Effective evaluation of benzydamine hydrochloride as a mouth wash in subjects with plaque induced gingival inflammation

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Abstract

Purpose: Benzydamine hydrochloride is a nonsteroidal anti-inflammatory drug that has shown topical anti-inflammatory, analgesic, anesthetic, and antimicrobial activities most often used in radiation induced oral mucositis. The aim of this study was to assess the effectiveness of 0.15% benzydamine hydrochloride as a mouth wash in subjects with severe generalized gingivitis on comparison with 0.2% chlorhexidine.

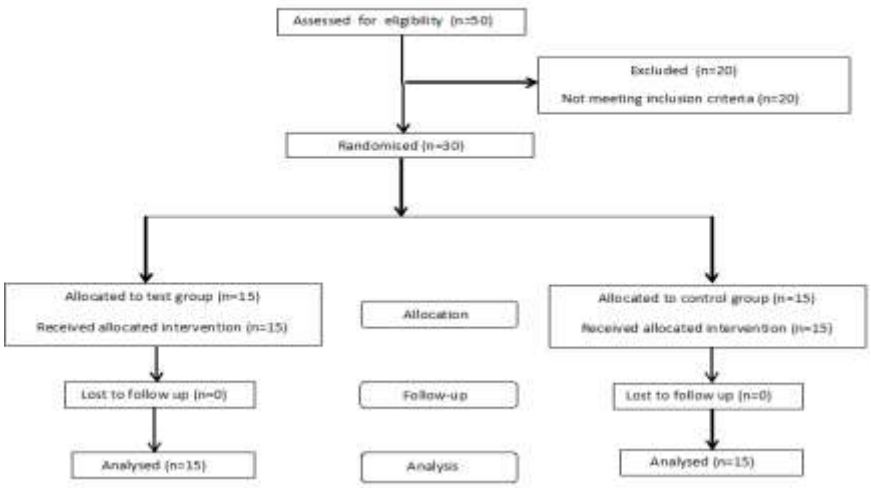
Methods: In this double-blind, randomized, clinical trial, 30 patients were equally divided into two groups. Patients in Group I were advised to rinse their mouths with 10 ml of 0.2% chlorhexidine(CHX) twice daily, Group II with 10 ml of benzydamine (BZD) mouth wash twice daily for two weeks. The clinical parameters measured were plaque index (PI), gingival index (GI), modified sulcular bleeding index (mSBI). These parameters were recorded at baseline, I week, 2 weeks and 1 month.

Results: There was no significant difference when the efficacy of benzydamine hydrochloride was compared to 0.2% chlorhexidine in subjects with severe gingivitis. A statistically significant decrease was observed in PI, GI, mSBI scores at 1 week, 2 weeks and 1 month when compared to baseline ($P<0.05$) in both the groups although intergroup comparison did not reveal statistical significant difference between the test and the control group. ($P>0.05$)

Conclusions: Benzydamine hydrochloride 0.15% as a mouth wash was as effective as chlorhexidine digluconate 0.2% in reducing gingival inflammation induced due to plaque accumulation thus, controls further disease progression. This chemical agent is also cost effective, easily available, and well tolerated with no reported side effects.

Keywords: Benzydamine, Chlorhexidine, Gingival Inflammation, Mouth Wash, NSAID, Periodontal disease

Graphical Abstract



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Introduction

Dental plaque has been proved by extensive research to be a paramount factor in initiation and progression of gingival and periodontal diseases.[1] A direct relationship has been reported to exist between plaque levels and the severity of gingivitis. The most rational methodology toward the prevention of periodontal diseases would be regular, effective removal of plaque by the personal oral hygiene protocol.[2] The

removal of plaque is a determining component in the prevention and treatment of periodontal diseases. The most effective method towards the prevention of periodontal diseases would be regular, effective removal of plaque by the personal oral hygiene protocol.

Procedures for plaque control include mechanical and chemical means. Mechanical plaque control is a simple and cost-effective method that has been reported to be effective in the control of gingivitis. Supragingival plaque control is largely the responsibility of the subject using tooth brushes and interdental cleaning devices, however high percentage of populations all over world do not practice a satisfactory standard of mechanical plaque removal due to lack of dexterity in executing oral hygiene methods. Thus, chemical plaque control can be used as an adjunct to mechanical plaque control procedures.

Observations made by various authors[3,4,5,6] suggested that mechanical cleaning alone by individuals is insufficient to maintain gingival health and to prevent periodontal disease occurrence and progression or recurrence.[2,3,4,5] This supports the concept of using agents to control plaque and require minimal co-operation and skill in their use. Recently, a number of chemical agents have been advocated which are either available in a toothpaste/dentifrices or in the form of a mouthwash. Among them, chlorhexidine is regarded as gold standard in dentistry for the prevention of dental plaque. Chlorhexidine is, thus far, the most studied and effective anti-plaque and anti-inflammatory chemical agent when used twice daily as mouth rinse. But use of mouth rinse chlorhexidine as mouth rinse has been reported to have a number of side effects including: brown discoloration of the teeth, some of the restorative materials and mucosa, bitter taste and occasionally sloughing of oral mucosa which restricts its use[6]. Hence, there is a need of an alternative anti-inflammatory agent which is as effective as chlorhexidine as a mouth wash.

Benzydamine hydrochloride is a nonsteroidal drug that has shown topical anti-inflammatory, analgesic, anesthetic, and antimicrobial activities.[7,8,9] Results from several clinical studies suggest that topically applied benzydamine as a gel is effective in attenuating a variety of inflammatory conditions including oral mucositis induced by antineoplastic radiation or chemotherapy. Studies have suggested that benzydamine is a particularly effective inhibitor of TNF-α production, which may explain its anti-inflammatory effects.[9,10,11,12] Production of TNF-α and, to a lesser extent, IL-1 were consistently inhibited.[14,15] In addition, benzydamine was shown to reduce lethality in the mouse model of lipopolysaccharide-induced shock with a concomitant reduction of peak plasma levels of both TNF-α and IL-1 whereas IL-6 and IL-8 were unaffected.[16]

A recent study by **Roopashri et al.**[17] indicated when benzydamine hydrochloride used as a mouth wash in subjects with radiation induced oral mucositis, there was effective delay in the development of severe form of mucositis and appears more efficient in the management of radiation induced mucositis, in not just delaying the progression of mucositis but also reduces the intensity of pain.

Kazemian et al.[18] compared placebo versus benzydamine (non-steroidal analgesic and anti-inflammatory) oral rinse in the prevention of oral mucositis in head and neck cancer patients receiving radiotherapy. The authors reported incidence of oral mucositis 2.6 times higher in the placebo group. Benzydamine mouthwash was found helpful in another trial by **Epstein et al.**[19] in the prevention of oral mucositis in head and neck cancer patients receiving radiation therapy.

Nicolatou-Galitis et al.[20] conducted a systematic review on anti-inflammatory agents for the management of oral mucositis and concluded that benzydamine mouthwash may be helpful in prevention of oral mucositis in head and neck cancer patients receiving moderate-dose radiation therapy without concurrent radiotherapy.

Taking these fact in to consideration the present study was conducted to assess the anti-inflammatory effects of benzydamine hydrochloride as a mouth wash in subjects with plaque induced gingivitis, also to assess if this anti-inflammatory agent is as effective as chlorhexidine or superior to it.

Materials and Methods

Study Design: The present study comprised a pre-post repeated measures analytical design to assess impact of preventive measures on disease which is a two factor repeated measure study assessing two factors time and condition. This double-blind randomised controlled trial was conducted on patients who reported to the Department of Periodontics, Faculty of Dental Sciences M.S Ramaiah University of Applied science.

The approval of the Institutional Ethics Committee was obtained. Patients were explained about the study and enrolled in the study after written informed consent were given by them. Subjects were recruited from April 2016 to May 2016.

Sample Size: The study was powered at 80% to detect a mean gingival index score difference of 1.9 after treatment assuming a 60% within-group change in the primary outcomes Plaque index and gingival index. The minimum required sample size was calculated to be 10 patients for each group; to compensate for patient withdrawal, 15 patients were recruited for each group.

Eligibility Criteria: 50 patients who visited the out-patient Department of Periodontics, Faculty of Dental sciences M.S Ramaiah University of applied science were assessed for eligibility. Out which 30 subjects who fulfilled the inclusion criteria and exclusion criteria were taken as study population.

Subjects of both genders aged 18-25 years who had been diagnosed with chronic generalized gingivitis with a gingival index of greater than or equal to 2. Patients should not have received non-surgical periodontal therapy within past 6 months Patients were required to be nonsmokers.

Individuals with systemic diseases, personal habits like pan chewing and smoking, dental caries, hormonal imbalances or patients who are pregnant or lactating, subjects with malocclusion were excluded from the study.

30 subjects were randomly assigned to either the test group (15 subjects), who received a mouthwash containing benzydamine hydrochloride [**Garbenz Mouthwash** *Manufacturer: Win Healthcare,* Retailer: ANN Pharma and Food Solutions Pvt. Ltd.] or a control group (15 subjects) who received a mouth wash containing chlorhexidine digluconate [**Rexidin Mouth Wash** *Manufacturer: Indoco Remedies].

Clinical Parameters assessed: After the allotment of patients to the test and the control group. All the subjects underwent an initial examination consisting of oral hygiene measurement. Subjects were educated and motivated regarding the importance of oral hygiene maintenance. The Non- parametric measurements assessed were Plaque index (PI), Gingival index (GI), Modified Sulcus Bleeding index (mSBI). The same clinical parameters were recorded at 1 week, 2 weeks and 1 month after the treatment in both test and the control group. At every visit subject's oral hygiene maintenance was reinforced. The clinical parameters such as PI, mSBI, GI were checked on four sites per tooth [mesiobuccal, buccal, distobuccal, and palatal or lingual]. The sum of all the values was calculated, and then, the average value was calculated by dividing the sum by the total number of surfaces measured. The measurements were carried out as given below.

Intervention: All the subjects underwent an initial therapy consisting of full-mouth Scaling and Root planing (SRP). SRP was performed using hand and ultrasonic instrumentation as necessary, subjects were then educated and motivated regarding oral hygiene practice. After the intial therapy subjects were instructed to use mouth wash for 2 weeks. The study subjects were instructed to discontinue mouth washes in both the groups after a period of 2 weeks in order to avoid side effects of chlorhexidine. Subjects in Group II had to follow the same instructions to avoid any sought of bias. However clinical parameters continued to be assessed till a month in order to assess time of interaction of the agents.

Group I (Chlorhexidine group): The subjects were instructed to rinse their mouth with 10 ml solution of 0.2% chlorhexidine mouthwash twice daily for 60 seconds. After the completion of exact-rinsing time, the subjects were instructed to expectorate the mouth wash.

Group II (Benzydamine group): The subjects were instructed to rinse their mouth with 10 ml solution of 0.15% benzydamine hydrochloride mouthwash twice daily for 60 seconds. After the completion of exact-rinsing time, the subjects were instructed to expectorate the mouth wash.

Patients were instructed not to rinse the mouth with water or any other antiseptic agent or eat after the application of experimental material for half an hour.

At the subsequent visits of 1 week, 2 weeks and 1 month, the clinical parameters were recorded and reinforcement of oral hygiene practice was carried out.

Statistical Analysis

Statistical analysis of data was performed using the version 16 of SPSS software.

- Intragroup group comparison of the clinical parameters at different time intervals were carried out using paired t test.
- Comparison of non-parametric parameters between the studies groups were conducted using One-way ANOVA test otherwise called as **Kruskal Wallis test.**
- When ANOVA result was significant pair wise was carried out using tukey test.
- Descriptive statistics expressed as mean and standard deviation was derived.
- P value <0.05 was considered as statistically significant.

Results

Table 1: Comparison of baseline characteristic between the two groups

Variables Age Mean & SD	Categories	CHX Group		BZD Group		p-value
		2.3	1.7	21.1	1.6	
Gender, N & %	Males	9	60.0%	6	40.0%	0.39
	Females	9	60.0%	6	40.0%	1.00

Variables are represented as mean and SD. (SD- standard deviation)
N- Number of participants
%- percentage of males and females within the two groups

The demographic features of the patients are presented in Table 1. The mean age of the patients was 20.3 years in the control group and 21.1 years in the test group, which was not found to have a significant difference (*P*=0.39). The gender distribution also did not significantly differ between the groups (*P*=1.00).

Table 2: Comparison of baseline clinical parameters between the two groups

Comparison of mean Plaque Index, gingival index & m. sulcular bleeding index between the two groups at baseline						
Time Period	**Group**	**N**	**Mean**	**SD**	**Mean. Diff**	**p-Value**
Plaque index	CHX GRP	15	2.44	0.35	-0.08	0.51
	BZD GRP	15	2.52	0.31		
M. Sulcular bleeding index	CHX GRP	15	2.82	0.13	0.07	0.50
	BZD GRP	15	2.75	0.35		
Gingival Index	CHX GRP	15	2.40	0.35	0.06	0.63
	BZD GRP	15	2.34	0.32		

Variables are represented as mean and SD. (SD- standard deviation)
N- Number of participants
SD- Standard deviation

The baseline parameters such as plaque index, gingival index and modified sulcular bleeding index scores between the test and control group did not have significant difference with a (*P* value of 0.51) for the plaque index, (*P* value of 0.50) for the gingival index and a (*P* value of 0.63) for the modified sulcular index suggesting the baseline parameters did not have a statistical significant difference.

Table 3: Intra group comparison of plaque index for group 1

Time Period	Group	N	Mean	SD	Mean. Diff	p-Value
Base Line	CHX GRP	15	2.44	0.35	2.08	0.0051*
1 Week	CHX GRP	15	1.25	0.28	1.03	0.002*
2 Week	CHX GRP	15	0.95	0.21	0.93	0.001*
1 Month	CHX GRP	15	0.80	0.19	0.90	0.001*

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant.

Table 4: Intra group comparison of plaque index for group 2

Time Period	Group	N	Mean	SD	Mean. Diff	p-Value
Base Line	BZD GRP	15	2.52	0.31	2.08	0.001*
1 Week	BZD GRP	15	1.22	0.23	1.03	0.002*
2 Week	BZD GRP	15	0.95	0.21	0.80	0.003*
1 Month	BZD GRP	15	0.80	0.19	0.90	0.004*

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant.

There was a significant reduction in the plaque index scores for both the groups. This index score in Group I (CHX GROUP) decreased from 2.44±0.35 to 1.25±0.23 at 1 week to 0.95±0.21 at 2 weeks and a final reduction to 0.80±0.19 at 1 month follow up with a [*P* value of 0.001] suggesting a statistical significant difference. This index score in Group II (BZD GROUP) decreased from 2.52±0.31 at baseline to 1.22±0.23 at 1 week to 0.95±0.21 at 2 weeks and a final reduction to 0.80±0.19 at 1 month follow up with a statistical significant difference that has a [*P* value of 0.005].

Table 5: Intra group comparison of gingival index for group 1

Time Period	Group	N	Mean	SD	Mean. Diff	p-Value
Base Line	CHX GRP	15	2.40	0.35	2.05	0.002*
1 Week	CHX GRP	15	1.37	0.40	0.94	0.004*
2 Week	CHX GRP	15	1.07	0.43	0.96	0.003*
1 Month	CHX GRP	15	0.84	0.37	0.73	0.001*

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant.

Table 6: Intra group comparison of gingival index for group 2

Time Period	Group	N	Mean	SD	Mean. Diff	p-Value
Base Line	BZD GRP	15	2.34	0.32	2.06	0.003*
1 Week	BZD GRP	15	1.37	0.40	0.90	0.001*
2 Week	BZD GRP	15	1.07	0.43	1.00	0.002*
1 Month	BZD GRP	15	0.84	0.37	0.90	0.001*

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant.

There was a significant reduction in the gingival index scores for both the groups. This index score in Group I (CHX GROUP) decreased from 2.40±0.35 to 1.37±0.40 at 1 week to 1.07±0.43 at 2 weeks and a final reduction to 0.84±0.37 at 1 month follow up with a [*P* value of 0.001] suggesting a statistical significant difference. This index score in Group II (BZD GROUP) decreased from 2.34±0.32 at baseline to 1.37±0.40 at 1 week to 1.07±0.43 at 2 weeks and a final reduction to 0.84±0.37 at 1 month follow up with a statistical significant difference that has a [*P* value of 0.001].

Table 7: Intra group comparison of modified sulcular bleeding index for group 1

Time Period	Group	N	Mean	SD	Mean. Diff	p-Value
Base Line	CHX GRP	15	2.82	0.13	2.32	0.005*
1 Week	CHX GRP	15	1.52	0.38	1.23	0.002*
2 Week	CHX GRP	15	1.19	0.31	0.90	0.001*
1 Month	CHX GRP	15	0.79	0.20	0.96	0.002

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant.

Table 8: Intra group comparison of modified sulcular bleeding index for group 2

Time Period	Group	N	Mean	SD	Mean. Diff	p-Value
Base Line	BZD GRP	15	2.75	0.35	2.07	0.003*
1 Week	BZD GRP	15	1.52	0.38	1.00	0.004*
2 Week	BZD GRP	15	1.19	0.31	1.00	0.001*
1 Month	BZD GRP	15	0.79	0.20	1.02	0.001*

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant.

There was a significant reduction in the bleeding index scores for both the groups. This index score in Group I (CHX GROUP) decreased from 2.82±0.13 to 1.52±0.38 at 1 week to 1.19±0.31 at 2 weeks and a final reduction to 0.79±0.20 at 1 month follow up with a [*P* value of 0.002] suggesting a statistical significant difference. This index score in Group II (BZD GROUP) decreased from 2.75±0.35 at baseline to 1.52±0.38 at 1 week to 1.19±0.31 at 2

weeks and a final reduction to 0.79±0.20 at 1 month follow up with a statistical significant difference that had a [*P* value of 0.001].

Table 9: Inter group comparison of mean plaque index scores between the two groups at different time interval

Comparison of mean Plaque Index scores between 02 study groups at different time intervals						
Time Period	**Group**	**N**	**Mean**	**SD**	**Mean. Diff**	**p-Value**
Baseline	CHX GRP	15	2.44	0.35	-0.08	0.51
	BZD GRP	15	2.52	0.31		
1 week	CHX GRP	15	1.25	0.28	0.03	0.72
	BZD GRP	15	1.22	0.23		
2 weeks	CHX GRP	15	0.95	0.21	0.00	1.00
	BZD GRP	15	0.95	0.21		
1 Month	CHX GRP	15	0.80	0.19	0.00	1.00
	BZD GRP	15	0.80	0.19		

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.

BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.

*P<0.05 was considered significant.

Although Plaque index scores significantly decreased in both test and control groups at 1 week, 2 weeks and 1 month follow up, intergroup comparison did not reveal statistical significant difference. (*P*=1.00).

Table 10: Inter group comparison of mean gingival index scores between the two groups at different time interval

Comparison of mean Plaque Index scores between 02 study groups at different time intervals						
Time Period	**Group**	**N**	**Mean**	**SD**	**Mean. Diff**	**p-Value**
Baseline	CHX GRP	15	2.40	0.35	0.06	0.63
	BZD GRP	15	2.34	0.32		
1 week	CHX GRP	15	1.37	0.40	0.00	1.00
	BZD GRP	15	1.37	0.40		
2 weeks	CHX GRP	15	1.07	0.43	0.00	1.00
	BZD GRP	15	1.07	0.43		
1 Month	CHX GRP	15	0.84	0.37	0.00	1.00
	BZD GRP	15	0.84	0.37		

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.

BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.

*P<0.05 was considered significant.

Despite, statistical significant reduction in the gingival index score in both test and the control group, intergroup comparison of the gingival index scores did not reveal a statistical significant difference between the groups. (*P* = 1.00).

Table 11: Inter group comparison of mean modified sulcular bleeding index scores between the two groups at different time interval

Comparison of mean Plaque Index scores between 02 study groups at different time intervals						
Time Period	**Group**	**N**	**Mean**	**SD**	**Mean. Diff**	**p-Value**
Baseline	CHX GRP	15	2.82	0.13	0.07	0.50
	BZD GRP	15	2.75	0.35		
1 week	CHX GRP	15	1.52	0.38	0.00	0.81
	BZD GRP	15	1.52	0.38		
2 weeks	CHX GRP	15	1.19	0.31	0.00	1.00
	BZD GRP	15	1.19	0.31		
1 Month	CHX GRP	15	0.79	0.20	0.00	1.00
	BZD GRP	15	0.79	0.20		

Values are presented as mean, standard deviation and mean difference between the groups at baseline, 1 week, 2 weeks and 1 month.
BZD: Benzydamine, CHX: Chlorhexidine, N= number of participants, SD: Standard deviation.
*P<0.05 was considered significant

Even though post-treatment examination revealed statistically significant reduction in the bleeding index scores at 1, 2 weeks and 1 month follow up in both the groups, intergroup comparison of the bleeding index scores did not reveal statistically significant difference (*P*=1.00).

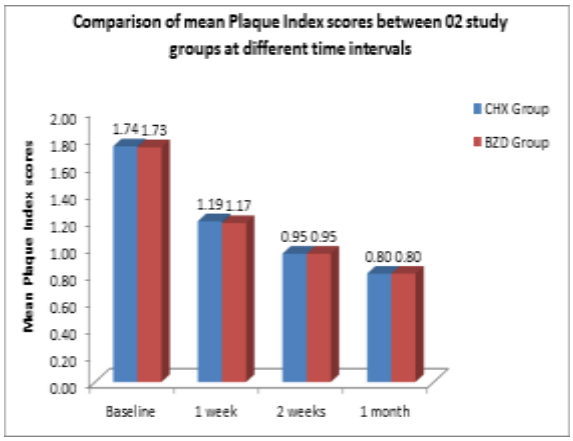

Fig. 1: Inter group comparison of mean plaque index scores between the two groups at different time interval

Bar diagram showing comparison of mean plaque index (PI) values for the two groups.

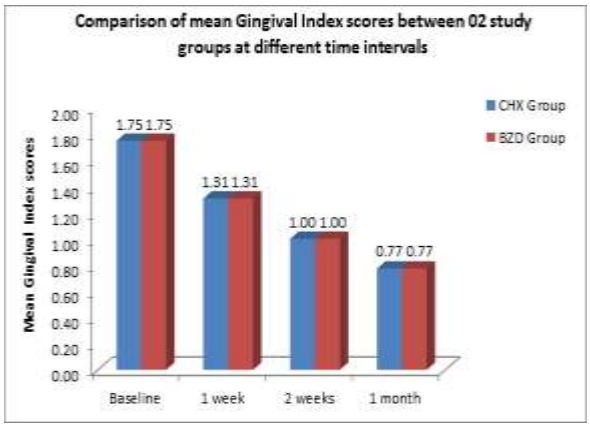

Fig. 2: Inter group comparison of mean gingival index scores between the two groups at different time interval

Bar diagram showing comparison of mean gingival index (GI) values for the two groups.

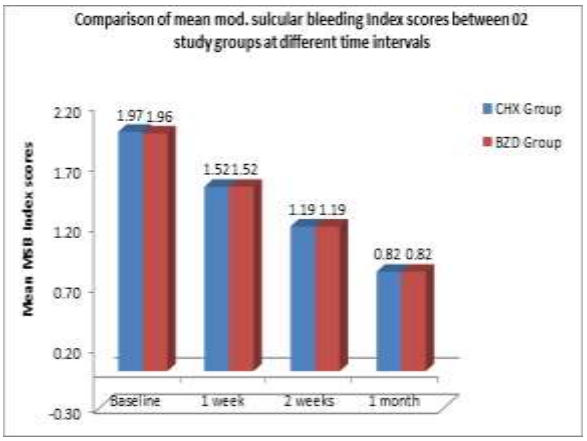

Fig. 3: Inter comparison of mean modified sulcular bleeding index scores between the two groups at different time interval

Bar diagram showing comparison of mean mod. Sulcular bleeding index (mSBI) values for the two groups.

Discussion

This clinical trial is the first study conducted to assess the effectiveness of 0.15% benzydamine hydrochloride in the reduction of inflammation induced by plaque in subjects with severe generalized gingivitis.

This paper presents the data of a short term, double-blind study where CHX and BZD solutions were used as an adjunct to mechanical debridement in a group of patients with chronic generalized gingivitis. Theses mouth rinses improved the supragingival plaque control and had an additional useful effect on the degree of gingival inflammation.

Dental plaque is a complex, specific but highly variable structural entity resulting from colonization of microorganisms embedded in a gelatinous extracellular matrix on tooth surfaces, restorations and other parts of oral cavity.[26] Chlorhexidine is the leading antiplaque agent till date, because of its many ideal properties, and its efficacy has been established by various studies in the literature.[4,5,6] Chlorhexidine acts by damaging the cell membrane of prokaryotes and by disrupting the cytoplasmatic constituents.[25] This agent is the most widely investigated and used oral product. Short-term trials predominantly demonstrate the superior efficacy of CHX on plaque regrowth and numerous other outcome measures. Plaque reductions of 16%-45% and gingivitis reduction from 27%-80% have been demonstrated in six-month trials.[24] On the basis of collection of positive clinical research findings, CHX rinses are often used as a standard control, meaning a product already in use and/or effectiveness evaluated, thus providing information regarding another agent's relative activity.

Similarly chlorhexidine rinses are used as a positive control, indicating that they are accepted as the most effective, or the "gold standard"[25].

On the other hand, Benzydamine hydrochloride is a well-established mouth rinse solution for radiation induced oral mucositis. This is an non-steroidal anti-inflammatory agent with analgesic, anesthetic and antimicrobial activity which is often used in the treatment of oral mucositis induced by radiation therapy.[7,8,9] The exact mechanism of action is not fully understood but it probably affects the prostaglandin and thromboxane production and decrease pro-inflammatory cytokine production. The ability of benzydamine as a preventive agent for radio-chemotherapy-induced oral mucositis has been studied in some double-blind randomized studies conducted in the last decades.[7,8,9,13,17,18,19,20]

Benzydamine HCl was first reported to be an effective intervention for oral mucositis in 1985.[19] In one phase III trial, benzydamine hydrochloride mouthwash reduced the severity of mucositis in patients with head and neck cancer undergoing radiation therapy of cumulative doses up to 50 Gy radiation therapy.[19]

Worthington et al and Clarkson et al.[29,30,31] published meta-analyses of interventions for preventing oral mucositis. Ten interventions showed some statistically significant evidence of benefits for either preventing or reducing the severity of mucositis when used as a mouth rinse compared to either a placebo or control group. One of these interventions was benzydamine hydrochloride mouth rinse.

Kazemian et al.[18] investigated the prophylactic efficacy of benzydamine mouthwash against oral mucositis induced by radiation. They found benzydamine to be a safe, well-tolerated and effective treatment for mucositis which significantly reduced its incidence during Radiation therapy.

Kamian et al.[32] also investigated benzydamine for the prophylaxis of radiation induced oral mucositis in head and neck cancers. They also concluded that an oral rinse of benzydamine was effective, safe and well-tolerated in the prophylaxis of radiation-induced oral mucositis in head and neck tumours, as did Epstein et al.[19] in the prevention of oral mucositis in head and neck cancer patients receiving radiation therapy.

Mody R.N and Talukdar S[33] studied the efficacy of Benzydamine hydrochloride oral rinses in radiation mucositis and reported that its mouth rinse helped in reducing the severity and the faster recovery of mucositis. Kim et al.[9] also observed that Benzydamine hydrochloride when used as a rinse/gargle provided a significant and clinically meaningful alleviation of oropharyngeal mucositis.

However in two studies, 0.15% w/v benzydamine hydrochloride has showed to be less effective than 0.2% w/v chlorhexidine gluconate in term of occurrence and severity of oral ulcerations in a pediatric population[34,35] whereas our study found benzydamine hydrochloride to be as effective as 0.2% chlorohexidine gluconate in reducing gingival inflammation induced by plaque.

Nicolatou-Galitis et al.[20] conducted a systematic review on anti-inflammatory agents for the management of oral mucositis and concluded that benzydamine mouthwash may be helpful in prevention of oral mucositis in head and neck cancer patients receiving moderate-dose radiation therapy without concurrent radiotherapy.

Furthermore, our study is accordance with studies by Wesley et al.[36] they assessed the clinical efficacy of a single sub-gingival irrigation of Chlorhexidine and Benzydamine in advanced Periodontitis. An observation of this study indicated that gingival inflammation index is reduced to 50% within 24 hours and the same level is maintained throughout the subsequent weeks when irrigated with Benzydamine. Another observation of this study by Wesley et al. Irrigation with Chlorhexidine showed a reduction of the Gingival bleeding index score, which was maintained up to two weeks only, while Benzydamine maintained reduced scores till the end of the four weeks. Chlorhexidine irrigation reduced the pocket depth by 25% in the first two weeks while Benzydamine irrigation reduced the pocket depth by 25% during the first two weeks and by 15% during the last two weeks.

Another study by the same author[37] evaluated the microbial effect of a single subgingival irrigation of chlorhexidine and benzydamine in advanced periodontitis results revealed benzydamine can be preferred to chlorhexidine due to their prolonged response as the results revealed the subgingival irrigation of the periodontal pocket with benzydamine hydrochloride showed a decrease in spirochetes up to 45% towards the end of 4 weeks. The level of coccoid after the irrigation of benzydamine was 273 at the end of 24 weeks, 402 and 457 at the end of 1 & 2 weeks as the coccoid cells predominate in healthy suggesting the role of benzydamine hydrochloride against the subgingival disease inducing microflora.

From the evidences mentioned above, it can be said the reduction in gingival inflammation in the present study (p value 0.005) for benzydamine group could be due to its anti-inflammatory as well antimicrobial effects. The present study also revealed its beneficial effect on reduction in the plaque formation at subsequent visits. Thus this agent can be successfully used as an antiplaque as well as antigingivitis agents to prevent future progression of the disease to periodontal breakdown, though future trials with long term follow up needed to establish this hypothesis.

Conclusion

Within the limitations of this study it could be concluded mouthwash containing 0.15% benzydamine hydrochloride was a safe and easy-to-use vehicle with potential therapeutic effects. Benzydamine Hydrochloride mouth wash was as effective a

chlorhexidine digluconate in reducing gingival inflammation induced by plaque. The results further revealed its significant action against plaque accumulation suggesting its antiplaque effectiveness. However further long term trials with larger sample size needed to establish the use of benzydamine hydrochloride as an antiplaque agent.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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