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Clinical Efficacy of Subgingivally Delivered Cranberry Gel in Chronic Periodontitis Patients

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Abstract

Cranberry has a unique combination of phytochemicals which are used for treatment of various systemic diseases including oral diseases like caries, periodontitis and oral cancer. Many in vitro studies have outlined the potential health benefits of cranberry but in vivo studies are still inconclusive. This study aimed to evaluate and compare the effects of subgingival delivery of cranberry gel and chlorhexidine gel as an adjunct to scaling and root planing (SRP) on clinical parameters in the management of patients with chronic periodontitis. In total, 15 systemically healthy individuals with age group ≥30 years diagnosed with chronic periodontitis were included in the study. This randomized split-mouth study comprised of two groups with 42 sites which were randomly allocated to experimental and control sites. After full-mouth SRP, subgingival delivery of cranberry gel in experimental sites and chlorhexidine gel in control sites was done. At 15 days, 1 and 3 months site-specific periodontal parameters were measured. The mean change in the Pocket depth (PD), Plaque Index (PI), Bleeding Index (BI) and Gingival Index (GI) within the groups when compared from baseline to 3 months was reduced in test group found to be statistically significant except probing depth and bleeding index. There was a significant improvement in the oral hygiene index which was statistically significant. Herbal products like cranberry gel can be recommended as an adjunct to SRP therapy for the treatment of patients with

localized, moderate chronic periodontitis can prove to be effective and better alternatives to Chlorhexidine in improving the oral health with minimal side effects.

Keywords: Chlorhexidine, cranberry, proanthocyanidins (non- dialyzable fraction/material (NDM)), periodontitis.

Introduction

Periodontal disease is a chronic inflammatory disease characterised by destruction or the loss of the supporting structures of the teeth.[1] Periodontitis is caused by dental plaque and the micro-organisms that are present in it. Although scaling and root planing (SRP) is an essential part of periodontal treatment, SRP alone fails to eliminate tissue invading pathogens due to difficulty in the ability of the dentist to gain access to deep and tortuous pockets, as well as a bacterial invasion into gingival and dental tissues often results in substantial variation in the effectiveness of scaling and root planing.[2] This led to the search for the need of adjuvant antimicrobial therapy which includes chemotherapeutic agents and neutraceuticals.

Among various local drug delivery agents, chlorhexidine is considered as gold standard as it is the most effective antimicrobial agent. Its antiseptic, which adheres to organic matter and effective in plaque inhibition as it is well-retained in the oral cavity by reacting reversibly with receptors in the mouth due to its affinity for hydroxyapatite and anionic salivary proteins. It has good substantivity, very low systemic toxicity in humans shows no resistance to oral micro-organisms and no teratogenic effects.[3,4]

There has been a rise in research for novel herbal formulations to avoid side effects of allopathy medications. So the dentistry is now oriented towards the phytotherapy by using food products like amla, strawberry and cranberry.Cranberry, Vaccinium macrocarpon, is a native North American fruit. Cranberries consist of 80% water and 10% carbohydrates, while the other 10% are proanthocyanidins (non- dialyzable fraction/material (NDM)), anthocyanins flavonoids, catechins, triterpenoids, organic acids and ascorbic acid. Citric acid, gallic acid, quinic acid, also a lesser content of benzoic acid and glucuronic acid are the organic acids present[5]. Proanthocyanidins, particularly A-type refer to a larger class of polyphenols, called flavanols. More complex polyphenols, having the same polymeric building block, form the group of tannins. Cranberries have one of the highest flavanol content among berries of 50-200mg/kg fresh weight. It has good medicinal properties such as anti-bacterial, anti-adhesion, anti-tumorigenic, anti-inflammatory and anti-oxidant activity[5,6,7]. A type proanthocyanidins of cranberry acts against RANKL dependent osteoclast differentiation.

In this study, an attempt was made to evaluate the clinical efficacy of formulated cranberry gel and chlorhexidine gluconate gel as an adjunct to SRP in the treatment of chronic periodontitis.

Materials And Methods

The study was conducted on the patients who visited the Outpatient Department of Periodontology and Implantology,Dr Sudha and NageswaraRao Siddhartha Institute of Dental Sciences, Chinaoutpally. This randomized split-mouth study comprised of two groups with 42 sites in 15 subjects. Each group includes 21 sites with pocket depth more than or equal to 4mm and less than 8mm were selected. Informed consent was obtained from every participant.

Inclusion criteria

1)Males and females of age 30-58 years,2)chronic gingivitis with localised pockets PD $\geq$ 4 in either maxillary or mandibular, 3) patients with a minimum of 20 natural teeth, 4) patients who had no history of non-surgical or surgical periodontal therapy in the past six months were included.

Exclusion criteria

1)Subjects using mouthwash or dental floss, 2)tobacco consumers,3)pregnant and lactating women, 4) systemically compromised individuals and 5)subjects with the medical or pharmacological history which can compromise the conduct of the study were excluded.

Group I (control group): Thirty sites on one quadrant were treated with SRP followed by chlorhexidine gluconate gel(Hexigel 1%w/w) placement in the periodontal pocket

Group II (experimental group): Thirty sites on the contralateral side were treated by SRP followed by cranberry gel placement in the periodontal pocket.

Gel preparation

9% cranberry gel was prepared by adding one gram of carbopol 934 to 1.25ml of propylene glycol. Carbopol was then neutralized with triethanolamine (TEA) by stirring. In an pre-weighted amounts of i.e 23ml of cranberry juice was dissolved. Then, the dispersion was subjected to trituration. pH was adjusted with 98% triethanolamine (TEA) until it reaches (6.8-7). During pH adjustment, the mixture was stirred gently with a spatula until a homogeneous gel was formed.

Procedure

Clinical examination was done, and the baseline values were recorded priorly by a single calibrated examiner. After thorough SRP, PPD was re-determined followed by the local drug delivery in both control and experimental sites. In Group I and Group II, the area was dried entirely using oil-free air syringe, and then the site was isolated with cotton rolls to prevent contamination from saliva. The local drug delivery system consisting of 0.2% chlorhexidine gel and cranberry gel was placed in the periodontal pockets by syringe with a needle attached to it in the sites of respective groups.

Pocket depth (PD), Plaque Index (PI), Bleeding Index (BI), Gingival Index (GI) and Oral Hygiene Index Simplified (OHI-S) were assessed at baseline, 15 days, one month and after three months.

Statistical analysis

All data were entered into a standardised format and analysed to evaluate the efficacy of chlorhexidine gel (Group I) and cranberry gel (Group II) from baseline to 15 days, one month and three months. SPSS 22.0 version. Mean of standard deviation (SD) of parameters such as pocket depth, GI, PI, BI and OHI-S was computed, and then the comparison between the study groups done using unpaired *t*-test. The within-group comparison made using a paired *t*-test. Test of significance was set at $P < 0.05$.

Results And Discussion

In table 1, the mean PD scores, when compared from baseline to 15 days for control and test groups, were 2.211 and 1.064, respectively. When compared from baseline to 3months, the mean PD found to be 1.160 in the control group and test group 2.185, respectively. The mean difference within the groups found to be statistically significant at 15 days in both the groups and at three months statistically, significant results are seen only in the control group.

The mean PI scores, when compared from baseline to 15 days for control and test groups, were 0.299 and 0.135, respectively. When compared from baseline to 3months, the mean PD found to be 0.014 in the control group and test group 0.086, respectively. The mean difference within the groups found to be statistically significant at 15 days in both the groups and at three months statistically, significant results are seen only in the test group (Table 1).

The mean GI scores, when compared from baseline to 15 days for control and test groups, were 0.164 and 0.228, respectively. When compared from baseline to 3months, the mean GI found to be 0.103 in the control group and test group 0.038, respectively. The mean difference within

the groups found to be statistically significant in both the groups and at 15 days and three months (Table 1).

The mean BI scores, when compared from baseline to 15 days for control and test groups, were 2.811 and 0.728, respectively. When compared from baseline to 3months, the mean BI found to be 0.176 in the control group and test group 0.001, respectively. The mean difference within the groups found to be statistically significant at 15 days in the control group only. At three months, no statistically significant results seen in both groups (Table 1).

On intergroup comparison (Table 2), the mean PD scores reduced significantly from baseline to 3 months, respectively. Still, statistically significant results were seen at 15 days, one month and three months between the control and test group.

The mean PI scores decreased significantly from baseline to 3 months respectively, but no statistically significant results seen at all the time intervals between control and test groups except at 15 days (Table 2).The mean GI scores decreased significantly from baseline to 3 months respectively, but statistically significant results seen between control and test groups at one month (Table 2).The mean BI scores decreased significantly from baseline to 3 months, respectively. Still,statistically significant results seen between control and test groups at 15 days (Table 2).

The paired t-test comparison scores showed that the mean OHI-S increased from 15 days to the three months, and the results are statistically significant (Table 3).

The local delivery of therapeutic agents into the periodontal pocket has prolonged availability of the drug resulting in its sustainability and thereby attaining 100 folds of higher concentrations in the subgingival site[8].

Among the various antimicrobials used as LDD agents, chlorhexidine has been the gold standard for subgingival chemical plaque control regimens[9]. It has found to be effective against subgingival bacteria when delivered through a sustained release device. It is useful when rinsed as it inhibits dental plaque and gingivitis has been well-established in for about two years without evidence of the development of any bacterial resistance[10].

Cranberry is a newer therapeutic approach against oral biofilm because of its anti-adhesive property. It inhibits of the production of organic acids produced by bacteria, and the formation of dental biofilm which justifies the use of such newer agent for the treatment and prevention of biofilm-dependent oral infections[11].

In vivo, animal studies stated that cranberry extracts can reduce C-reactive protein (CRP)[12] and proinflammatory interleukins and increase NO synthesis[13] . It decreases angiotensin converting enzyme, angiotensin II, and angiotensin II type 1 receptor. It also suppress Helicobacter pylori infection[12]; and improve pancreatic b-cell glucose responsiveness and functional b-cell mass. Cranberry products can lower LDL cholesterol (LDL-C) and total cholesterol, increases HDL cholesterol (HDL-C). It lowers glycemic responses and elevates plasma antioxidant capacity.

The results of the present investigations showed comparable improvement in the clinical parameters like pocket depth, gingival index and bleeding index in the test group compared to that of the control group at the end of three months and the results are not statistically significant. Plaque index scores reduced in the control group compared to that of the test group, and the results are not statistically significant.

Authors[12] conducted a study to compare the effect of three different types of mouthwash cranberry, hiora and chlorhexidine in the management of periodontal diseases. They stated that the mean change in the GI, PI within the groups when compared from baseline to 21 days found to be statistically significant. At 21 days, the mean PD

reduced in the cranberry group. The mean % difference in the microbial count Aggregatibacter actinomycetes comitans and P.gingivalis is less in hiora when compared with chlorhexidine and cranberry groups at 15 days.

Maria C. Sanchez etal[13]stated that cranberry had a moderate anti-bacterial effect against periodontal pathogens in biofilms, but relevant anti-biofilm properties, by affecting bacteria adhesion in the first six hours of development of biofilms. The NDM fraction prevents the adhesion of P. gingivalis to various proteins including type I collagen thus reducing bacterial co-aggregation in periodontal diseases[14]. Cranberry acts against the proteolytic activity of the red complex specifically the gingipain activity of P. gingivalis, the trypsin-like movement of T. forsythia thus inhibits their growth resources from amino acids, peptides and inhibits the tissue destruction mediated by bacterial proteinases[15,16].

Rajeswari etal[17] compared the effect of cranberry gel and chlorhexidine gel (0.2% cervitec) against micro-organisms (Porphyomonas gingivalis (PG), Tanerella forsythia (TF), Aggregatibacter actinomycete comitans (AA)) developed in culture media. They stated that cranberry shows similar to inhibition against a panel of micro-organisms associated with periodontal and periapical infections. Cranberry is known to inhibit co-aggregation of bacteria to host cells. A high molecular weight non-dialysable material (NDM) of cranberry juice shown to reverse co-aggregation of many oral bacterial species[18].

Tipton DA etal[19] stated that low non-dialysable material (NDM) concentrations inhibit NF-kB and MMP-3, suggesting that cranberry components may regulate AgP fibroblast inflammatory responses.

Cranberry juice may fight oral diseases, but its high dextrose and fructose content in addition to its hyperacidity limits its potential. However, the NDM fraction of cranberry is highly effective in the control of periodontitis. NDM fraction of cranberry incorporated in mouthwashes or toothpaste may have shown a lot of promising results in the management of periodontitis.

To the best of our knowledge, a very few studies in the scientific literature compared the efficacy of cranberry and chlorhexidine on subgingival delivery along with SRP. The periodontal parameters are assessed at 15 days, one month and three months in chronic periodontitis patients. Although the aim and objectives of the present study are met, however, few limitations were also noted like small sample size and no microbiological assessment.

Future perspectives are aimed at conducting studies with a larger sample size with 6-month follow-ups. To assess the long-term effectiveness of cranberry gel as an adjunct in non-surgical periodontal therapy, they may be incorporated into a biodegradable matrix of crosslinked hydrolysed gelatin and made into a chip for its more extended bioavailability.

Conclusion

Within limitations of the study, herbal products like cranberry gel can be recommended as an adjunct to SRP therapy for the treatment of patients with localized, moderate chronic periodontitis can prove to be effective and better alternatives to Chlorhexidine in improving the oral health with minimal side effects.

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Legend Tables and Figures

Table 1: Intra Group Comparison Of Pocket Depth, Plaque Index, Gingival

Parameter	Time interval	Control group			Test group		
		Mean	F value	P-value	Mean	F value	P-value
Pocket depth	Baseline-15days	2.211	17.876	.000	1.064	4.057	.025
	Baseline- 1 month	1.116	5.495	.008	.470	3.244	.050
	Baseline-3months	1.160	5.598	.007	.264	2.185	.126
Plaque index	Baseline-15days	.299	19.309	.000	.135	9.225	.000
	Baseline- 1 month	.072	3.549	.024	.096	5.665	.003
	Baseline-3months	.014	.776	.515	.086	6.323	.001
Gingival index	Baseline-15days	.164	14.071	.000	.228	15.996	.000
	Baseline- 1 month	.173	5.076	.005	.044	2.138	.096
	Baseline-3months	.103	4.802	.006	.038	3.424	.018
Bleeding index	Baseline-15days	2.811	20.927	.000	.728	3.001	.091
	Baseline- 1 month	.056	.214	.647	.269	1.216	.277
	Baseline-3months	.176	.787	.380	.001	.007	.931

Table 2: Inter Group Comparison Of Pocket Depth, Plaque Index, Gingival Index And Bleeding Index

Clinical Parameters	Time Interval	Intergroup Comparison		Mean	p-value
Probing Depth	At baseline	Group 1	Group 2	.146	.057
	At 15 days	Group 1	Group 2	-.293	.003
	At one month	Group 1	Group 2	-.390	.000
	At 3 months	Group 1	Group 2	-.317	.003
Plaque index	At baseline	Group 1	Group 2	-.0415	.572
	At 15 days	Group 1	Group 2	-.0805	.045
	At one month	Group 1	Group 2	-.0268	.474
	At 3 months	Group 1	Group 2	.0073	.822
Gingival index	At baseline	Group 1	Group 2	-.0195	.798
	At 15 days	Group 1	Group 2	-.0220	.581
	At one month	Group 1	Group 2	-.0951	.012
	At 3 months	Group 1	Group 2	-.0488	.117
Bleeding index	At baseline	Group 1	Group 2	-.024	.822
	At 15 days	Group 1	Group 2	-.805	.000
	At one month	Group 1	Group 2	-.171	.147
	At 3 months	Group 1	Group 2	-.073	.498

Table 3: Comparison of Oral Hygiene Index-Simplified From Baseline to 3 Months

Clinical parameters	Time interval	N	Mean	P-value
OHI-S	Baseline-15days	15	.233	.000
	Baseline- 1 month	15	.240	.000
	Baseline-3months	15	.280	.000

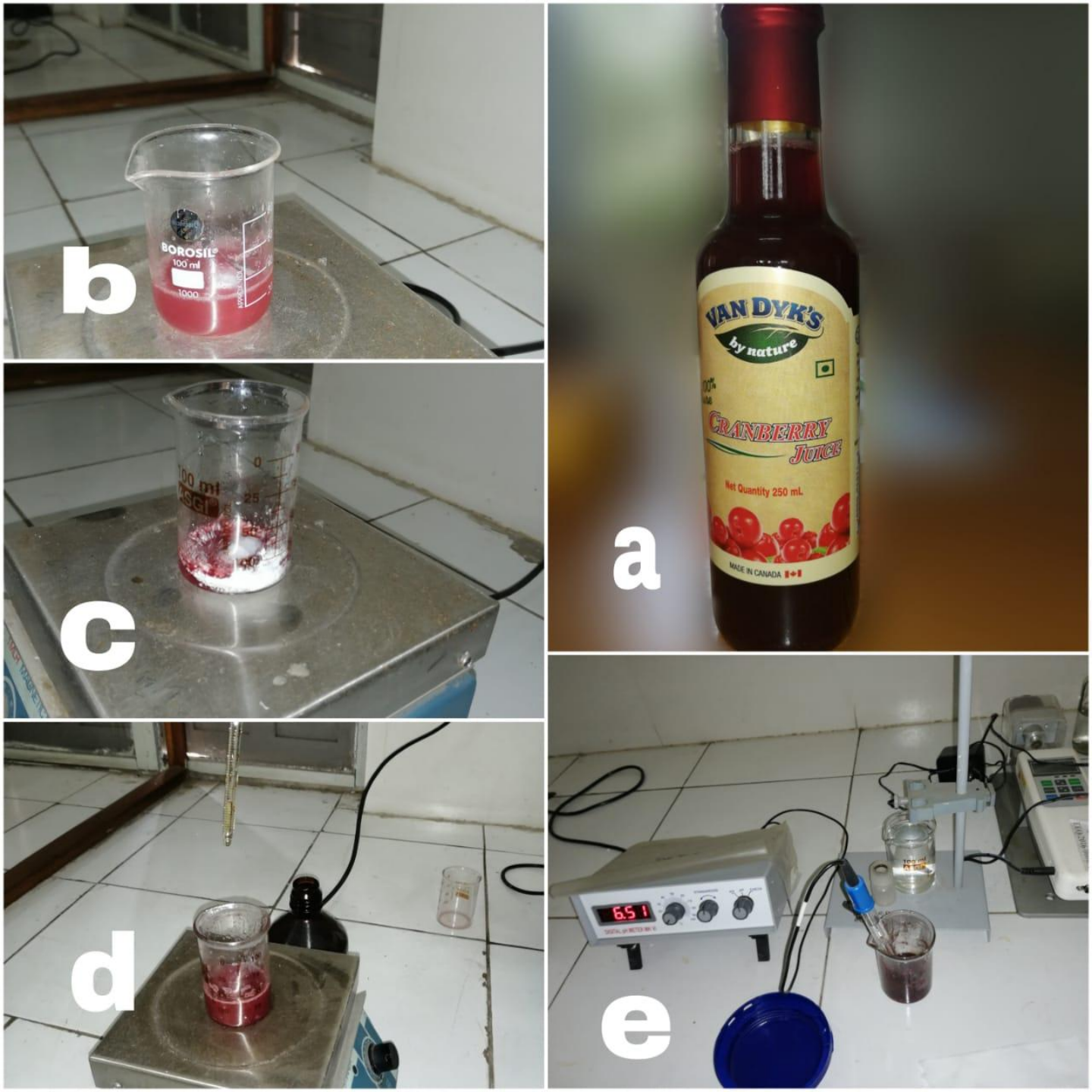

Fig 1: a)commercially available 100% concentrated cranberry juice, b)cranberry juice is added to the carbopol and propylene glycol, c) mixture is stirred on a magnetic strirrer, d)triethanolamine is added to the mixture to adjust the pH, e)showing the pH of the prepared gel**.**

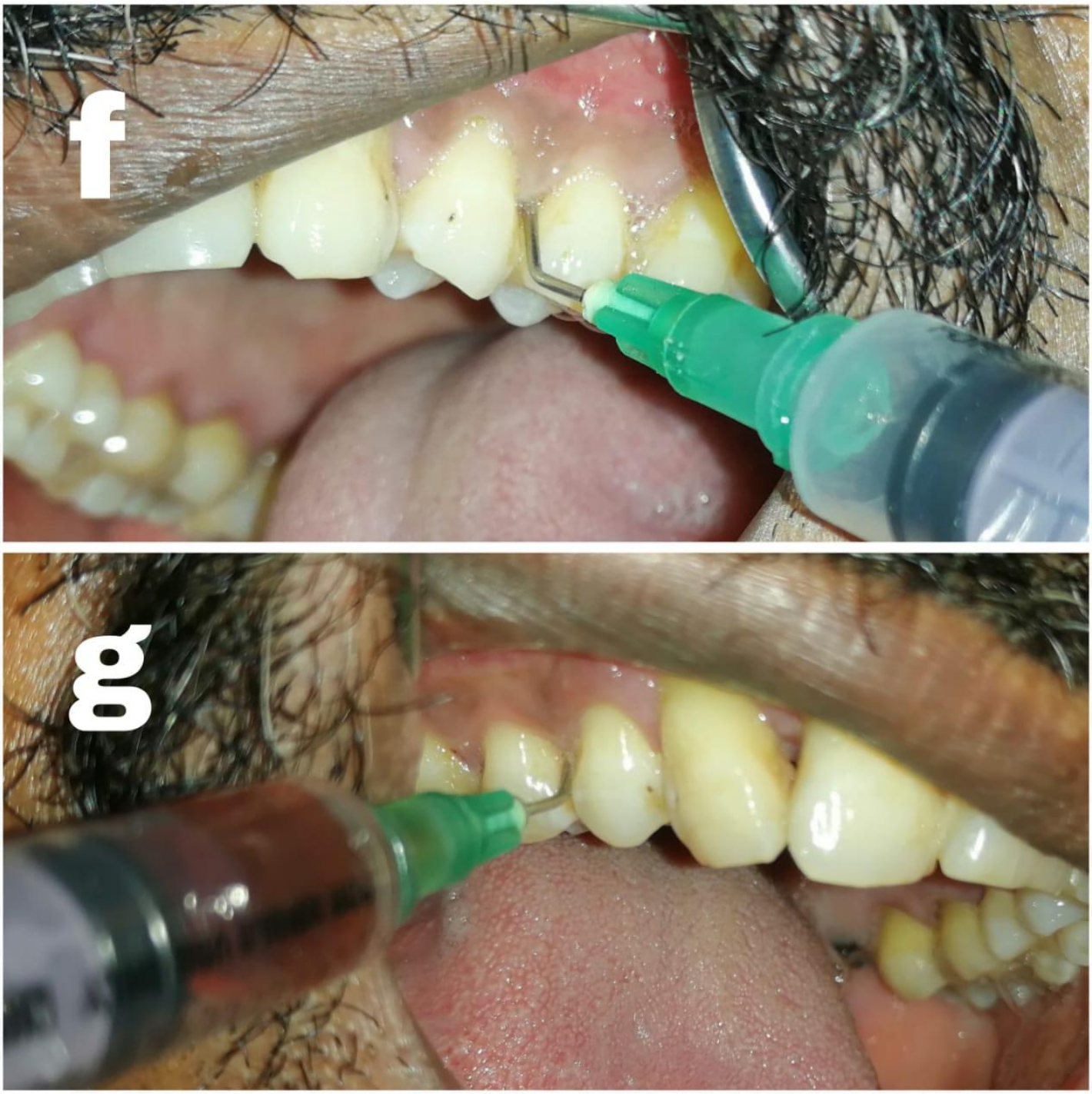

Fig 2: f &g shows the subgingival delivery of chlorhexidine and cranberry gel delivery at the premolar sites

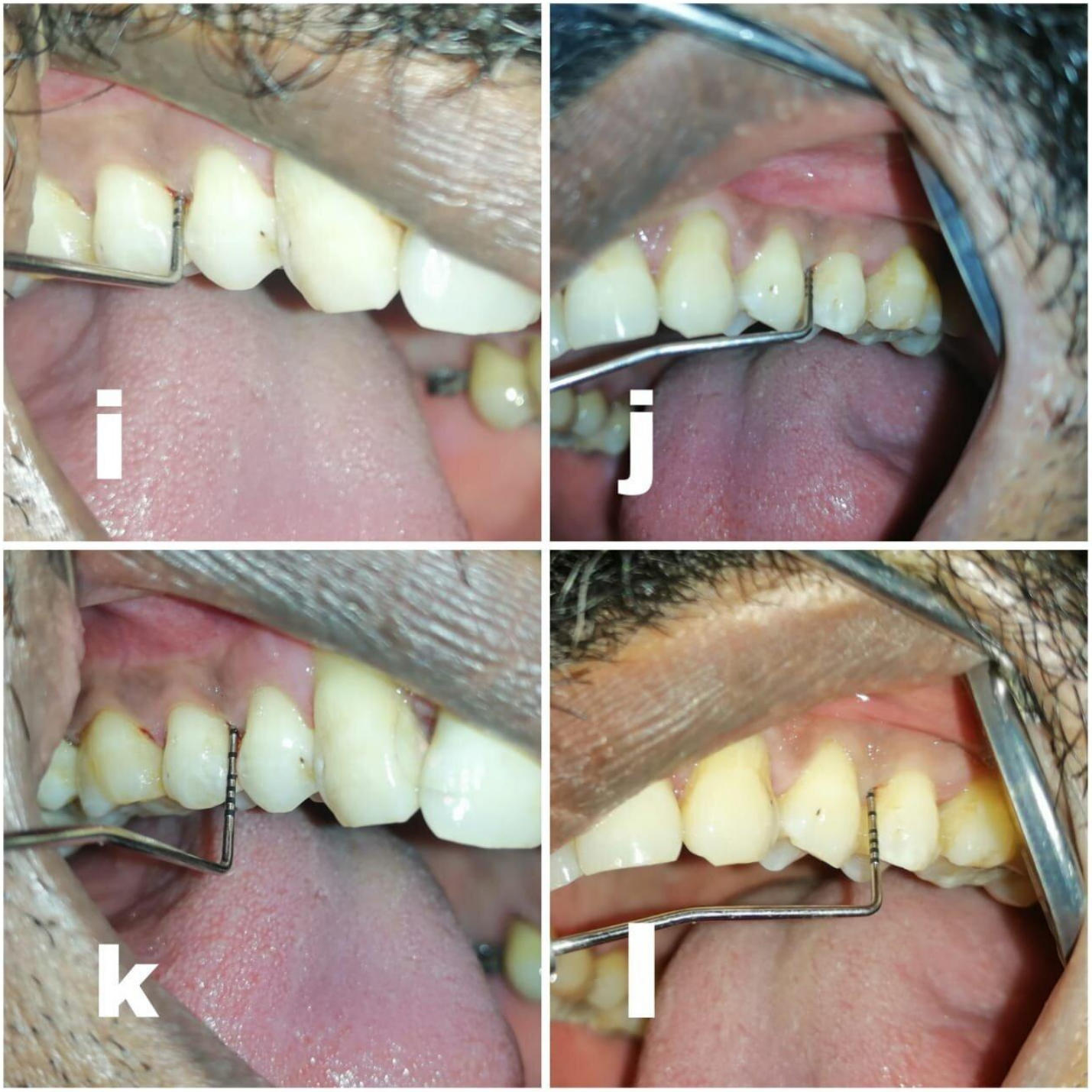

Fig 3: I & j) shows the preoperative probing depths, k & l)shows the post operative probing depths at 3months.