percentage of “the probability of avoiding caries” (Green) sector as the bigger the green sector, the lesser is the risk of caries and better oral hygiene and dental health *vice versa*.

#### Caries defects, filling, and missing (DMFT) (Secondary outcome)

DMFT was counted and calculated, where D score was measured according to ICDAS II scores. DMFT scores were evaluated in four visits:  $T_0$ ,  $T_3$ ,  $T_6$ , and  $T_{12}$ .

### Statistical analysis

The mean and standard deviation values were calculated for each group. Data were explored for normality using Kolmogorov–Smirnov and Shapiro–Wilk tests, data showed non-parametric (not normal) distribution (Scores). Kruskal–Wallis was used to compare between more than two groups in non-related samples Mann–Whitney which was used to compare between two groups in non-related samples. Friedman test was used to compare between more than two groups in related samples. Wilcoxon was used to compare between two groups in related samples. The significance level was set at  $p \leq 0.05$ . Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

## Results

According to cariogram, there was a statistically significant difference between participants which were exposed to a regimen including dual zinc plus arginine-based toothpaste (Group A1), participants were exposed to a regimen including zinc-based toothpaste (Group A2), and participants were exposed to a regimen including fluoride-based toothpaste (Group A3), where  $p < 0.001$ . A statistically significant difference was found between caries prevention regimen including dual zinc plus arginine-based toothpaste (Group A1), and each of regimen including zinc-based toothpaste (Group A2), and regimen including fluoride-based toothpaste (Group A3), where  $p < 0.001$ . Furthermore, a statistically significant difference was found between regimen including zinc-based toothpaste (Group A2) and regimen including fluoride-based toothpaste (Group A3), where  $p < 0.001$ . The highest mean value was found in regimen including dual zinc plus arginine-based toothpaste (Group A1) followed by regimen including zinc-based toothpaste (Group A2), the lowest mean value was found in regimen including fluoride-based toothpaste (Group A3). However, DMF scores of all groups showed no statistically significant difference between them.

### Cariogram results

#### Effect of time on cariogram for each group

Regarding all intervention regimens, there was a statistically significant difference between T<sub>0</sub>, T<sub>3</sub>, T<sub>6</sub>, and T<sub>12</sub> where p < 0.001, while the highest mean value was found in T12 followed by T<sub>6</sub>, T<sub>3</sub>, and the lowest mean value is found in T<sub>0</sub> Table 1 and Figure 1.

**Table 1: The mean, standard deviation values of cariogram (Green %)**

Variable	Cariogram Green (%)									P
	Group A1			Group A2			Group A3			
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	
T <sub>0</sub>	18.23	2.05	17.50	17.82	2.15	17.00	18.82	2.67	17.50	< 0.001*
T <sub>3</sub>	78.23	5.91	78.50	73.00	5.68	73.00	47.18	6.87	43.00	< 0.001*
T <sub>6</sub>	85.73	5.00	87.00	80.86	4.23	81.00	58.73	7.61	58.00	< 0.001*
T <sub>12</sub>	91.23	3.28	92.00	83.32	3.00	82.00	60.18	7.16	59.00	< 0.001*
p	< 0.001*			< 0.001*			< 0.001*			

\*Significant (p < 0.05). NS: Non-significant (p > 0.05).

#### Effect of different groups on cariogram for each time period

Regarding to T<sub>0</sub>, there was no statistically significant difference between Groups A1, A2, and A3, where p = 0.385. Regarding to T<sub>3</sub>, T<sub>6</sub>, and T<sub>12</sub>, there was a statistically significant difference between all intervention regimens, where p < 0.001.

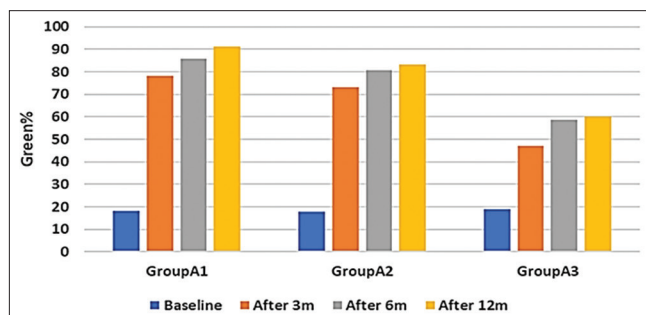


Figure 1: Bar charts representing the effect of time on cariogram (Green%) for each group

While, the highest mean value was found in Group A1 followed by Group A2, the lowest mean value is found in Group A3 Table 1 and Figure 2.

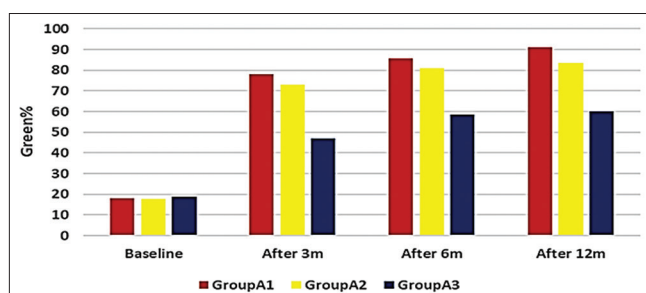


Figure 2: Bar charts representing the effect of different groups on cariogram (Green%) for each time period

### ICDAS results

Regarding all intervention regimens, there was no statistically significant difference between T<sub>0</sub>, T<sub>3</sub>, T<sub>6</sub>, and T<sub>12</sub> Table 2 and Figure 3.

**Table 2: The mean, standard deviation values of international caries detection, and assessment system scores**

Variables	ICDAS									p
	Group A1			Group A2			Group A3			
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	
Baseline	2.060	0.600	2.000	2.000	0.720	2.000	1.833	0.763	2.000	0.157 (NS)
After 3 months	2.060	0.600	2.000	2.018	0.680	2.000	1.867	0.650	2.000	0.213 (NS)
After 6 months	2.060	0.600	2.000	2.055	0.678	2.000	1.850	0.685	2.000	0.133 (Ns)
After 12 monthsh	2.060	0.600	2.000	2.055	0.678	2.000	1.867	0.676	2.000	0.178 (NS)
p	1 (NS)			0.425 (NS)			0.781 (NS)			

\*Significant (p < 0.05). NS: Non-significant (p > 0.05). SD: Standard deviation, ICDAS: International caries detection and assessment system, NS: Non-significant.

### Discussion

Dental caries is a biofilm-induced dental disease as the presence of cariogenic microorganisms is essential to destruction of the mineralized tooth structure. Therefore, mechanical and therapeutic approaches against cariogenic biofilm should disrupt the biofilm matrix to kill or interfere with cariogenic bacteria within the biofilm [12].

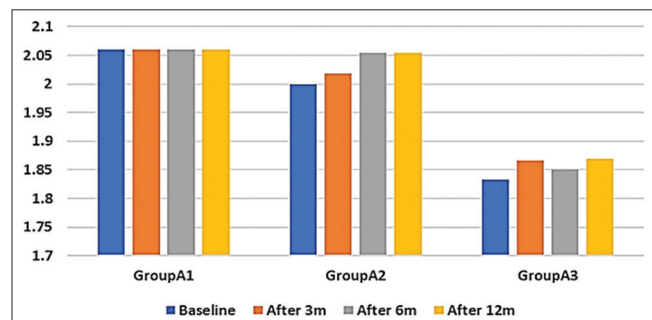


Figure 3: Bar charts representing the effect of time on ICDAS score for each group

New strategies work against cariogenic biofilm have been raised and developed in recent years. Using arginine containing formulations to modulate cariogenic biofilm ecology through alkali production by oral bacteria, through bacterial arginine deiminase system (ADS) as it is responsible for pH raising effect as ADS metabolizes arginine with producing ammonia then protonation of ammonia to ammonium leads to a rise of pH. It considered an effective new therapeutic strategy in the prevention of dental caries. As alkali producing specific bacteria would provide protection against the acidification of cariogenic plaque through fermentation of exogenous amino acid (arginine), which can neutralize acids and raising pH within the biofilm and oral cavity [9].



Zinc-based oral health care products provide a new innovative and interesting era to control and prevent dental caries. Zinc salts as zinc acetate and citrate have been used in oral care dentifrice composition aiming to gain antibacterial and anticaries effect by reducing colonization of bacteria on the tooth surface, inhibition of glucose metabolism, and interaction with the bacterial cell wall [7].

The present study has shown that both caries prevention regimen including dual zinc plus arginine-based toothpaste and regimen including zinc-based toothpaste influence CRA in high caries risk patient more than caries prevention regimen including fluoride-based toothpaste. In addition, preventive regimen including dual zinc plus arginine-based toothpaste was statistically and clinically significant higher when compared with preventive regimen including zinc-based toothpaste. However, DMF scores of all groups showed no statistically significant difference between them. Hence, the hypothesis was accepted.

Studies done by Delgado *et al.* [8] and Sreenivasan [9] supports the paradigm changes in the prevention of dental caries using dual zinc plus arginine-based dentifrices. Based on multiple mechanisms of action, dual zinc plus arginine-based toothpaste has immediate, prolong antibacterial action and reduction of dental plaque with continued use. The antibacterial effect of it is built over time to modify the oral biofilm to maintain the natural balance of the oral microbiome, therefore, offering multiple oral health benefits during regular tooth brushing. Manus *et al.* [13] also found a significant reduction in oral bacterial metabolism and growth using zinc-based toothpaste. Combining L-arginine with zinc will increase the delivery of zinc by enhancing the uptake of it. Therefore, both of them will enhance the antibacterial effect and improving the preventive effect of different regimens against caries.

The result of the study conducted by Lavaee *et al.* [7] and Lim *et al.* [14] evaluated the interaction of zinc and the growth of streptococcus mutans and showed that zinc is a new method for inhibiting cariogenic bacteria. In addition, they did not show significant differences in antibacterial effect between zinc, chlorhexidine, and penicillin. A study done by Sreenivasan *et al.* [15] revealed a significant reduction in lactate dehydrogenase, gingival index, and dental plaque scores, on brushing with 0.96% zinc-based toothpaste when compared to fluoride toothpaste after 12 weeks.

The results of the studies done by Karabekiroğlu and Ünlü [1] and Al Dehailan *et al.* [16] showed the same results of the present study as it was confirmed the use of preventive regimen included within it 1450 ppm fluoride-based toothpaste, fluoride varnish, and chlorhexidine would reduce participants caries risk as evaluated by cariogram and dental caries assessed by ICDAS criteria. Even if not the preventive regimen prevents the occurrence of dental caries, it would

slow the lesion progression. A study done by Sam [17] demonstrated the anti-cariogenic effect of fluoride and chlorhexidine through effective reduction of cariogenic bacteria after 6 months than herbal toothpastes and mouthwashes.

Studies done by Petersson *et al.* [10], Hayes *et al.* [18], and Garg *et al.* [19] were validated the usage of cariogram for CRA and DMFT for measuring the caries incidence. As the suitability of developing new caries, lesion was decreased from high to low caries risk participants after 1 year follow-up. Although study was done by Birpou [20] showed that the accuracy of cariogram with high caries risk participants was limited, as its setting showed low accuracy for predicting dental caries and unrelated with caries experience. Despite study done by Dou *et al.* [21] revealed using cariogram even without saliva tests would provide high caries predictive value, and it is considered a rapid assessment of dental caries.

The hypothesis is accepted in this study as both preventive regimens could enhance patient's caries risk better than preventive regimens including fluoride-based toothpaste. In addition, preventive regimen including dual zinc plus arginine-based toothpaste was statistically and clinically significant higher when compared with preventive regimen including zinc-based toothpaste.

The present clinical trial has some limitations that must be discussed. First, this study is mainly based on patient centered care that may provide variations in following the instructions of preventive regimens. Second, the multifactorial nature of dental caries and behavioral changes of the participants can affect the end results.

## Recommendation

Caries preventive regimens contain dual zinc plus arginine-based toothpaste and zinc-based toothpaste are recommended to be included in different preventive regimens for the prevention of dental caries as an alternative to fluoride-based toothpaste, especially with high caries risk patients. Further studies of different caries preventive regimens are advised to evaluate its clinical performance over a longer period of time using different vehicles.

## Conclusions

Based on the results of this study, it could be concluded that preventive regimens containing different toothpastes are positively influencing caries prevention

in high caries risk patients. Dual zinc plus arginine-based toothpaste is a superior caries preventive regimen in high caries risk patients.

## Clinical Significance

The benefits of preventive regimen to the practitioner will be providing a non-invasive, conservative, time saving, safe, and cost-efficient method to prevent dental caries and reduce patient caries risk. Benefits to the patient will be an improvement of oral hygiene, prevention of dental caries, reducing caries risk, and maintain healthy dental supporting structures. Furthermore, to follow, a caries prevention regimen, using time saving, safe, and cost-efficient antimicrobial toothpaste is proved their potency against mutans streptococci. This will dramatically improve the oral health of patients and will prevent the development of dental caries.

## Author Contributions

All authors had contributed equally and finally approved the manuscript and given consent for publication.

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