

COMPARISON OF THE EFFICIENCY OF ALOE VERA MOUTHWASH WITH ALCOHOL-FREE CHLORHEXIDINE ON PERIODONTAL DISEASE: A RANDOMIZED, DOUBLE- BLIND, CONTROLLED, CLINICAL TRIALAmirhossein Farahmand¹, Ferena Sayar*², Nafiseh Naghdi³, Bahareh Jafrazadeh Esfahani³ and Navid youssefi³¹Assistant Professor, Department of Periodontics, Department of Periodontics, Dental School, Islamic Azad University of Medical Sciences, Tehran, Iran.²Associate Professor, Department of Periodontics, Department of Periodontics, Dental School, Islamic Azad University of Medical Sciences, Tehran, Iran.³Dentist, Private Practice.***Corresponding Author: Ferena Sayar**

Assistant Professor, Department of Periodontics, Department of Periodontics, Dental School, Islamic Azad University of Medical Sciences, Tehran, Iran. Email ID:

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ABSTRACT

Background and Aim: the use of mouthwash has become Prevalent as a part of regular oral hygiene. Chlorhexidine has in fact been proven to be a gold standard oral care; the aim of this study was to compare the clinical periodontal parameters effectiveness and the side-effect profiles of an Aloe- Vera (AV) and an Alcohol-Free chlorhexidine (AF.CHX) -containing mouthwash. **Methods and Materials:** Using a double-blind, randomized clinical trial, a total of 32 healthy individuals with probing depth (PD) >4 mm and clinical attachment level (CAL) $\geq 1-3$ mm; were allocated to treatment with SRP followed by Alcohol-Free chlorhexidine (CHX) mouthwash (A) or Aloe Vera (AV) mouthwash (B) for 15 days; Plaque index (PI) using a Silness & Loe index; bleeding index (BI) by Carter and Barnes; (PD), (CAL) were recorded at baseline and after 15 days. Adverse events were monitored. **Results:** (CHX) mouthwash reduced plaque formation significantly; ($P < 0.001$). The decrease in BI score was greater in group A (0.02 ± 0.03) compared to group B (0.13 ± 0.12) at 15 days; the meaningful reduction in PPD was in the (CHX) group was from 3.54 ± 0.58 to 1.69 ± 0.37 mm, meaningfully greater than with (AV) mouthwash; however Inter-group comparison showed that CAL was a significantly more meaningful reduction in CAL from baseline to 15 days in the (CHX) group than the (AV) group ($P < 0.0001$). **Conclusions:** (AV) mouthwash can be an effective antiplaque agent and with proper purification in taste, can be effective as adjunctive periodontal therapy; the two types of mouthwash seemed to be equally effective as antiplaque agents.

KEYWORDS: Aloe Vera; Alcohol-Free chlorhexidine; periodontal diseases; mouthwash.**INTRODUCTION**

Periodontitis is an infectious inflammatory disease. Bacteria modulate the inflammatory response and alter the diversity of periodontal disease.^[1] Periodontal diseases appear to occur when pathogenic microbial plaque acts on a sensitive host.^[2] Many host-response modulation therapies and local drug therapies have been promoted to block the pathways responsible for the periodontal tissue breakdown.^[1] Total plaque removal is difficult to obtain, and prevention of periodontal disease can be improved either by reducing the amount of plaque below the individual's threshold for disease or altering the quality of plaque to a more tissue-favorable mixture.^[3] For effective plaque control, several mechanical oral hygiene aids, as well as a number of anti-plaque agents such as chlorhexidine and Aloe Vera, are available. Chlorhexidine (CHX) has shown its distinct advantages and proved its efficacy,^[3] However, CHX has been reported to have a number of side effects

namely brown discoloration of teeth, salt taste perturbation, oral mucosal erosions, and enhanced supragingival calculus formation, which limits its long-term use,^[4,7] even so, side effects such as staining of the teeth and increased calculus formation often deter its users over long periods.^[3] Aloe Vera is a perennial succulent plant belonging to the Aloe Cease family (the subfamily of the Asphodelaceae),^[8] Aloe Vera is the most preferred species for a number of medical, cosmetic, and nutraceutical purposes,^[9] It is helpful in the treatment of both gingivitis and periodontitis. It reduces bleeding, inflammation, and swelling of the gingival tissue. It is a powerful antiseptic in pockets where normal cleaning is difficult and inaccessible,^[10] In 2012 Geetha et al. conducted a study on Aloe Vera and highlighted its property when used as a medicament in the periodontal pocket. They deduced that subgingival application of Aloe Vera gel leads into the healing of the periodontal tissue,^[11] In another study conducted by

Barrantes and Guinea in 2003, it was suggested that the aloe formatives could inhibit the MMPs through a mechanism related to that of inhibitory tetracycline's.^[12] A study, conducted by Villalobos et al. In 2001, evaluating the clinical influence of (AV) presented a notable reduction of gingivitis and plaque accumulation after use as a mouth rinse containing this natural product.^[13] Although the medical uses of Aloe Vera have been reported, there is no published literature on compared use of Aloe Vera and Alcohol-Free chlorhexidine for the treatment of chronic periodontitis. Considering the mentioned facts, the aim of this double-blind, placebo-controlled, randomized clinical trial was to evaluate the efficacy of Aloe Vera's mouthwash in comparison with Alcohol-Free chlorhexidine as an adjunct to mechanical debridement during periodontal therapy.

METHODS

Study Design and Population

A total of 32 (16 Male, 16 Female, aged 28 to 62 years) healthy subjects were selected from the patient volunteers of the Periodontics Department of the Islamic Azad University, Dental Branch of Tehran. The research protocol was reviewed and approved by The Ethical Committee of the Dental School. The study was registered at Clinical Trials. Gov as NCT02560870. The current study was arranged according to the principles outlined in the Declaration of Helsinki on human medical experimentation. Written informed consent was obtained from all participants; who were enrolled for this double-masked, parallel, randomized controlled clinical trial.

Inclusion: Diagnosed suffering from early - moderate chronic periodontitis [having at least two residual places with a probing pocket depth (PPD)>4 mm] in two opposite quadrants, and clinical attachment level (CAL) \geq 1-3 mm), more than 28 years old with at least 20 remaining teeth and at three teeth in each quadrant; The following clinical outcome variables were recorded at baseline, within seven days for three weeks at the selected teeth, at six sites per tooth, by means of a periodontal probe (William's® probe, Hu-Friedy, USA) by two calibrated blinded examiners; Plaque index (PI) using a Silness & Loe index.^[14] Bleeding on probing (BOP), through the visual inspection 30s after probing, (Score 0: No bleeding after probing. Score 1: A single discrete bleeding point appears after probing).^[15]

Exclusion: Patients with known allergies to the constituents of the formulation, systemic illness; pregnant and lactating females; patients undergoing orthodontic treatment; multiple bridges, having partial denture or multiple caries and those with smoking habits were excluded.

Clinical Parameters

The subsequent periodontal clinical parameters were noted at baseline; SRP and polishing were performed for

all the objects participating in the study. Oral hygiene instructions were given that included brushing twice a day with a soft brush. After 2 weeks, they were randomly (Balanced Block Randomization with a block size of 4 and an allocation ratio of 1:1 block randomization was chosen to prevent excessive variability in the number of a reasonably steady flow of patients to each treatment group) equally divided into two groups; Group A: Aloe Vera mouthwash (Alodent Co. UK) for every patient, Group B: Non-alcoholic Chlorhexidine (Perio-Kin, Livar CO. Spain). Patients routinely used 10 ml of mouthwash twice a day for about 30 seconds and continued this routine for 15 days. Every 7 days periodontal parameters were evaluated. This was a double-blind study (neither the patients nor the clinicians were aware of the rinsing solution used). Consequently, all durations of treatment, clinical parameters were recorded by an examiner who was blinded to the kind of treatment received by the patients while another clinician gave treatment for both groups. The patients were recalled at weekly intervals in order to get examined for periodontal clinical parameters.

Sample Size Estimation

According to previous studies and the sample size calculation is based on detecting changes in the primary outcome of periodontal disease measurements- probing depth (PD) from baseline to the end of follow-up; The sample size of the study was calculated using "two-sample t-test sample size calculation" tab of MINITAB software considering $\alpha=0.05$, $\beta=0.05$ mean a difference of equal to 1.65 and pooled standard deviation=1.4 ;Therefore at least 15 cases in each group was necessary.

Statistical Analyses

Statistical software was used to analyze the data. The values of different parameters collected are expressed as means \pm SD. At several follow-up meetings in both groups; Repeated measure two-way ANOVA was used for the comparison of quantitative indices, while P-value <0.001 was considered statistically significant. The data were analyzed by SPSS version 21.

RESULTS

All of the patients in the non-alcoholic Chlorhexidine and aloe Vera groups completed the study. In that location was no significant differences between the Non-alcoholic Chlorhexidine and aloe Vera groups, all participants tolerated the drug without any complications. Neither at the beginning nor at the balance of the study period, with differences to the periodontal parameters evaluated. Thirty-six of 40 patients (one site per participant) (Fig. 1) completed the survey. Four patients failed to follow up during the entire course of the study. Thirty-two treatment sites (16 in each group) were evaluated for clinical parameters at the baseline (before SRP) and after seven and 15 days. There was an improvement in both site-specific and full-mouth PI in both groups(A, B) but only at seven and 15 days,

there was a statistically significant difference in site-specific PI ($P=0.0497$). However, a greater reduction in Plaque index scores was detected in Group A compared with Group B as declared in (table1). Meanwhile, at the baseline, BI scores showed no deviation in both groups while a statistically significant decrease was found in BI from baseline to 15 days in both groups. Moreover, Table1 illustrates the decrease in BI score as greater in group A (0.02 ± 0.03) compared to group B (0.13 ± 0.12) at 15 days ($P = 0.0144$). There was a statistically significant reduction in PD and CAL value in both groups compared to baseline at the final interval (Tables

1). CAL gain was significantly greater in group A compared to group B at all periods (Tables 1). The mean value and standard deviation of probing pocket depth (PD) at baseline in the test side were 3.54 ± 0.58 mm and after therapy, it was 1.69 ± 0.37 mm. As a result, there was a highly statistically significant difference between values of PD before and after treatment (at $P = 0.0499$, $P < 0.0001$).

Adverse Events

No adverse events were noted during the entire study process.

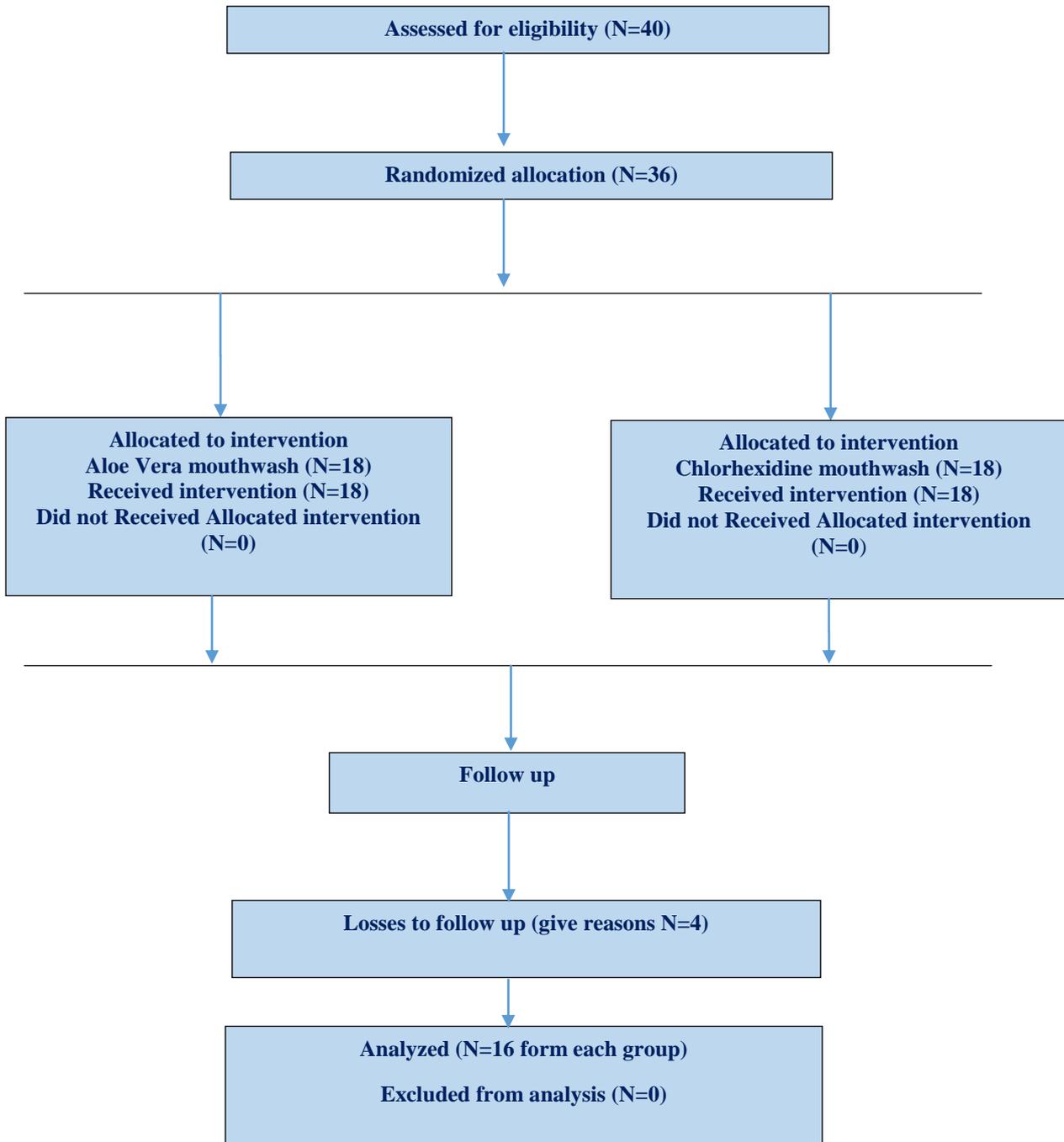


Fig. 1: Flowchart of the study participants.

Table 1: Gender and age distribution of the study participants.

Age Groups	Number of participants And gender	Minimum	Maximum	Mean	Std. Deviation
Group AV	16 (8 male & 8 female)	25	59	38.25	11.323
Group CHX	16 (8 male & 8 female)	24	62	35.53	12.524

Table 2: Indices Scores (Mean \pm standard deviation).

Index	Formulation	Baseline	One week	Two weeks	Three weeks
Plaque	AV	2.98 \pm 1.01	2.84 \pm 0.89	2.25 \pm 0.88	1.96\pm0.54*
	AF.CHX	3.62 \pm 0.92	3.16 \pm 0.67	2.05 \pm 0.86	1.52\pm0.67*
Bleeding	AV	0.61 \pm 0.21	0.48 \pm 0.19	0.27 \pm 0.14	0.13\pm0.12†
	AF.CHX	0.53 \pm 0.18	0.34 \pm 0.15	0.09 \pm 0.10	0.02\pm0.03†
Pocket depth	AV	2.99 \pm 0.40	2.93 \pm 0.43	2.64 \pm 0.39	1.98\pm0.25‡
	AF.CHX	3.5 \pm 0.58	3.32 \pm 0.54	2.27 \pm 0.46	1.69\pm0.37‡
CAL	AV	1.66 \pm 0.63	1.53 \pm 0.59	0.91 \pm 0.71	0.79\pm0.15§
	AF.CHX	1.17 \pm 0.74	1.14 \pm 0.74	0.74 \pm 0.46	0.41\pm0.11§

***P=0.0497 (AF.CHX VERSUS AV), this difference is considered to be statistically significant.**

† **P = 0.0013 (AF.CHX VERSUS AV), this difference is considered to be statistically significant.**

‡ **P = 0.0144 (AF.CHX VERSUS AV), this difference is considered to be statistically significant.**

§ **P = 0.0499 (AF.CHX VERSUS AV), this difference is considered to be statistically significant.**

DISCUSSION

There is an increase in the use of conventional and chemical plaque control agents to prevent dental caries and periodontal disease. Various chemical mouthwashes are available in the market but are associated with side-effects like immediate hypersensitivity reactions, toxicity, tooth staining, etc. Other medicines may be developed from medicinal plants as these plants contain natural phytochemicals, and potentially can replace synthetic drugs.^[16-18] Conventional non-surgical periodontal therapy is based on the elimination of foci of infections by mechanical debridement, including SRP, as well as local drug delivery (LDD) of therapeutic agents, such as herbal products into periodontal pockets. Use of medicinal herbs or their extracts is effective in preventing and treating oral conditions.^[19] Aloe Vera is an herbal plant, used in dentistry for the treatment of oral lichen planus,^[20] burning mouth syndrome,^[21] gingivitis,^[22] and periodontal diseases.^[23] Aloe Vera is a natural product contained in herbal dentifrices, which effect on the control of plaque and gingivitis. Aloe latex has Anthraquinones and enzymes like Brady kinase, which are chemical complexes that are used in healing and arresting pain because of their anti-inflammatory nature. Aloe Vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Also, Aloe Vera includes 6 antiseptic agents: Lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenol, and sulfur. They all have an inhibitory action on fungi, bacteria, and viruses.^[24-26] Although Mlachkova *et al.* (2014),^[27] revealed following non-surgical periodontal therapy, a relevant reduction of plaque and gingival inflammation was found in all treated participants; they also found a statistically important reduction of periodontal pockets with clinically measured depth < 5 mm. The current study evaluated the effects of using Aloe Vera's mouthwash in comparison with Alcohol-Free chlorhexidine for controlling periodontal diseases and

found the improvement in clinical parameters to be significantly more with the Alcohol-Free chlorhexidine compared to Aloe Vera's mouthwash. In addition, the outcomes of our study indicated a significantly greater reduction of PD in the Alcohol-Free chlorhexidine group (A) compared to Aloe Vera (B) which were in agreement with the following study. Chandrasah *et al.* (2012) described that mouthwash containing Aloe Vera showed significant reduction of plaque and gingivitis, There was the statistically significant decrease in PI, MGI, and BI scores, but when compared with chlorhexidine the effect was less significant.^[28] Our results were also in accordance with studies by Ajmera *et al.* (2013) which suggested mouthwash containing Aloe Vera showed a consequential reduction of plaque and gingivitis but when compared with chlorhexidine the effect was less significant.^[29] While on the contrary, Bhat *et al.* (2014) believed that herbal mouthwash can be a good alternative to chlorhexidine in order to reduce the side effects in the treatment of gingivitis and PI.^[30] Additionally, our results were consistent with those were found by Karim *et al.* (2014), who revealed that Aloe Vera mouth rinse was equally effective in reducing periodontal indices as Chlorhexidine and there was a significant reduction in plaque and gingivitis in both Aloe Vera and chlorhexidine groups and no statistically significant difference was observed among patient.^[31] Gupta *et al.* (2014) exhibited that Aloe Vera mouth rinse is equally effective in reducing plaque as Chlorhexidine compared to placebo over a period of 4 days; there was a significant reduction of plaque in Aloe Vera and chlorhexidine groups and no statistically significant difference was observed among them.^[32] Storti (2012) *et al.* stated that chlorhexidine reduced the PI in patients significantly.^[33] In contrast to the findings of the present study Parkar *et al.* (2014) indicated that using Aloe Vera mouthwash leads to improvement of chronic periodontitis and the periodontal parameters the same way as chlorhexidine.^[34] Viridi *et al.* (2012) used Aloe

Vera gel and suggested there was a significant improvement in the pocket depth and the GI readings after six weeks and In the PI. However, the significant improvement was observed in both groups and the difference between the groups was not significant.^[35] Moreover, we have noticed a reduction in plaque, probing pocket depth scores in both groups; this effect could be due to the SRP and proper oral hygiene maintenance. The results of this study were in agreement with those presented by Bhat *et al.*,^[36] and Vidya Dodwad and Komal Arora,^[37] who used subgingival delivery of Aloe Vera gel in chronic periodontitis treatment, where there was a significant reduction in bleeding index, probing pocket depth after treatment of patients with chronic periodontitis. Furthermore, it has been reported that chlorhexidine is cytotoxic to human periodontal ligament cells, inhibits protein synthesis, and affects mitochondrial activity. Thus it could have serious harmful effects on vital tissues,^[38,39] and the herbal mouthwash may be used therapeutically in the future to inhibit oral microbial growth. As CHX rinsing can cause a number of local side-effects, including extrinsic tooth and tongue brown staining, taste disturbance enhanced supragingival calculus formation and, less commonly, desquamation of the oral mucosa. Finally, Investigators are interested in the substitute therapies of plaque control using natural products as an alternative to the present artificial agents. The decrease in gingival scores can be attributed to components of Aloe Vera. Moreover, Aloe Vera extracts have exhibited inhibition of the cyclooxygenase pathway and decrease prostaglandin synthesis from arachidonic acid, consequently reducing inflammation. Vitamin C present in Aloe Vera is associated while collagen synthesis, improves the density of oxygen at the wound position because of dilation of blood capillaries,^[40] further, Aloe vera also decreases edema by controlling matrix metalloproteinases(MMP) blocking polymorphonuclear leucocyte (PMNs) release, cyclooxygenase, and lipoxigenase pathways. Those stimulated PMNs, in turn, inhibit free oxygen radicals.^[41] Within the limitations of this study, Aloe Vera has an anti-plaque and anti-gingivitis effect. If the potential benefit is established through long-term studies, Aloe Vera could be an alternative to chlorhexidine from its primary position and would be precious in patients who are looking for a chemical-free, natural, and patient-friendly oral hygiene supplement. Hence, herbal-based products are expected to replace chlorhexidine as soon as a reliable, effective, antibacterial, tasty and cost-effective substitute could be available. However, future studies (with a long-term rinsing period) can be in order to understand the advantages and disadvantages of this herbal product.

CONCLUSION

Aloe Vera, when used at the full strength, reduced accumulated plaque significantly. Within the limits of the clinical study, it may be concluded that the mouthwash containing Aloe Vera showed significant reduction of plaque and gingivitis, but when compared with chlorhexidine, this was less significant.

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