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Comparison of the Side Effects of Chlorhexidine and Honey Mouthwash among Dental Patients: A Randomized Controlled Trial

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ABSTRACT

Gingivitis, primarily caused by bacterial plaque buildup, was managed through mechanical removal, though this requires consistency. Chemical agents like chlorhexidine mouthwash were effective but have notable side effects. Honey, with its antibacterial properties, offers a potential alternative with fewer adverse effects. **Objective:** To compare the side effects of 0.12% chlorhexidine gluconate and 10% honey mouthwash to determine which offers a safer and more comfortable option for oral hygiene in young adults. **Methods:** This randomized controlled trial was conducted from June 2020 to December 2020 to compare the side effects of two oral care solutions, 0.12% chlorhexidine gluconate and 10% honey mouthwash, among young adults. Sixty subjects were recruited from the Department of Periodontology at a tertiary care hospital in Karachi. The primary focus of the study was to observe and document any side effects associated with each mouthwash during and after three weeks of usage for plaque removal and gingival health. **Results:** The study revealed that participants in Group A (chlorhexidine) reported a higher incidence of adverse effects, including a pronounced bad taste, numbness in the mouth, and noticeable tooth discoloration. In contrast, Group B (honey) participants generally reported a pleasant taste, with significantly fewer and milder side effects. **Conclusions:** Honey mouthwash offers a more comfortable user experience with fewer negative side effects, including a pleasant taste. This makes it a promising alternative for individuals seeking an effective and gentle approach to maintaining oral health.

INTRODUCTION

The progression of gingivitis has been long thought to be triggered and/or exacerbated by natural accumulation of dental plaque, consisting of relatively high loads of endogenous oral bacteria. Accumulating metabolites and byproducts from endogenous oral organisms could lead to inflammation [1]. The most successful approach to treating and preventing dental plaque and gingivitis is still the removal of the bacterial biofilm [2, 3]. It has been shown that the application of mechanical agents is an easy and affordable way to effectively reduce gingivitis [4]. Consequently, a chemical method for plaque control using mouthwashes is seen to be preferred to make up for potential shortcomings in maintaining regular dental hygiene. Mouth rinses are frequently utilized as adjuncts to oral care and in delivering active substances to the teeth and gums [3]. Chlorhexidine, commonly known as (CHX), is a biguanide that has a positive effect against bacteria, fungi, and hydrophobic viruses [5]. Investigators recommends CHX in the context of both the prevention and treatment of periodontal disorders due to its plaque

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inhibitory action [3, 6, 7]. Apart of its demonstrated initial bactericidal activity, chlorhexidine binds to the oral mucosa and progressively releases it, continuing its antibacterial impact [8]. Chlorhexidine mouthwash, is regarded the "gold standard," although it has side effects such as teeth discoloration and taste alteration, thus it is not a miracle cure [9]. But its use has been linked to a number of localized side effects, including discoloration of teeth caused by precipitation of anions from food chromogens, temporary shedding of the oral epithelium, taste disturbances, and enhanced accumulation of deposits, especially in the subgingival area [10]. Honey, a natural product, has long been used for both nourishment and medicinal purposes. It has shown broad-spectrum antibacterial activity with few adverse effects. The majority of investigations on honey antimicrobial properties have been undertaken in vitro. It has also been investigated for the ability to reduce dental plaque production [11]. The study was designed to compare the side effects of 0.12% chlorhexidine gluconate and 10% honey mouthwash among young adults.

The aim was to determine which mouthwash offers a more comfortable and safer option for oral hygiene.

METHODS

A clinical trial (ClinicalTrials.gov ID NCT05258955) through randomization was directed to compare the side effects of mouthwashes containing natural honey and chlorhexidine. This open-label study involved sixty patients in the age group 18 to 26 years, complaining of teeth discoloration and gums bleed at the Department of Periodontology, at a Tertiary care hospital of Karachi. Patients were enrolled through convenience sampling from the target population attending the department between June 2020 to December 2020. Convenience sampling was applied to effectively sample participants with an age between 18 and 26 years old, presenting gingival staining and bleeding. All patients gave their consent before they were enrolled into the study. In order to maintain confidentiality and prevent bias in the study, a sealed-envelope randomization procedure was implemented. Participants were asked to randomly select an envelope containing their group assignment, ensuring they were unaware of their assigned group. The envelopes were prepared in advance by independent individuals who were not involved in the study. These individuals sealed the envelopes properly and signed the back of each one to confirm that they had not been opened or tampered with. This process ensured the integrity of the randomization and preserved the confidentiality of the group assignment, minimizing any potential bias in the study results. The participants with 28 teeth (excluding wisdom teeth) and practicing oral hygiene through the modified Bass technique were included. Exclusion criteria included patients with numerous extractions; overhanging restorations; dental prostheses, periodontal pockets exceeding 3 mm, medication use within one month prior to study enrollment, non-compliance with oral hygiene instructions, smoking, habits like betel chewing, and any systemic health conditions causing dental issues, such as Diabetes and Sjögren's syndrome. The randomization process employed an opaque sealed envelope technique to maintain participant anonymity. Envelopes were prepared and securely sealed by individuals unassociated with the study, with stamps applied to ensure tamper-proofing. The study protocol was approved by the Ethical Review Committee of Liaquat College of Medicine and Dentistry on February 5, 2020 (Reference Number: EC/11/20). Each participant provided handwritten informed consent prior to inclusion. The sample size was determined via the OpenEpi, based on the mean and standard deviation of plaque levels in the honey and chlorhexidine groups at day 15, which were 2.85 ± 0.44 and 2.40 ± 0.51, respectively. To account for potential dropouts, at least 27 participants were calculated for each group, with an additional 10% added, bringing the total to 30 participants per group. The study was designed with a 95% confidence interval and 95% statistical power. Partakers were assigned amongst two groups in which Group A was given chlorhexidine Mouthwash while the Group B was given natural honey mouthwash. Natural sidr honey and 0.12% chlorhexidine gluconate mouthwashes were used in the study. Sidr honey, sourced from the Islamic Shehad Centre, was formulated in collaboration with Liaquat College of Medicine and Dentistry. Each 450 ml dark bottle contained 45 ml of honey mixed with 405 ml of lukewarm water to create a 10% honey-based mouthwash. The solution was prepared by diluting 10 ml of honey in 90 ml of lukewarm water. The chlorhexidine mouthwash (0.12%) used in the study was Protect® chlorhexidine gluconate solution, a commercially available brand. Bottles containing the assigned mouthwash were provided to the participants and they were instructed to practice 10 mL two times a day for 60 seconds. They were instructed to brush using the modified Bass technique and were not allowed to use any other mouthwashes during the study period. After 21 days, patients were assessed for the presence of the common side effects: bad taste, good taste, loss of taste, numbness in the tongue and mouth, soreness or burning in the tongue/mouth, dryness, and discoloration. SPSS version 21.0 was used for data analysis, considering mean values, standard deviations, frequencies, and percentages. Descriptive statistics were applied to continuous variables (e.g., age, represented by mean and SD), while categorical variables (e.g., gender, education level, and side effects) were analyzed through frequencies. The chi-square test was used to compare side effects

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between groups, with a significance level set at $p < 0.05$ for all statistical comparisons.

RESULTS

Sixty patients visited the Outpatient Department (OPD) at the Department of Periodontology, at a tertiary care hospital in Karachi. The participants were divided into two groups: Group A, treated with chlorhexidine, and Group B, treated with honey. The mean age in Group A was 23.53 ± 2.60 years, with 66.7% of participants being male and 33.3% female. Group B had a mean age of 24.0 ± 3.76 years, comprising 73.33% males and 26.67% females. The education level distribution was as follows: in Group A, 23% completed matriculation, 30% intermediate, 33.3% undergraduate, and 13.3% were graduates. In Group B, 30% completed matriculation, 26.6% intermediate, 20% undergraduate, and 23% were graduates, as detailed in Table 1.

Table 1: Population Statistics and Level of Education of the Study Participants in Group A and B

Participant Data	Group A Mean ± SD/N (%)	Group B Mean ± SD/N (%)
Age in Years	23.53 ± 2.60	24.0 ± 3.76
Gender		
Male	20 (66.7%)	22 (73.33%)
Female	10 (33.3%)	8 (26.67%)
Level of Education		
Matriculation	7 (23%)	9 (30%)
Intermediate	9 (30%)	8 (26.6%)
Undergraduate	10 (33.3%)	6 (20%)
Graduate	4 (13.3%)	7 (23%)

Group A: Participants receiving Chlorhexidine Mouthwash
Group B: Participants receiving Natural Honey Mouthwash
Age and Level of Education: Mean ± Standard Deviation
Gender: Frequency and Percentage

Table 2 showed that participants in Group A experienced a range of side effects, including a bad taste, which was reported by 15 individuals, and loss of taste, noted by 16 participants. Additionally, 9 participants in Group A reported numbness in the tongue and mouth, while 7 experienced soreness or burning sensations. Discoloration was also reported by 9 participants in Group A. In contrast, Group B, which used honey mouthwash, did not report these side effects. Notably, Group B participants reported a good taste in 15 cases, whereas only 5 participants in Group A reported a pleasant taste. The statistical analysis showed significant differences between the two groups for bad taste, good taste, loss of taste, numbness, soreness/burning, and discoloration (p-values <0.001 for most comparisons), with no significant difference in dryness (p=0.659).

Table 2: Side Effects Experienced by Participants in Groups A and B (n=60)

Side Effects	Number of Participants Group A N (%)	Number of Participants Group A N (%)	p-Value
Bad Taste	15 (50%)	0 (0%)	<0.001
Taste Satisfaction	5 (16.7%)	15 (50%)	<0.001
Loss of Taste	16 (53.3%)	0 (0%)	<0.001
Numbness in the Tongue and Mouth	9 (30%)	0 (0%)	<0.001
Soreness / Burning in Tongue/Mouth	7 (23.3%)	1 (3.3%)	0.004
Dryness	1 (3.3%)	2 (6.7%)	0.659
Discoloration	9 (30%)	0 (0%)	<0.001

Group A received the standard treatment.
Group B received the experimental treatment.
The number of participants indicates those who reported experiencing the specific side effect.
Chi-square test was applied

DISCUSSION

Chlorhexidine (CHX) mouthwash can cause adverse drug reactions (ADRs), with tooth staining being the most commonly reported effect. These ADRs are often underreported, as many studies rely on subjective patient reports rather than objective assessments [13]. According to studies, some self-reported adverse effects were associated with 21 days of CHX mouthwash use included taste change, numbness in the mouth and tongue, oral pain, a dry mouth, and discoloration. "Loss of taste" and "numbness" were much more common at higher concentrations (0.12% and 0.2%) than at 0.06%. However, no severe side effects such as erosion or ulceration of the oral mucosa were noted [14]. Some of the most common side effects of CHX mouthwash were xerostomia, hypogeusia, tongue discoloration, calculus buildup, and extrinsic tooth staining. The most prevalent side effect that prevents people from using chlorhexidine was tooth discoloration [15]. In the study by Guerra F et al., the chlorhexidine + cetylpyridinium Chloride group showed significant improvements in bleeding perception and burning sensations compared to the chlorhexidine alone group. The chlorhexidine alone group had higher reports of burning sensations and altered taste, and was less favored for mouthwash taste compared to the other groups. The chlorhexidine + anti-discoloration System group had better results in taste alteration but more reports of dryness [16]. A seven-day study compared two chlorhexidine concentrations, 0.2% and 0.12%. Both groups experienced no burning sensations on the first and third days, with a few incidences of mild burning recorded on the seventh day. The 0.2% chlorhexidine group had a higher rate of taste disturbances than the 0.12% chlorhexidine group, which had fewer mild taste disturbances [17]. This study assesses

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common complications from using chlorhexidine mouthwashes among 41 dentists in North Macedonia, revealing that 85.4% noted taste disturbance, 78.1% observed xerostomia, and 58.6% reported tooth discoloration. Most dentists (87.8%) recommend these mouthwashes, primarily for mouth odor and periodontal diseases, and 80.5% believe side effects correlate with usage duration [18]. In a study comparing different concentrations of chlorhexidine, the most prevalent reported side-effects were "loss of taste" and "numbness" [19]. Honey has been documented to exhibit broad-spectrum antibacterial properties, effectively targeting a wide range of bacterial strains. Its minimal side effects further enhance its appeal as an oral care solution. This efficacy was attributed to honey's natural components, such as hydrogen peroxide, which was known for its antimicrobial action, and its high sugar content, which creates an environment less conducive to bacterial growth [20]. Another study found that honey mouthwash was superior to chlorhexidine in terms of antibacterial efficacy [21]. Although chlorhexidine was widely used in medicine for a variety of oral treatments, it was also a common contact allergen with undesirable side effects.

CONCLUSIONS

Based on the study findings, honey proved to be a promising natural alternative for oral health care. It demonstrated significant benefits in reducing plaque and gingival bleeding, with fewer or no side effects compared to chlorhexidine. While chlorhexidine had been effective in oral care, it was frequently associated with adverse effects such as taste disturbances, dry mouth, and tooth discoloration. In contrast, honey's antimicrobial properties, along with its positive patient acceptance, positioned it as a viable option for maintaining oral health, making it a strong candidate for further consideration in dental care practices.

Authors Contribution

Conceptualization: MA
Methodology: MA, RR
Formal analysis: AS, SM
Writing, review and editing: AS, HAZ, UZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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