ORIGINAL ARTICLE

Efficacy of Colloidal Nanosilver Tooth Gel in the Management of Orodental Conditions: A Prospective, Randomized, Triple Arm, Parallel, Double-blind Controlled Interventional Clinical Study

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Received on: 26 March 2023; *Accepted on:* 19 June 2023; *Published on:* 29 August 2023

Abstract

Objective: Poor orodental health is a root cause of various oral conditions, viz., dental caries, periodontal diseases, malocclusion, orofacial anomalies, and many more that result in pain, suffering, and even disability. Around 3.5 billion population suffers from one or the other dental condition globally. Moreover, poor orodental health also contributes to many systemic diseases. The newer therapeutic agents are needed to prevent dental caries and plaque formation and thereby protect teeth from further damage. Colloidal Nanosilver (SilverSol®) Tooth Gel is a colloidal nanosilver preparation along with xylitol and peppermint oil with a unique biodisruptive nanotechnology having multidimensional activity due to its wound healing and antimicrobial properties.

Methodology: The present study was conducted on 120 patients suffering from different dental conditions to assess the efficacy of SilverSol® Tooth Gel.

Results: SilverSol® showed a significant effect in almost all the conditions monitored in the patients. There was a reduction in extrinsic tooth stains and pocket depth score in the mouth by 58.6 and 52.2% respectively. Breath malodor also showed improvement as the score reduced by 66%. Altogether, it contributed to the overall oral health improvement by 69%.

Conclusion: SilverSol® Tooth Gel is effective in several orodental conditions including periodontitis and gingivitis in comparison to chlorhexidine gel. Routine application of SilverSol® Tooth Gel will prevent these conditions and maintain the overall orodental health.

Keywords: Bleeding gums, Colloidal NanoSilver Tooth Gel (SilverSol®), Dental plaque, Gingivitis, Orodental health, Periodontitis, Tooth sensitivity.

Journal of Oral Health and Community Dentistry (2023): 10.5005/jp-journals-10062-0166

Introduction

Orodental health is a key to general health. If altered, it leads to various oral conditions, viz., dental caries, periodontal diseases, malocclusion, orofacial anomalies, and many more that result in pain, suffering, and even disability.[1,2] Besides socioeconomic status and awareness, many other factors, viz., diet, unsafe drinking water, alcohol consumption, and tobacco chewing contribute to poor Orodental health, and it can affect every age-group, irrespective of gender, socioeconomic status, literacy, etc. Around 3.5 billion population suffers from one or the other dental condition globally.[3] Wide prevalence of dental conditions is due to various bacteria growing in the oral cavity causing tooth decay (cavities, dental caries) and inflammation causing gum diseases, including gingivitis, and periodontitis respectively. Dental caries is caused by various streptococcal species – *Streptococcus mutans*, *Streptococcus sanguis*, and *Streptococcus salivarius*. Whereas the periodontal pockets support the colonization of diverse gram-negative facultative or obligate anaerobic microbes, viz. *Porphyromonas gingivalis*, *Bacteroides* spp., *Capnocytophaga* spp. and *Actinobacillus actinomycetemcomitans*.[4] Moreover, poor orodental health contributes to many systemic diseases due to the dissemination of microbes and their toxin from the oral cavity to the distant part of the body.[5]

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How to cite this article: Mahale SA, Walvekar AK, Tiwari S, *et al*. Efficacy of Colloidal Nanosilver Tooth Gel in the Management of Orodental Conditions: A Prospective, Randomized, Triple Arm, Parallel, Double-blind Controlled Interventional Clinical Study. J Oral Health Comm Dent 2023;17(2):49–56.

Source of support: Nil

The routine prevention measures for dental conditions are to maintain oral hygiene, involving the use of fluoride toothpaste and/or xylitol. Xylitol helps protect the teeth from damage, and fluoride helps repair any damage to the teeth. However, for severe manifestations, various dental procedures need to be used, which are painful, time-consuming, and may be costly.[6]

Earlier in dentistry, silver was mostly used in the form of amalgams,[7] which now have diverse dental applications in the form of silver nanoparticles,[8] owing to the improved microbicidal activity of silver nanoparticles.[9] Various studies have reported ex vivo inhibitory effects of differently synthesized silver nanoparticle preparations, used as an ionic solution[10] or as silver nanoparticle gel[11] for effective elimination of *Enterococcus faecalis* biofilms.

SilverSol® is a colloidal nanosilver preparation developed by American Biotech Labs (ABL), USA using a patented technology.[12] A nano-sized (5–50 nm) metallic silver particles with their unique structure with water molecules confer SilverSol® multidimensional bioactivity, high safety, and stability.[13] SilverSol® in various dosage forms—wound wash/gels/creams/ointments have shown excellent wound healing activity including complex infected wounds of diverse etiology. It acts through its antimicrobial activity even against multidrug-resistant microbes.[14,15] A large number of patients, over 22,000 undergoing various dental procedures, treated with SilverSol® showed quicker healing time with relief from post-surgical pain and swelling.[13] Based on these data, the present clinical study was undertaken to assess if SilverSol® has any effect on various dental conditions, such as dental caries, gingivitis, and periodontitis that can prevent further complications, viz., teeth damage and subsequent loss.

Oral health being a global concern, newer therapeutic agents are needed to prevent dental caries and plaque formation and thereby protect teeth from further damage. Colloidal Nanosilver (SilverSol®) Tooth Gel is a colloidal nanosilver preparation along with xylitol and peppermint oil with a unique biodisruptive nanotechnology having multidimensional activity due to its wound healing and antimicrobial properties. The present study was conducted in 120 patients with different dental conditions to assess the efficacy of a colloidal nanosilver tooth gel in comparison with chlorhexidine gel as a reference and Placebo.

Methodology

Colloidal Nanosilver (SilverSol®) Tooth Gel is an advanced formulation containing besides SilverSol®, two more commonly used active ingredients are xylitol and peppermint oil. SilverSol® Tooth Gel and identical Placebo Gel were manufactured and supplied by Viridis BioPharma Pvt. Ltd. and the marketed product of Chlorhexidine Gel was used as a reference product.

The primary objective of the study was to assess the efficacy of SilverSol® Tooth Gel in the management of orodental hygiene in comparison to chlorhexidine gel and placebo. The secondary objective of the study was to ensure the tolerability of SilverSol® Tooth Gel in the management of orodental hygiene in comparison to Chlorhexidine Gel and placebo.

The prospective, randomized, triple arm, parallel, double-blind placebo-controlled clinical study was planned with a total of 120 subjects, 40 in each arm, viz., SilverSol® Tooth Gel (Test Product), Placebo Gel (Placebo), and Chlorhexidine Gel (Reference Product)] suffering from one or more of the following conditions.

- Tooth sensitivity (tooth decay (cavities or caries), fractured teeth, worn fillings, worn tooth enamel, exposed tooth root)
- Gingivitis
- Periodontitis
- All dental concerns including bleeding gum, dental plaque (calculus or tar tar)

The sample size was calculated by PASS11 software. The test used for calculation is the Test of The Difference of Two Means. In a study by Pradeep et al., it was reported that the mean gingival index score at 6 weeks interval in the Metronidazole gel group was 1.43 ± 0.27 while the mean gingival index score in Metronidazole and Chlorhexidine combination gel was 1.01 ± 0.38.[16] Keeping this difference at the level of significance (α) at 5% and power of study 85%, we needed at least per group 32 observations. Considering 25% dropout, the total number of subjects per group was decided as 40. Since, we had three experimental groups, a total number of 120 subjects were planned to conduct the study. The Power Analysis of a Non-Inferiority Test of The Difference between Two Means was calculated by a method described by Chow et al.[17] Group sample sizes of 40 and 40 achieve 85% power to detect non-inferiority using a one-sided, two-sample *t*-test. The margin of non-inferiority is –0.170. The true difference between the means is assumed to be 0.078. The significance level (alpha) of the test is 0.05000. The data were drawn from populations with standard deviations of 0.511 and 0.270. The subjects were screened for oral health by dentists using Oral Health Assessment Tool for Dental Screening.

The study was conducted at 4 centers—MGV's KBH Dental College and Hospital, Nashik, India; Coorg Institute of Dental Sciences, Virajpet, India; Shree Samarth Hospital, Pune, India and MV Hospital & Research Center, Lucknow, India. The study was approved by the respective Institutional Ethics Committee and was registered under CTRI (CTRI/2022/01/039411). The trial was conducted as per the ICMR (2006) Guidelines for Biomedical Research on Human subjects, ICH GCP Guidelines, New Drugs and Clinical Trials Rules 2019, Declaration of Helsinki (Brazil, 2013), and in accordance with other applicable guidelines.

A randomization list was generated for this study by using the statistical program in the SAS environment by the random number generation method. Patients fulfilling inclusion/exclusion criteria were enrolled in the study after signing informed consent. A total of 120 patients were enrolled, 40 patients in each arm upon enrollment in the study, patients were randomly assigned to the Test Product or Reference Product or Placebo. Patients were asked to apply the material on the gums, twice a day using a finger or swab and were asked to avoid drinking or eating for 30 minutes after applying the gel for 14 days and followed up after 10 days after discontinuation of treatment, that is, on the 24th day.

The patients were followed up at regular intervals during the treatment period, that is, 4th and 14th day from the start of the treatment. The subjects were later followed up on 10th day after discontinuing the treatment (i.e., on 24th day). During the follow-up, besides physical examination and vital sign assessments, on 14th and 24th day orodental assessment was done for oral health, gingivitis, periodontal status, and stain index.

Following endpoints were considered for the study:

Conflict of interest: Mr. Anirudh Mehta is Director, Viridis BioPharma Pvt. Ltd. and Dr. Shashank S. Jadhav was Med. Director, Viridis BioPharma Pvt. Ltd. Rest of the authors have no competing interests to declare.

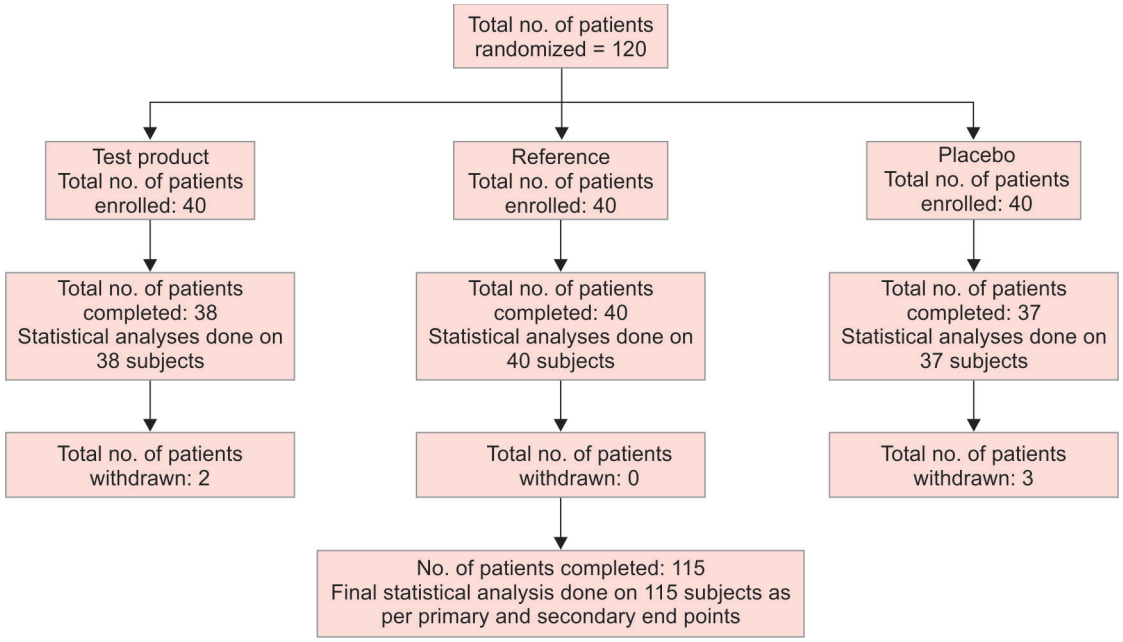

Fig. 1: CONSORT 2010 flow diagram

Primary Endpoints

- Assessment of change in Breath odor from the screening to the end of the treatment using a hedonic malodor evaluation.[18,19]
- Evaluation of the changes in extrinsic tooth stains from screening to the end of treatment by Lobene Stain index.[20]
- Reduction in plaque formation in the mouth from baseline to the end of the treatment.

  Plaque score was determined by using the scoring system for tooth surfaces as follows:

  0 = No Plaque on the tooth surface
  1 = 1/3 of the tooth surface covered
  2 = Between 1/3 and 2/3 of the tooth surface covered
  3 = More than 2/3 of the tooth surface covered
- Reduction in pocket depth in periodontitis is measured by the periodontal probe and the score is assessed using the scale.

Secondary Endpoints

- Improvement in the overall oral health performance as assessed by Oral Health Assessment Tool for Dental Screening and Oral Care Assessment Guide from baseline to the end of the treatment.[21]
- Reduction in gingival index.[22]
- Incidence and rate of adverse events.

All the data were expressed as the mean and standard deviation (SD) of the score of each variant. Change from the baseline to the end of treatment was calculated. The data were analyzed with a 5% significance level and 80% power for study using SAS® version 9.1.3 Inc, CARY, USA. Descriptive statistics was presented for all continuous efficacy indicators obtained during the study and frequency distribution is presented for all categorical variables available in the data. The normality of the data was tested using Kolmogorov–Smirnov test. Wilcoxon rank-sum test (for ordinal interval parameters with non-normal distribution) or χ^2-test (for attributes) was used. In case statistically significant differences are found, differences between treatment groups were estimated with the use of 95% confidence intervals at a 5% level of significance.

Table 1: Demography of the subjects at the time of enrollment ($N = 120$)

Gender	*Females*	*Males*
Number (*N*)	53 (1 dropped out)	62 (4 dropped out)
Age (years) (Mean ± SD/Range)	33.7 ± 11.5/18–63	35.5 ± 11.9/19–74
Weight (kg) (Mean ± SD/Range)	66.6 ± 9.9/43–90	69.6.1 ± 10.7/50–90
Hight (cm) (Mean ± SD/Range)	157.7 ± 6.1/142–172	165.5 ± 9.4/140–188
BMI (kg/m^2) (Mean ± SD/Range)	25.2 ± 4.5/17.01–39.34	25.5 ± 3.5/19.06–34.61
Breath odor	53	62
Extrinsic tooth stain	45	46
Plaque formation	44	43
Pockets in the mouth	44	44
Bleeding gum	4*	3*
Gingivitis	11	21
Gingivitis and periodontitis	24	19
Periodontitis	13	21
Tooth sensitivity	3	2

*1subject had biofilm-induced gingivitis

Results

A total of 120 subjects suffering from one or more orodental problems were enrolled for the study by dentists, using Oral Health Assessment Tool for Dental Screening. Among the 120 subjects' 54 were females in the age-group 18–63 years and 66 were males in the age-group 21–64 years (Fig. 1). The demography of all subjects at the enrollment is given in Table 1.

Table 2: Assessment of various parameters from baseline to end of the treatment in the respective groups

Treatment groups	*N*	*Baseline*	*End of treatment*
Breath odor			
SilverSol® Gel	38	7.08 ± 3.73	2.37 ± 2.34
Placebo	37	6.08 ± 2.62	3.89 ± 2.28
Chlorhexidine Gel	40	7.28 ± 3.08	4.53 ± 3.39
Extrinsic tooth stains			
SilverSol® Gel	29	1.16 ± 0.44	0.48 ± 0.51
Placebo	29	1.31 ± 0.76	1.14 ± 0.74
Chlorhexidine Gel	33	1.09 ± 0.38	0.76 ± 0.50
Plaque formation			
SilverSol® Gel	30	1.69 ± 0.67	1.07 ± 0.42
Placebo	26	1.78 ± 0.70	1.50 ± 0.67
Chlorhexidine Gel	31	1.70 ± 0.76	0.8 ± 0.56
Pocket depth			
SilverSol® Gel	31	1.15 ± 0.43	0.55 ± 0.51
Placebo	28	1.32 ± 0.77	1.04 ± 0.19
Chlorhexidine Gel	31	1.13 ± 0.34	0.84 ± 0.45
Gingival index			
SilverSol® Gel	26	1.65 ± 0.49	1.19 ± 0.40
Placebo	26	1.62 ± 0.50	1.46 ± 0.51
Chlorhexidine Gel	27	1.52 ± 0.51	1.33 ± 0.48
Overall oral health			
SilverSol® Gel	38	3.74 ± 2.72	1.16 ± 1.52
Placebo	37	3.84 ± 2.91	2.97 ± 2.18
Chlorhexidine Gel	40	3.80 ± 2.99	2.58 ± 2.41

Values in Mean ± SD; SD, standard deviation

All the patients had breath odor as a prominent symptom, followed by extrinsic tooth stains, plaque formation, and pockets in the mouth. There was no predominance seen in males or females as to these symptoms.

Enrollment of the subjects was followed by a randomization for the three treatment arms as 40 subjects each receiving placebo, reference product, and test product. However, 1 female and 1 male subject in the test product group and three male subjects from the placebo group were lost to follow-up and hence dropped out. So, a total of 115 cases, with 37 in placebo, 38 in the test product group, and 40 in the reference product group completed the study.

All the subjects received either the test product, reference product, or placebo as per the randomization and were asked to apply the material on the gums twice daily and were followed up on day 4th, 9th, and 14th day of treatment and followed up on the 10th day after the end of treatment (i.e., 24 days of treatment). The major symptoms, viz., plaque formation, reduction in pocket depth, breath odor, and tooth stains along with orodental assessment and overall oral health were monitored using standard methods of scoring as described, *vide supra.*

Plaque Formation

Plaque formation was observed in 26 cases in the placebo group, 30 cases in SilverSol® Gel group, and 31 cases in the Chlorhexidine Gel group. The score for the plaque formation on the tooth surface in these patients varied from 0 to 4. The average scores in the three treatment groups were 1.78 ± 0.7 in placebo, 1.69 ± 0.67 in the SilverSol® Gel group, and 1.7 ± 0.76 in the Chlorhexidine Gel group (Mean ± SD). These values were statistically not significant, suggesting that patients in all the groups were equally affected due to plaque formation. The plaque formation score was assessed at every visit for all the patients in the three treatment groups. Table 2 presents data at the baseline and at the treatment.

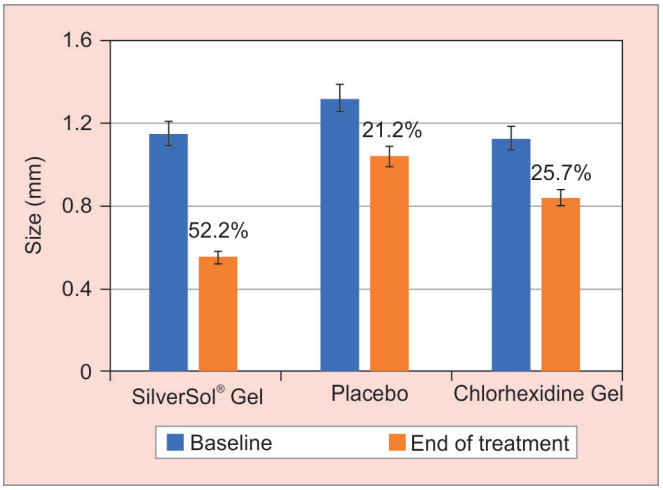

Fig. 2: Pocket depth assessment in the three treatment groups

The comparison of scores of plaque formation in the SilverSol® Gel group and the Reference group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0453) and between SilverSol® Gel group and the placebo group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0306). Whereas when the mean change from baseline to the end of treatment was compared between all three groups, it was found that SilverSol® Gel is more effective in comparison to placebo at 0.05 level of significance. There was a 36.7% reduction in plaque formation with the use of SilverSol® Tooth Gel.

Pocket Depth

Pocket depth was observed in 28 cases in the placebo group, 31 cases in SilverSol® Gel group, and 31 cases in the Chlorhexidine Gel group. Reduction in pocket depth in periodontitis is measured by the periodontal probe and assessed using a scale. The size of pocket depth in these patients varied from 1 to 4 mm. The average scores in the three treatment groups were 1.31 ± 0.76 in placebo, 1.15 ± 0.43 in the SilverSol® Gel group, and 1.13 ± 0.34 in the Chlorhexidine Gel group (Mean ± SD). These values were statistically not significant, suggesting that patients in all the groups were equally affected due to the extrinsic tooth stains. The pocket depth in mm was assessed at every visit for all the patients in the three treatment groups. Table 2 presents data at the baseline and at the treatment and Figure 2 shows a graphical representation of the data.

The comparison of the size of pocket depth in the SilverSol® Gel group and the Reference group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0340) and between SilverSol® Gel group and the placebo group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0094). Whereas when the mean change from baseline to end of treatment was compared between all the three groups, it was found that SilverSol® Gel is more effective in comparison to Chlorhexidine Gel and Placebo at 0.05 level of

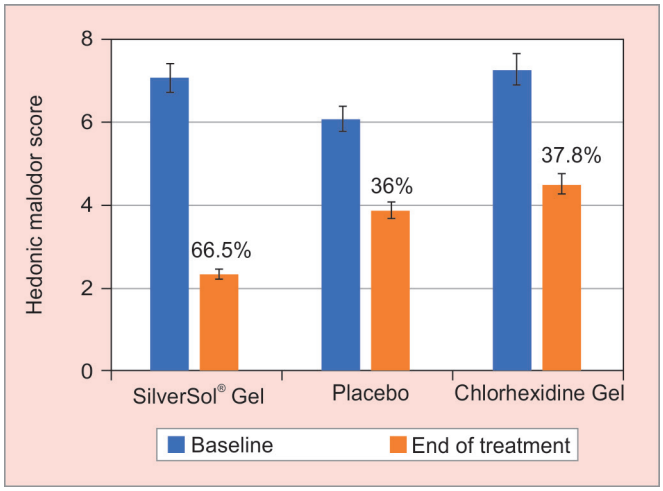

Fig. 3: Breath odor assessment in the three treatment groups

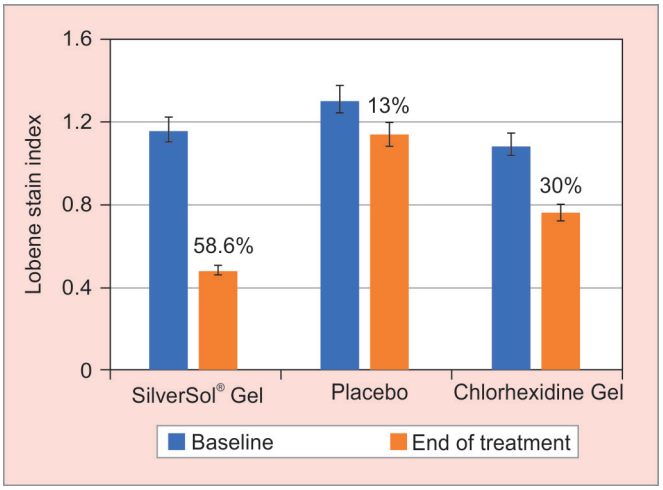

Fig. 4: Extrinsic tooth stains assessment in the three treatment groups

significance. There was a 52% reduction in pocket depth with the use of SilverSol® Tooth Gel.

Breath Odor

All the patients in the three arms had breath odor irrespective of their orodental problem. It was assessed using a hedonic malodor evaluation method.[18,19] Hedonic malodor scores in these patients varied from 1 to 17. The average scores in the three treatment groups were 6.08 ± 2.62 in placebo, 7.08 ± 3.73 in the treatment group, and 7.28 ± 3.08 in the reference group (Mean ± SD). These values were statistically not significant, suggesting that patients in all the groups were equally affected due to malodor of breath. The hedonic malodor score was assessed at every visit for all the patients in the three treatment groups. Table 2 depicts data at the baseline and the end of treatment. Figure 3 shows a graphical representation of the data.

The comparison of scores of hedonic malodor score for breath score assessment in the SilverSol® Gel group and the Reference group showed statistically significant difference between baseline and end of treatment (*p*-value 0.048) and the comparison between SilverSol® Gel group and the placebo group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0068). Whereas when the mean change from baseline to end of treatment was compared between all the three groups, it was found that SilverSol® Gel is more effective in comparison to Chlorhexidine Gel and Placebo at 0.05 level of significance.

Extrinsic Tooth Stains

Extrinsic tooth stains were observed in 29 cases in the placebo group, 29 cases in SilverSol® Gel group, and 33 cases in the Chlorhexidine Gel group. It was assessed using Lobene Stain index.[20] Lobene Stain index in these patients varied from 1 to 4. The average scores in the three treatment groups were 1.31 ± 0.76 in placebo, 1.16 ± 0.44 in the SilverSol® Gel group, and 1.09 ± 0.38 in the Chlorhexidine Gel group (Mean ± SD). These values were statistically not significant, suggesting that patients in all the groups were equally affected due to the extrinsic tooth stains. The Lobene Stain index was assessed at every visit for all the patients in the three treatment groups. Table 2 presents data at the baseline and at the treatment and Figure 4 shows a graphical representation of the data.

The comparison of scores of Lobene Stain index in the SilverSol® Gel group and the Reference group showed statistically significant

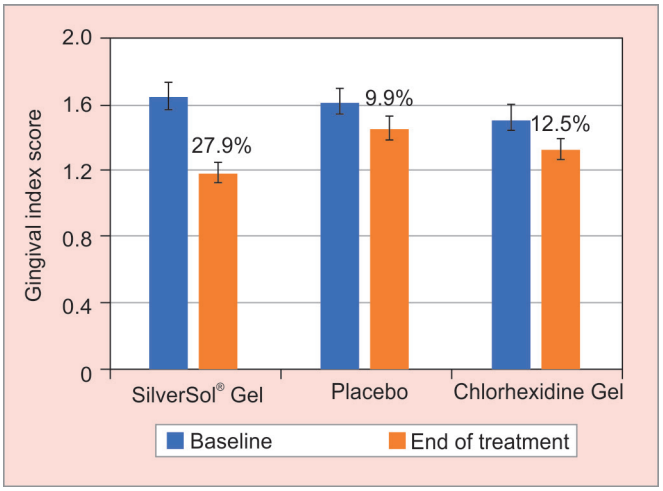

Fig. 5: Gingival index assessment in the three treatment groups

difference between baseline and end of treatment (*p*-value 0.0402) and between SilverSol® Gel group and the placebo group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0064). Whereas when the mean change from baseline to end of treatment was compared between all three groups, it was found that SilverSol® Gel is more effective in comparison to Chlorhexidine Gel and Placebo at 0.05 level of significance. There was an improvement of 58.6% with the use of SilverSol® Tooth Gel.

Gingival Index

Gingival index was assessed in 26 cases in the placebo group, 26 cases in the SilverSol® Gel group, and 27 cases in the Chlorhexidine Gel group. Improvement in gingivitis was assessed by the method described by Harad in 1967.[22] Gingival index in these patients varied from 1 to 3. The average scores in the three treatment groups were 1.62 ± 0.5 in placebo, 1.65 ± 0.49 in the SilverSol® Gel group and 1.52 ± 0.51 in the Chlorhexidine Gel group (Mean ± SD). These values were statistically not significant, suggesting that patients in all the groups were equally affected due to the extrinsic tooth stains. The gingival index was assessed at every visit for all the patients in the three treatment groups. Table 2 presents the data at the baseline and at the treatment and Figure 5 shows a graphical representation of the data.

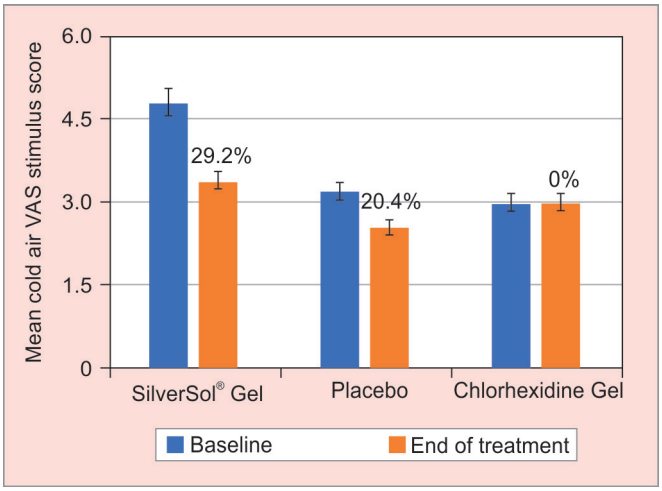

Fig. 6: Tooth sensitivity assessment in the three treatment groups

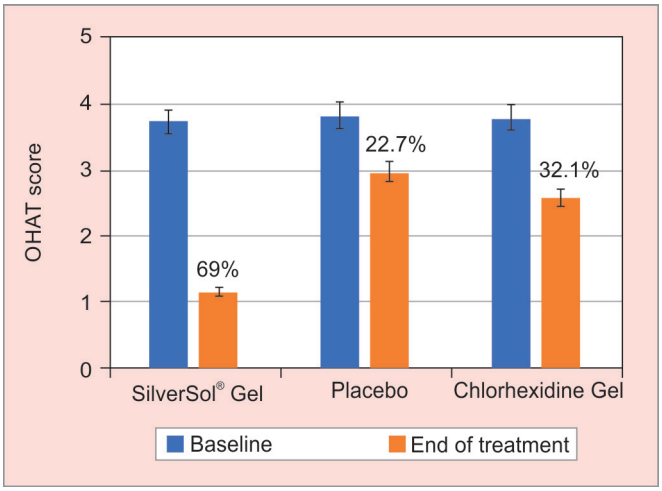

Fig. 7: Overall oral health assessment in the three treatment groups

The comparison of scores of Gingival indexes in the SilverSol® Gel group and the Reference group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0397) and between SilverSol® Gel group and the placebo group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0374). Whereas when the mean change from baseline to end of treatment was compared between all three groups, it was found that SilverSol® Gel is more effective in comparison to Chlorhexidine Gel and Placebo at 0.05 level of significance.

Bleeding Gum

Two patients in each placebo and SilverSol® Gel group had bleeding gums with the baseline score of 3 and 3.2 in the placebo group and 3.5 and 3.8 in the SilverSol® Gel group. The Chlorhexidine Gel group patients did not show bleeding gum issues. At the end of treatment, the score reduced to 2.5 in both the patients in the placebo group and to 2.8 and 3.2 in each patient of the SilverSol® Gel group.

Tooth Sensitivity

Tooth sensitivity problem was observed in all the three groups. Evaluation of tooth sensitivity reduction was measured by Mean Cold Air VAS Stimulus Score using Heft Parker Visual Analog Scale. The average scores for tooth sensitivity in the three treatment groups were 3.2 in Placebo, 4.8 in the SilverSol® Gel group, and 3.0 in the Chlorhexidine Gel group. The tooth sensitivity was assessed at every visit for all the patients in the three treatment groups. Figure 6 shows a graphical representation of the data. The tooth sensitivity was found to be improved in SilverSol® Gel and the placebo group, but the Chlorhexidine Gel treatment did not show any improvement at the end of treatment.

Overall Oral Health

The overall oral health performance as assessed by Oral Health Assessment Tool (OHAT) for Dental Screening and Oral Care Assessment Guide from baseline to end of treatment.[21] It was recorded in all the patients – 37 cases in the placebo group, 38 cases in SilverSol® Gel group, and 40 cases in the Chlorhexidine Gel group.

The OHAT score in these patients varied from 1 to 4. The average scores in the three treatment groups were 3.84 ± 2.91 in placebo, 3.74 ± 2.72 in the SilverSol® Gel group, and 3.8 ± 2.99 in the Chlorhexidine Gel group (Mean ± SD). These values were statistically not significant, suggesting that patients in all the groups were equally affected due to the extrinsic tooth stains. The assessment was done at every visit for all the patients in the three treatment groups. Table 2 presents the data at the baseline and at the treatment and Figure 7 shows a graphical representation of the data.

The comparison of scores of the overall oral health performance in the SilverSol® Gel group and the Reference group showed statistically significant difference between baseline and end of treatment (*p*-value 0.045) and between SilverSol® Gel group and the placebo group showed statistically significant difference between baseline and end of treatment (*p*-value 0.0127). Whereas when the mean change from baseline to end of treatment was compared between all the three groups, it was found that SilverSol® Gel is more effective in comparison to Chlorhexidine Gel and Placebo at 0.05 level of significance.

Adverse Event/s

Two patients reported dull aching in the teeth during the treatment period in the SilverSol® Gel group. However, the symptoms disappeared on their own within 3 hours and no concomitant medication was required. None of the patients reported any adverse event or untoward reaction in any of the treatment groups.

Limitations

In the current study, the number of subjects in each dental condition was not uniform and, in some conditions, it was even inadequate. This study can be considered as a pilot study to evaluate the efficacy of Colloidal Nanosilver Tooth Gel in the management of various orodental conditions. Based on these results, further double-blind placebo-controlled comparative studies need to be conducted with each orodental condition on a larger sample size.

Discussion

Silver has long been known for its antimicrobial activity.[23] Recent development in nanotechnology has further augmented its antimicrobial and anti-inflammatory properties when used in nanoform with several applications in dentistry, such as resins, implants, and other biomaterials.[8,24] This proprietary colloidal nanosilver tooth gel used in the present study is composed of SilverSol®, a patented colloidal nanosilver, xylitol, and peppermint

oil as active ingredients. SilverSol® results in superior microbiocidal activity as compared with other AgNP formulations. The efficacy of SilverSol® in wound healing, and against even resistant microbes has been demonstrated in various *in vitro*, *in vivo*, and human studies.[13] SilverSol® has been demonstrated to have the profound ability to treat oral infections and speed up wound healing during dental procedures in about 22,000 patients without negatively impacting the oral microbiome (and probiotic bacteria) or gut health.[13] *In vitro* studies show strong bactericidal activities of this nanosilver gel (even at low concentrations of 1–3 ppm) with comparable potency to several prominent antibiotics. Additive, as well as synergistic effects of this nanosilver gel were observed in combination with different antibiotics.[14,25]

The current study shows significant improvement in almost all the clinical symptoms monitored in the patients treated with SilverSol® Tooth Gel in comparison to Chlorhexidine Gel. SilverSol® Tooth Gel improved extrinsic tooth stains by 58.6%, followed by a reduction in pocket depth by 52% and 36.7% reduction in plaque formation. This reduction in extrinsic tooth stains was persistent on the 10th day after the end of treatment and remained statistically significant compared with Chlorhexidine (data not shown). SilverSol® Tooth gel was found to be effective in gum bleeding, tooth sensitivity, and gingivitis as the reduction in the respective score was much more than that of the placebo and/or Chlorhexidine Gel. Chlorhexidine Gel did not show any improvement in tooth sensitivity. The improvement was maximum in the breath odor as there was 67% reduction in the baseline score compared with only 37.8% for the Chlorhexidine Gel-treated patients. This effect can be attributed to the superior antimicrobial effect[15] of colloidal nanosilver.

SilverSol® is highly effective in adhering *C. glabrata* and the respective biofilms. On *C. albicans*, the effect was not so evident, but there was also a reduction in the number of viable biofilm cells. Silver nanoparticles have the potential to be an effective alternative to conventional antifungal agents for future therapies in *Candida*-associated denture stomatitis.[26] SilverSol® has also been clinically proven to be effective in the management of various fungal skin infections.[27]

The effect on biofilm-forming ability of bacteria was studied through scanning electron microscopy by Tran et al.[28] It was demonstrated that SilverSol® inhibited biofilm formation by three major bacteria – *S. mutans*, *S. sanguis*, and *S. salivarius*. In addition, it also inhibited biofilm formation by these three bacteria when mixed, as confirmed by scanning electron microscopy. In another *in vitro* study, the colloidal silver gel in combination with betadine antiseptic solution was effective in inhibiting the growth of bacterial biofilms.[29]

This property of SilverSol® is likely to help in plaque formation on long-term use. This will also improve overall oral health, preventing periodontitis and gingivitis. Periodontitis is an inflammatory condition, and SilverSol® has been shown to be an effective anti-inflammatory agent.[13]

In an *in vitro* study, when the silver nanoparticles were added to poly (methyl methacrylate) [PMMA] discs, it was observed that there was reduced adherence of *C. albicans* and it did not affect metabolism or proliferation of human lymphocyte cell line. It also appears that silver nanoparticles do not cause genotoxic damage to the cells.[30] In another *in vitro* study, the colonization and penetration of specific bacteria on nanosilver-impregnated GTR (guided tissue regeneration) membranes were proven to be of value when controlling membrane-associated infection.[31] Incorporating silver nanoparticles into dental materials enhances the mechanical features and antibacterial properties of the dental materials.[32]

Silver nanoparticles have been studied as an alternative strategy for reducing bacterial adhesion and preventing biofilm formation thanks to their antimicrobial properties.[15] Silver nanoparticles have been included in devices used in alveolar bone surgery with promising results. Membranes and scaffolds for bone regeneration containing silver nanoparticles have the potential to reduce the incidence of postoperative bacterial contamination. One of the most interesting applications of silver nanoparticles in dentistry is for preventing or delaying peri-implantitis. Silver nanoparticle coatings could be applied to the whole dental implant surface or to selected areas, such as the most coronal area of the implant or the inner threaded surface. Another strategy to reduce biofilm formation on dental implants and the related prosthetic components in the oral cavity might be to apply silver nanoparticles to prosthetic devices, such as the healing screws, abutments, and fixing screws.[33]

In the recent years, there is an increased awareness among the researchers for the application of silver nanoparticles in dentistry. The usage of silver nanoparticles in dentistry and dental implants, therapeutic abilities, such as wound dressings, silver-impregnated catheters, ventricular drainage catheters, combating orthopedic infections, and osteointegration are being analyzed.[34] An increasing number of dental materials with the inclusion of silver nanoparticles are being developed that improve the overall oral health status of patients.[35] In a recent review article, the superiority of silver nanoparticle compounds in the prevention and arrest of dental caries without the adverse effect of dental pigmentation was observed.[36] Most of the published studies reveal that silver nanoparticles on dental implant surfaces reduce cytotoxicity as well as provide a prolonged antibacterial effect.[37] Even the search for patents (restricted to the A61K code) reaffirmed the growth of the silver nanotechnology and the dominance of the USA pharmaceutical industry over silver nanoparticles product development.[38] Hence, it can be rightly said that Colloidal Silver nanotechnology is a promising area in dentistry with several applications.

The other active ingredients in the SilverSol® Tooth Gel are xylitol and peppermint oil. Xylitol is known to prevent dental caries and reduce plaque formation. It also prevents the adhesion of mutant streptococci to teeth surface and in plaques and saliva kills them through bacterial energy disruption. Peppermint oil, one of the commonly used essential oil adds to the taste of tooth gel, increases freshness in the mouth, and eliminates foul breath odor. It increases saliva secretion and reduces dryness of the mouth and prevents halitosis. Overall, this product, through the combined effects of these active ingredients makes an excellent tooth gel that can maintain orodental health.

Conclusion

In conclusion, the SilverSol® Tooth Gel containing colloidal nanosilver, xylitol, and peppermint oil is effective in several orodental conditions including periodontitis and gingivitis in comparison to Chlorhexidine Gel. It can improve most common problems like tooth sensitivity, gum bleeding, breath malodor and reduces extrinsic tooth stains which have social issues too. Routine application of SilverSol® Tooth Gel will prevent these conditions and maintain overall orodental health.

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