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Research Protocol

Dentistry Section

Evaluation of Mangosteen Gel as an Adjunct to One Stage Full-mouth Disinfection in Stage II Periodontitis Patients: A Research Protocol of Randomised Controlled Clinical Trial

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ABSTRACT

Introduction: Periodontitis is a long-term inflammatory disease that deteriorates the tissues supporting teeth. A new staging and grading system helps improve understanding and management of its severity and progression. Stage II periodontitis is characterised by moderate Clinical Attachment Loss (CAL) and Probing Depths (PD) with horizontal bone loss. One Stage Full-Mouth Disinfection (FMD), using agents like Chlorhexidine (CHX), aims to eliminate intraoral reservoirs of pathogens and improve periodontal outcomes. Recent interest has emerged in natural adjuncts such as Garcinia mangostana (mangosteen), known for its antioxidant and anti-inflammatory properties, for their potential role in periodontal therapy.

Need of the study: Although FMD has shown benefits over conventional therapy, the adjunctive use of herbal agents like mangosteen gel remains underexplored. Considering the reduced antioxidant capacity observed in periodontitis patients, investigating a potent natural antioxidant like mangosteen as an adjunct to one stage FMD could improve clinical outcomes.

Aim: To evaluate the effectiveness of mangosteen gel in one-stage FMD treatment of Stage II periodontitis patients, focusing on improvements in PD, CAL and Bleeding On Probing (BOP).

Methods and Materials: This randomised controlled parallel arm clinical trial will involve 30 systemically healthy individuals diagnosed with Stage II periodontitis, recruited from the outpatient Department of Periodontics at Sharad Pawar Dental College, Sawangi (Meghe), Wardha. The study proposal (ref. no. DMIHER(DU)/IEC/2024/51) has been approved by the DMIHER Institutional Ethical Committee (IEC). The patients will be randomly divided into two groups and the planned overall duration of the study will be one year from December 2024 to November 2025, while it will include a follow-up period of six months. Group-A will receive one-stage FMD, performed within 24 hours and consisting of subgingival Scaling and Root Planing (SRP) with adjunctive measures described in the original FMD protocol by Quirynen M et al., including CHX mouth rinse, tongue brushing, and pocket irrigation. Group-B will undergo the same FMD regimen as Group-A, with the addition of subgingival application of mangosteen gel in all periodontal pockets one week postoperatively. Since CHX is an integral component of the established FMD protocol, the present study specifically evaluates the adjunctive effect of mangosteen gel beyond this standard regimen. Clinical data, including the Probing Pocket Depth (PPD), CAL, BOP will be recorded at baseline, three months, and six months. To determine the importance of variations within and across groups, the data will be analysed using appropriate statistical methods, including the Wilcoxon signed-rank test. Using IBM SPSS Statistics, SPSS v17 statistically significant p-value is defined as being less than 0.05.

Keywords: Chlorhexidine, Full mouth disinfection, Mangosteen gel, Periodontitis, Root planing, Scaling

INTRODUCTION

Periodontitis is a multifactorial disease that impacts the periodontium and affects people of all ages, ethnicities, and genders. This inflammatory condition of the tooth's supporting tissues is caused by bacteria or clusters of particular microorganisms, and it causes recession, pocket formation, or both as the periodontal ligament and alveolar bone gradually deteriorate. The new classification system offers a comprehensive, multidimensional approach to diagnose and treat periodontitis, enabling clinicians to better assess disease severity and create more effective treatment plans. The staging and grading method can assist in identifying people at risk for illness progression who may require more intensive therapy [1]. The staging method in periodontitis classification considers not only disease severity but also the complexity of care and risk of progression. Stage II periodontitis is characterised by horizontal bone loss, no tooth loss due to the disease, PD of 5 mm or less and CAL of 3-4 mm. The aim of effective periodontal therapy is to reduce harmful bacteria to halt inflammation. To ensure periodontal treatment is successful, the smear layer-which consists of bacteria, contaminated root cementum, bacterial endotoxins and supragingival and subgingival bacterial biofilms- must be completely eradicated [2,3].

Periodontitis can be treated by FMD. By avoiding infection of intraoral bacterial reservoirs, including tongue, tonsils and other mucous membranes, as well as periodontal pathogens, this treatment aims to control periodontal pockets and prevent a return of the disease. This treatment uses antimicrobial chemicals like CHX and SRP to disinfect the entire mouth in a single session. Numerous clinical trials have been conducted to examine the efficacy of this approach [4]. In addition to having low irritation, CHX shows substantivity to the oral mucosa and tooth surfaces. According to a number of studies, full-mouth SRP within 24 hours with a disinfectant decreased the likelihood of bacterial cross-contamination and produced microbiologic and therapeutic benefits over traditional stepwise therapy [5-7].

Patients with periodontitis generally have diminished antioxidant capabilities both locally and systemically. The antioxidant defense

system can prevent and/or mitigate the detrimental effects of free radicals and nonradical reactive species [8,9]. The Guttiferae family encompasses Garcinia mangostana (MGA), often known as Mangosteen (MG) or the "queen of fruits." The pericarp of Garcinia mangostana L. comprises several chemicals, including chrysanthemin, garcinone A, B, and C, gartanin, sesquiterpenoids, fructose, sucrose, xanthones, tannins, and their derivatives. Mangostana mostly consists in its antioxidant, antibacterial, anti-inflammatory, anticancer, antiproliferative, pro-apoptotic, and aromatase inhibitory qualities [10].

Objectives

To evaluate the effectiveness of MG gel in one stage FMD treatment in terms of BOP, PD, and CAL.

Primary objective: To evaluate the effect of 4% MG gel adjunct to FMD on PPD.

Secondary Objective: To assess the impact of 4% MG gel on BOP, CAL, Plaque Index (PI) and Papillary Bleeding Index (PBI).

Null Hypothesis: There is no statistically significant difference in PD, CAL, BOP, or PI between patients treated with FMD alone and those treated with FMD plus 4% MG gel.

Alternate Hypothesis: There is a statistically significant improvement in PPD, CAL, BOP, PI, and PBI in patients treated with FMD plus 4% MG gel compared to those treated with FMD alone.

REVIEW OF LITERATURE

Kulkarni M et al., [10] in their double-blinded, split-mouth, randomised, placebo-controlled trial evaluated the efficacy of 4% mangosteen gel as an adjunct to SRP in 13 patients with Stage II, Grade B chronic periodontitis (26 sites), comparing clinical periodontal outcomes and Gingival Crevicular Fluid (GCF) Matrix Metalloproteinase-9 (MMP-9) levels at baseline and after three months; while both the treatment (SRP+4% MG gel) and control (SRP+placebo gel) sites showed improvement in PI, gingival bleeding index, PD, Relative Attachment Levels, and reductions in GCF MMP-9, the MG gel test sites demonstrated significantly greater reductions in PD, greater gains in attachment levels (RAL/CAL), and a statistically significant decrease in GCF MMP-9 compared to controls—highlighting that adjunctive 4% MG gel enhances clinical and biochemical outcomes in managing chronic periodontitis [11].

Manjunatha VA et al., in their placebo-controlled split-mouth trial evaluated the clinical and antioxidant efficacy of 4% MG gel as an adjunct to SRP in chronic periodontitis [11]. Fifty sites from 25 patients were treated either with SRP plus 4% MG gel or SRP plus placebo. Clinical parameters such as PI, gingival bleeding index, PD, and RAL were assessed, along with GCF Total Antioxidant Capacity (TAOC). After three months, both groups showed significant clinical improvement, but sites treated with MG gel demonstrated greater reductions in PD, improved attachment gain, and a marked increase in GCF TAOC compared with controls. The findings suggest that adjunctive 4% MG gel enhances both clinical and biochemical outcomes, supporting its role as a promising local drug delivery system in the management of chronic periodontitis.

Husna M et al., in a placebo-controlled clinical study evaluated the efficacy of 4% MG (Garcinia mangostana) peel extract gel as an adjunct to SRP in Stage III, Grade B periodontitis patients by assessing Interleukin-6 (IL-6) levels in GCF and related clinical parameters [12]. Test sites treated with SRP plus MG gel showed significantly greater reductions in IL-6 levels compared to placebo (48.91±19.89 pg/mL vs. 8.83±12.17 pg/mL) along with marked improvements in gingival index, PD, and CAL over seven days. Additionally, IL-6 reductions correlated positively with clinical improvements, indicating that adjunctive use of 4% MG gel enhances both anti-inflammatory and clinical outcomes, supporting its potential as a local drug delivery agent in the management of periodontitis.

MATERIALS AND METHODS

This will be a randomised controlled parallel-arm clinical trial conducted over a 6-month follow-up period at the Department of Periodontics, Sharad Pawar Dental College, Datta Meghe Institute of Higher Education and Research (DMIHER), Sawangi (Meghe), Wardha, India. The study has received approval from the Institutional Ethical Committee (IEC) of DMIHER (Ref. No. DMIHER (DU)/IEC/2024/51). The planned overall duration of the study will be one year, while it will include a follow-up period of six months. A total of 30 systemically healthy individuals diagnosed with Stage II periodontitis will be recruited.

Sample size: We calculated the sample size based on the difference in mean values for the variable PI as a primary variable between two of the treatment groups (FMD alone) against treatment group (FMD+Mangosteen gel).

Formula Using Mean Difference:

$$n1=n2=2\frac{(Z_\alpha+Z_\beta)^2\sigma^2}{(\delta)^2}$$

Z_α=1.96 at 5% error and CI at 95% Z_β=2.34 =Power at 99%

Primary Variable: Plaque Index (PI)

Mean score difference pre-post (1.423- 0.634)=0.789 at control group [10]

Mean score difference pre-post (1.308- 0.076)=1.232 at trial group [10]

Pooled standard deviation=(0.277+0.299+0.355+0.120)/4=0.2627

Mean difference δ=(1.232-0.789)=0.443

$$\text{Sample size } N=n1=n2=2\frac{(1.96+2.34)^2(0.2627)^2}{(0.443)^2}=13 \text{ per group}$$

Total samples 26 per group.

Considering 10% drop out=Approx.2

Total sample required 2* (13+2)=30

n1=15 per group.

Preparation of Mangosteen Gel

The MG gel used in this study is prepared at the Department of Rasashastra, Mahatma Gandhi Ayurved College, DMIHER, Sawangi, following previously published protocols (Manjunatha VA et al., 2017) [11]. The formulation consisted of *Garcinia mangostana* pericarp extract standardised to contain 4% w/w α-mangostin, the principal xanthone with antioxidant, anti-inflammatory, and antimicrobial activity. The extract is incorporated into a carboxymethyl cellulose-based gel with glycerol, providing appropriate viscosity and sustained subgingival delivery. Standardisation and quality control are performed using High-Performance Liquid Chromatography (HPLC) to confirm the concentration of α-mangostin. The gel is sterilised by filtration and dispensed into sterile syringes before use. It is stored at cool temperature conditions (2-8°C) to maintain stability and efficacy, and was used within seven days of preparation.

For clinical application, 0.1 mL of the gel will be delivered subgingivally into each periodontal pocket using a sterile syringe. The gel will be applied once, at one week postoperatively, after completion of the FMD regimen.

Inclusion criteria:

1. The presence of interproximal clinical attachment loss in at least three teeth, excluding molars and first incisors.
2. Patients diagnosed with Stage II periodontitis will be included in the study.
3. The amount of microbial deposits that is not consistent with the degree of damage of periodontal tissue.
4. Individuals having at least 20 teeth.
5. Patients who have two sites of at least 12 teeth with PDs ≥ 4 mm and CAL.

6. Systemically healthy participants should be enrolled in the trial.
7. Individuals without a history of antibiotic treatment or periodontal treatments within the previous six months.
8. Patients that are willing to complete the follow-up for six months and are motivated to receive therapy.

Exclusion criteria:

1. Individuals who have a suspected or confirmed allergy.
2. Individuals who had received periodontal therapy during the previous six months.
3. Individuals who suffer from any systemic condition that compromises their periodontal health.
4. Individuals suffering from infectious diseases other than periodontitis.
5. Chronic alcoholics
6. Patients who smoke or use tobacco products in any way.
7. Patients with systemic illnesses and impaired immune systems.
8. Women in pregnancy or lactation.

Study Protocol

The specifically designed chart will encompass details on nutritional status, systemic context, oral hygiene habits, gingival and periodontal health, along with additional standard clinical information. A mouth mirror and the UNC-15 probe will be utilised to evaluate individuals in adequately illuminated settings. Prior to the commencement of the clinical study, patients will be educated about its objectives and methodology, and they will all provide their signatures on an informed consent form.

CLINICAL MEASUREMENTS

I) Indices:

1) PI (Turesky-Gilmore-Glickman Modification of Quigley-Hein 1970) [13].

Following the application of a disclosing agent, plaque will be evaluated on the lingual and buccal surfaces of each tooth based on the following standards.

Score Criteria

0 No plaque;

1 Separate flecks of plaque at the cervical margin of the tooth;

2 A thin, continuous band of plaque near the cervical edge that is up to 1 mm;

3 A band of plaque wider than 1mm but covering less than one third of the crown;

4 Plaque covering at least one third but less than two thirds of the crown;

5 Plaque covering two thirds or more of the crown.

Calculations: The PI score of a tooth is determined by dividing the total of the surrounding values by two. The PI score for each individual is obtained by adding the data from each tooth and dividing by the total number of teeth assessed.

2) PBI (Muhlemann HR 1977) [14]

A periodontal probe will be advanced coronally to the tip of the papilla after being cautiously inserted into the gingival sulcus at the mesial side of the base of papilla. On the distal side of same papilla, this will be done again. A 0-4 scale will be used to record the severity of any bleeding that is thereby induced.

Score Criteria

0- No bleeding;

1 Appearance of single discrete bleeding point;

2 Appearance of several isolated bleeding points/a single fine line of blood;

3 The interdental triangle fills with blood shortly after probing;

4 After probing profuse bleeding occurs; blood flows immediately into marginal sulcus.

Calculations: The total of all papillary bleeding scores will be divided by the quantity of investigated papillae to ascertain the PBI score for each individual.

II) Probing measurements:

To evaluate the outcomes, the following clinical parameters such as PPD, CAL will be assessed. A UNC-15 (Hu-Friedy) will be used to quantify PPD and CAL. Every probing measurement will be noted at the tooth's greatest pocket depth. Only the teeth undergoing treatment will have these clinical parameters documented at baseline, three, and six months.

Procedure

Group-A

The patient will have a one-stage whole mouth disinfection after a week of supragingival scaling. Full mouth subgingival SRP will be performed in one day using curettes and an ultrasonic scaler, under local anaesthetic. According to one-stage FMD protocol by Quirynen M et al., CHX will be utilised in the intraoral niches for disinfection, alongside mechanical debridement [7]. Subsequent to each instrumentation session, the operator will apply 1% CHX gel to the dorsum of the patient's tongue for one minute, rinse the oral cavity twice with a 0.2% CHX solution for one minute each, administer a 0.2% CHX spray to the pharynx, irrigate all periodontal pockets three times within 10 minutes using a 0.2% CHX solution, and receive a prescription for 0.2% CHX mouthwash to be used at home for one week following comprehensive FMD.

Group-B

After a week of supragingival scaling, the patient will have a single-stage thorough oral disinfection therapy. The comprehensive subgingival SRP of the whole oral cavity will be completed in one day under local anaesthesia with curettes and an ultrasonic scaler. Alongside mechanical debridement, the intraoral niches will be sanitised with CHX. Following each instrumentation session, the patient will receive a prescription for 0.2% CHX mouthwash to be used for one week. They must thoroughly disinfect their mouth, brush the dorsum of their tongue for one minute with 1% CHX gel, rinse their mouth twice for one minute each with a 0.2% CHX solution, spray the pharynx with a 0.2% CHX spray, and irrigate all pockets three times within 10 minutes using a 0.2% CHX solution. One week post-surgery, each pocket will get a subgingival injection of 0.1 mL of 4% MG gel.

STATISTICAL ANALYSIS

The means and standard deviations (Mean±SD) of each clinical parameter will be calculated. A typical statistical approach will be used to analyse the mean data's statistical significance. Version 17.0 of the Statistical Package for the Social Sciences (SPSS) software will be used to conduct all statistical analyses. Data at baseline and six months for each treatment group will be compared using the Wilcoxon sign rank test. At baseline, three months, and six months, the PI, BOP CAL, and PD will be compared. If the observed difference is less than 0.05, it will be deemed significant; if the probability value (p) is more than 0.05, it will be deemed non-significant.

The primary outcome is the change in PPD from baseline, 3 months to 6 months after treatment, comparing patients receiving one-stage FMD alone versus FMD with adjunctive 4% MG gel.

Secondary outcome: Secondary outcomes will include changes in CAL, BOP, PI, and PBI.

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