

ORIGINAL RESEARCH

Comparative Evaluation of 1% Metformin Gel as an Adjunct to Scaling and Root planing in the Treatment of Chronic Periodontitis with Scaling and Root planing Alone: A Randomized Controlled Clinical Trial

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ABSTRACT

Introduction: Periodontal diseases are multifactorial in etiology, and bacteria are one among these etiologic agents. Thus, an essential component of therapy is to eliminate or control these pathogens. This has been traditionally accomplished through mechanical means (scaling and root planing), which is time consuming, difficult, and sometimes, ineffective. From about the past 30 years, locally delivered, anti-infective pharmacological agents, most recently employing sustained release vehicles, have been introduced to achieve this goal.

Purpose: The purpose of this study is to investigate the effects of metformin (a popular biguanide antidiabetic) on periimplant healing.

Methods: A total of 30 patients were assigned to two groups: (1) Control and (2) test group

Keywords: Periodontitis, Metformin, Pocket depth, Subgingival, Diabetes Mellitus, Local drug delivery.

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INTRODUCTION

Periodontal disease is characterized by tissue inflammation and destruction of the tooth-supporting structures that eventually lead to the loss of affected teeth.^[1] Lesions in the periodontal tissues are clinically identified and diagnosed based on the signs such as (i) presence of

bleeding following periodontal pocket probing and (ii) reduced tissue resistance to pocket probing (i.e., probing depth [PD] of >4 mm). These signs develop as a result of the tissue response to the presence of a subgingival biofilm, resulting in an inflammatory lesion, rich in leukocytes and poor in collagen, in the gingival connective tissue adjacent to the tooth surface.^[2] There are no conventional periodontal and surgical treatments which can regenerate lost periodontal tissue to a significant clinical degree. Hence, establishing new therapeutic procedures that enable the complete regeneration of periodontal tissue once destroyed by the periodontal disease progression is an important task.^[3]

Elevated proportions of some subgingival microbial species have been associated with destructive periodontal disease activity. These highly organized bacterial populations form the apically advancing front of periodontal pockets in close proximity to connective tissue and alveolar bone destruction. Hence, elimination or adequate suppression of putative periodontopathogenic microorganisms in the subgingival microbiota is essential for periodontal healing.^[4]

A thorough understanding of the etiopathogenesis of periodontal disease has provided the clinicians and researchers with a number of diagnostic tools and technique that has widened the treatment options.^[5] The most widely used approach has been scaling and root planing (SRP). Debridement of the root surface by SRP came into relatively common use in the first half of the past century and has become the central feature held in common by all currently used forms of periodontal therapy.^[6]

Metformin (1, 1-dimethylbiguanide) is one of the commonly used oral antihyperglycemic agents for the treatment of type 2 diabetes mellitus and is now known to stimulate osteoblasts and reduce alveolar bone loss.^[3,7] In 1995, the Food and Drug Administration approved metformin for use in the United States, which led to a significant increase in clinical use. Metformin is one of the insulin-sensitizing agents most commonly used for the management of different conditions associated with insulin resistance, such as type 2 diabetes mellitus,

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metabolic syndrome, and polycystic ovary syndrome.^[3] It is currently recommended as first-line therapy in overweight or obese patients with this condition. Several sites of action have been proposed for metformin, including decreased hepatic glucose output, increased peripheral glucose uptake, and improved insulin secretion.^[7]

Metformin is shown to inhibit cytosolic and mitochondrial reactive oxygen species production induced by advanced glycation end products in endothelial and smooth muscle cells (Rao NS *et al.*, 2006).^[7] Treatment of two osteoblast-like cells (UMR106 and MC3T3E1) with metformin (25–500 mM) for 24 h led to a dose-dependent increase of cell proliferation and also promoted osteoblastic differentiation: It increased Type I collagen production in both cell lines and stimulated alkaline phosphatase activity in MC3T3E1 osteoblasts. In addition, metformin markedly increased the formation of nodules of mineralization in 3-week MC3T3E1 cultures.^[6,9]

Metformin-induced activation and redistribution of phosphorylated extracellular signal-regulated kinase in a transient manner and dose dependently stimulated the expression of endothelial and inducible nitric oxide synthases.^[6,8]

Metformin increases the *in vitro* osteoblastic differentiation of bone marrow progenitor cells. Under proper stimuli, these cells have the capability to differentiate into different types such as osteoblasts, chondrocytes, and adipocytes.^[9]

Considering the above facts, the current study is designed as a single-center, randomized, controlled clinical trial to evaluate the efficacy of 1% metformin gel as an adjunct to SRP in the treatment of chronic periodontitis patients with SRP.

Source of Data

A total of 30 patients were selected from the outpatient department (OPD) of the Department of Periodontology and Implantology, D.J. College of Dental Sciences and Research, Modinagar. The whole study protocol was explained to them, and it was made clear to the potential patients that participation is voluntary. Written informed consent was obtained from patients, and ethical clearance for the study was received from the Institutional Ethical Committee and Review Board of the OPD of the Department of Periodontology and Implantology, D.J. College of Dental Sciences and Research, Modinagar.

Inclusion Criteria

The following criteria were included in the study:

- Patients with no systemic diseases
- Patients with sites showing PD ≥ 5 mm and clinical

attachment loss ≥ 4 mm in chronic periodontitis patients.

- No history of periodontal therapy for the past 6 months.
- Patients between the ages of 25 and 55 years.
- No history of use of antibiotics for the past 6 months.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients with a known or suspected allergy to the metformin/biguanide group.
- Patients on systemic metformin or other oral antidiabetic therapy.
- Patients with aggressive periodontitis or diabetes.
- Patients using tobacco in any form.
- Patients having habit of alcoholism.
- Immunocompromised patients.

Clinical Parameters

1. Modified sulcus bleeding index (mSBI) (Mombelli, Van Oosten, Schurch, and Land, 1987).

The severity of gingival bleeding is a sign of inflammation and is associated with periodontal disease. The tissues surrounding each tooth are divided into four gingival scoring units: distofacial, facial, mesiofacial, and entire lingual gingival margin. To minimize examiner variability in scoring, the lingual surface was not subdivided because it is mostly likely being viewed indirectly with a mouth mirror. A periodontal probe was used and passed along the gingival margin to provoke bleeding, and the clinical findings were recording to the following scores and criteria.

0 - No bleeding when a periodontal probe is passed along the gingival margin

1 - Isolated bleeding spots visible

2 - Blood forms a confluent red line on margin

3 - Heavy or profuse bleeding.

2. PD (UNC-15 periodontal Probe [Hu Friedy® U.S.A]). It is measured as the distance from the gingival margin to the bottom of the gingival sulcus
3. Clinical attachment level (CAL) (custom-made occlusal stent).

A customized acrylic stent was made for each patient with the cold cure acrylic by the sprinkle on method. It covered the occlusal 1/3 on the buccal and lingual side. The thickness of the stent was about 2–3 mm. The vertical grooves were made on the stent on buccal side using straight fissure bur number 566 and air-rotor handpiece to guide the UNC-15 probe at selected sites. The stent was made to the occlusal surfaces of teeth, and the measurement was made using UNC-15 probe by placing it in the groove made on the stent. Mark was made on the

stent with permanent marker so as to facilitate recording at subsequent recalls.

PREPARATION OF ORAL SOFT GEL

All the required ingredients of the formulation were weighed accurately. Dry gellan gum powder was dispersed in 50 mL of distilled water maintained at 95°C. The dispersion was stirred at 95°C for 20 min using a magnetic stirrer (Remi magnetic stirrer 2MLH, Mumbai, India) to facilitate hydration of gellan gum. The required amount of mannitol was added to the gellan gum solution with continuous stirring, and the temperature was maintained above 80°C. Metformin was added with stirring. Then, sucralose, citric acid, and preservatives (methylparaben and propylparaben) were added with stirring. Finally, required amount of sodium citrate was dissolved in 10 mL of distilled water and added to the mixture. At last, raspberry flavor was added. The weight of the gel was monitored continuously during manufacturing, and finally, it was adjusted to 100 g with distilled water. The mixture containing gellan gum, metformin, and other additives was packed in polyethylene bag [Figures 1-7].

Treatment Protocol

- Thirty patients, diagnosed with chronic periodontitis, aged between 25 and 55 years were enrolled in this study from the OPD of the Department of Periodontology and Implantology, D.J. College of Dental Sciences and Research, Modinagar.
- Patients were selected as per the inclusion criteria and exclusion criteria, and complete pre- and post-operative records were made with the help of cast models.
- Clinical parameters, including mSBI, probing pocket depth (PPD), and CAL, were recorded at baseline (before the SRP) and at 1 and 3 months with the help of UNC-15 probe.
- Complete phase 1 therapy was performed, and in the test groups, sites were treated with SRP, followed by 1% metformin gel local drug delivery, whereas in the control group, sites were treated with SRP alone. Multiple sites from maxillary and mandibular teeth per patient were to be enrolled for either the metformin or SRP group.
- No antibiotics and/or anti-inflammatory agents were prescribed after treatment.
- A custom-made acrylic stent and a color-coded UNC 15 periodontal probe were used to standardize the measurement of clinical parameters.

Local Drug Delivery

For standardization, 10 μ L prepared metformin gel was injected into the periodontal pockets using a syringe



Figure 1: Armamentarium (for clinical use)



Figure 2: 1% metformin



Figure 3: Group I (scaling and root planing): Pre-operative clinical measurements

with a blunt cannula. Patients were instructed to refrain from chewing hard or sticky foods, brushing near the treated areas, or using any interdental aids for 1 week. Adverse effects were noted at recall visits, and any supragingival deposits were removed.

- The mSBI, PD, and clinical attachment loss were evaluated at baseline, 1 month, and 3 months.



Figure 4: Group II (1% metformin): Pre-operative clinical measurements



Figure 6: Subgingival delivery of



Figure 5: Root planing

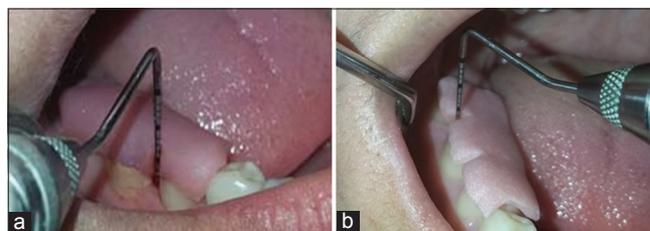
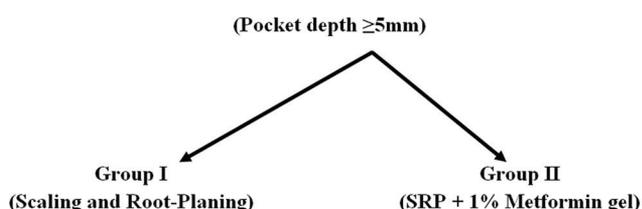


Figure 7: (a and b) Post-operative clinical measurements

- Individually customized bite blocks were used.
- Data were collected, and statistical analysis was carried out.

A blunt end needle of 24-gauge and a disposable syringe was used. The tip of the needle was gently placed without pain at least 3 mm deep (marking made at 3 mm on needle) inside the pocket, parallel to the long axis of the tooth, and 1 μ L of the solution was irrigated in 20 s.

Patients with Chronic Periodontitis [Table 1]



RESULTS

The statistical analysis was performed using Statistical Package for the Social Sciences version 16.0 statistical

analysis software. The scores were represented as number (%) and mean (\pm) SD.

Table 2 shows the descriptive analysis for Group I (SRP).

1. mSBI

The mean scores with standard deviation of Group I (SRP) at:

- a. Baseline: 2.59 \pm 0.53
- b. 1 month: 1.81 \pm 0.37
- c. 3 months: 1.22 \pm 0.30.

2. PD

The mean scores with standard deviation of Group I (SRP) at:

- a. Baseline: 6.39 \pm 0.48
- b. 1 month: 5.26 \pm 0.31
- c. 3 months: 4.19 \pm 0.51.

3. CAL

The mean scores with standard deviation of Group I (SRP) at:

- a. Baseline: 6.21 \pm 0.43
- b. 1 month: 5.34 \pm 0.54
- c. 3 months: 4.40 \pm 0.74.

Table 3 shows the descriptive analysis for Group II (SRP+1% metformin).

1. mSBI

The mean scores with standard deviation of GROUP II (SRP+1% Metformin) at:

- a. Baseline: 2.71 \pm 0.10
- b. 1 month: 1.39 \pm 0.18
- c. 3 months: 0.32 \pm 0.05.

2. PD

Table 1: Study design

Clinical parameter (mSBI, PD, and CAL)	At baseline	Clinical parameter (mSBI, PD, and CAL)
Scaling and root planing		SRP+1% Metformin gel
Clinical parameter (mSBI, PD, and CAL)	At 1 month	Clinical parameter (mSBI, PD, and CAL)
Clinical parameter (mSBI, PD, and CAL)	At 3 months	Clinical parameter (mSBI, PD, and CAL)

Table 2: Descriptive analysis

Group I (scaling and root planing),			
Clinical Parameters	Baseline mean±SD	1 month mean±SD	3 months mean±SD
mSBI	2.59±0.53	1.81±0.37	1.22±0.30
Probing depth	6.39±0.48	5.26±0.31	4.19±0.51
CAL	6.21±0.43	5.34±0.54	4.40±0.74

CAL: Clinical attachment level

Table 3: Descriptive analysis

Group II (SRP+1% metformin),			
Clinical Parameters	Baseline mean±SD	1 month mean±SD	3 months mean±SD
mSBI	2.71±0.10	1.39±0.18	0.32±0.05
Probing depth	6.44±0.38	4.17±0.52	2.13±0.38
CAL	6.25±0.23	4.59±0.97	2.17±0.29

CAL: Clinical attachment level

The mean scores with standard deviation of Group II (SRP+1% metformin) at:

- Baseline: 6.44±0.38
 - 1 month: 4.17±0.52
 - 3 months: 2.13±0.38.
3. CAL

The mean scores with standard deviation of Group II (SRP+1% metformin) at:

- Baseline: 6.25±0.23
- 1 month: 4.59±0.97
- 3 months: 2.17±0.29.

Table 4 shows an intergroup comparison of change in gingival bleeding index scores between the different intervals - baseline, 1 month, and 3 months.

1. The statistical analysis of the changes in mSBI in Group I (SRP) from baseline to 1 month, baseline to 3 months, and 1 month to 3 months was as follows:

- Baseline to 1 month: 0.62±0.32
- Baseline to 3 months: 1.2±0.33
- 1 month to 3 months: 0.66±0.17.

The percentage of change in Group I (SRP) was as follows:

- Baseline to 1 month: 23.28%
- Baseline to 3 months: 51.29%
- 1 month to 3 months: 35.91%.

2. The statistical analysis of the changes in mSBI in Group II (SRP+ 1% metformin) from baseline to 1 month, baseline to 3 months, and 1 month to 3 months was as follows:

- Baseline to 1 month: 1.31±0.25
- Baseline to 3 months: 2.3±0.12
- 1 month to 3 months: 1.07±0.19.

The percentage of change in Group II (SRP+ 1% metformin) was as follows:

- Baseline to 1 month: 48.28%
- Baseline to 3 months: 88.17%
- 1 month to 3 months: 76.74%.

Independent *t*-test for the significance of change in mSBI in intergroup analysis shows that statistically there was difference in both SRP and SRP+ 1% metformin group. However, the statistical difference is more significant in Group II (SRP+ 1% metformin). Thus, SRP+ 1% metformin is more efficient in decreasing gingival bleeding.

Graph 1 shows the intragroup comparison of mSBI for Group I (SRP) and Group II (SRP+1% metformin) between three intervals - baseline, 1 month, and 3 months. There is a reduction in the mean scores for mSBI in both the groups at all intervals, but the reduction is more significant in Group II (SRP+ 1% metformin). Thus, it shows that 1% metformin is more efficient in reducing gingival bleeding.

Table 5 shows an intergroup comparison of change in PD scores between the different intervals - baseline, 1 month, and 3 months.

1. The statistical analysis of the changes in PD in Group I (SRP) from baseline to 1 month, baseline to 3 months, and 1 month to 3 months was as follows:

- Baseline to 1 month: 1.13±0.29
- Baseline to 3 months: 2.20±0.52
- 1 month to 3 months: 1.06±0.56.

The percentage of change in Group I (SRP) was as follows:

- Baseline to 1 month: 17.53%
- Baseline to 3 months: 34.30%
- 1 month to 3 months: 20.11%.

2. The statistical analysis of the changes in PD in Group II (SRP+ 1% metformin) from baseline to 1 month, baseline to 3 months, and 1 month to 3 months was as follows:

- Baseline to 1 month: 2.27±0.61
- Baseline to 3 months: 4.31±0.58
- 1 month to 3 months: 2.03±0.57.

The percentage of change in Group II (SRP+ 1% metformin) was as follows:

- Baseline to 1 month: 35.08%
- Baseline to 3 months: 66.72%
- 1 month to 3 months: 48.19%.

Table 4: Intergroup comparison of Gingival Bleeding Index scores between the different intervals -baseline, 1 month, and 3 months

Time intervals	Group I (mean±SD)	Group II (mean±SD)	P value	Significance
Baseline-1 month	-0.62±0.32 (-23.28%)	-1.31±0.25 (-48.28%)	0.001	Significant
Baseline-3 months	-1.2±0.33 (-51.29%)	-2.3±0.12 (-88.17%)		
1 month-3 months	-0.66±0.17 (-35.91%)	-1.07±0.19 (-76.74%)		

Table 5: Group-wise comparison of change in PD scores between the different intervals - baseline, 1 month, and 3 months

Time intervals	Group I (mean±SD)	Group II (mean±SD)	P value	Significance
Baseline - 1 month	-1.13±0.29 (-17.53%)	-2.27±0.61 (-35.08%)	0.001	Significance
Baseline - 3 months	-2.20±0.52 (-34.30%)	-4.31±0.58 (-66.72%)		
1-3 months	-1.06±0.56 (-20.11%)	-2.03±0.57 (-48.19%)		

PD: Probing depth

Independent *t*-test for the significance of change in PD in intergroup analysis shows that statistically there was difference in both SRP and SRP+ 1% metformin group. However, the statistical difference is more significant in Group II (SRP+ 1% metformin). Thus, SRP+ 1% metformin is more efficient in decreasing the PD.

Graph 2 shows the intragroup comparison of pocket depth for Group I (SRP) and Group II (SRP+1% metformin) between three intervals - baseline, 1 month, and 3 months. There is a reduction in the mean scores for pocket depth in both the groups at all intervals, but the reduction is more significant in Group II (SRP+ 1% metformin). Thus, it shows that 1% metformin is more efficient in reducing pocket depth.

Table 6 shows an intergroup comparison of change in CAL scores between the different intervals - baseline, 1 month, and 3 months.

1. The statistical analysis of the changes in CAL in Group I (SRP) from baseline to 1 month, baseline to 3 months, and 1 month to 3 months was as follows:

- a. Baseline to 1 month: 0.87±0.37
- b. Baseline to 3 months: 1.80±0.68
- c. 1-3 months: 0.93±0.50.

The percentage of change in Group I (SRP) was as follows:

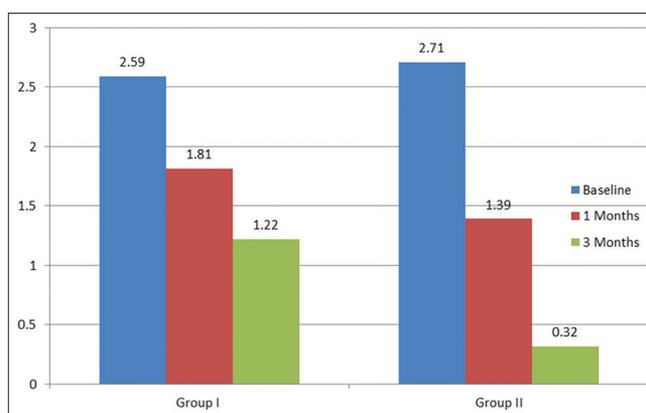
- a. Baseline to 1 month: 14.03%
- b. Baseline to 3 months: 29.06%
- c. 1-3 months: 17.62%.

1. The statistical analysis of the changes in CAL in Group II (SRP+ 1% metformin) from baseline to 1 month, baseline to 3 months, and 1 month to 3 months was as follows:

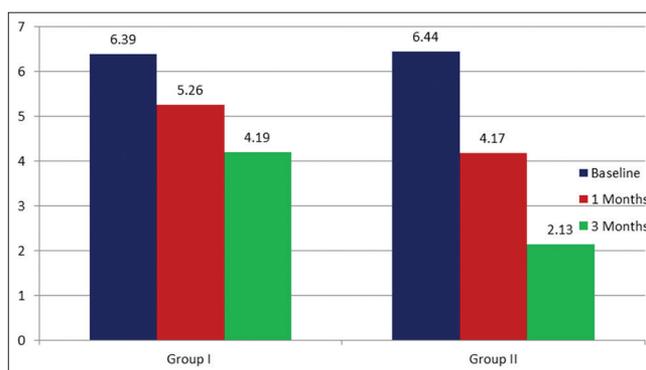
- a. Baseline to 1 month: 1.65±1.00
- b. Baseline to 3 months: 4.07±0.41
- c. 1 month to 3 months: 2.41±0.85.

The percentage of change in Group II (SRP+ 1% metformin) was as follows:

- a. Baseline to 1 month: 26.41%
- b. Baseline to 3 months: 65.13%



Graph 1 : Intragroup comparison of modified sulcus bleeding index between three intervals for Groups I and II



Graph 2: Intragroup comparison of probing depth scores between three intervals for Groups I and II

- c. 1 month to 3 months: 51.19%.

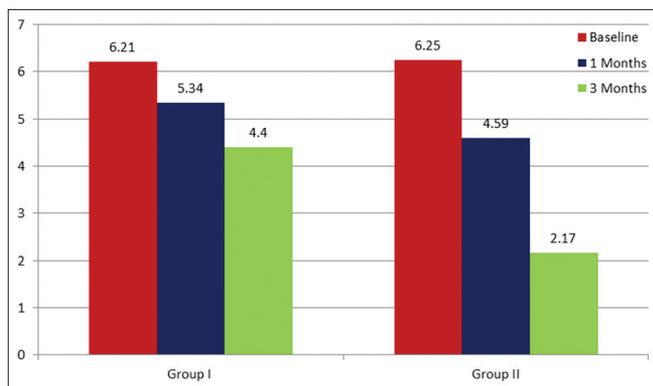
Independent *t*-test for the significance of change in CAL scores in intergroup analysis shows that statistically there was difference in both SRP and SRP+ 1% metformin group. However, the statistical difference is more significant in Group II (SRP+ 1% metformin). Thus, metformin is more efficient in gaining the CAL.

Graph 3 shows the intragroup comparison of CAL for Group I (SRP) and Group II (SRP+ 1% metformin) between three intervals - baseline, 1 month, and 3 months. There is a significant reduction in the mean scores for CAL in both

Table 6: Intergroup comparison of change in CAL scores between the different intervals - baseline, 1 month, and 3 months

Time intervals	Group I (mean±SD)	Group II (mean±SD)	P value	Significance
Baseline-1 month	-0.87±0.37 (-14.03%)	-1.65±1.00 (-26.41%)	0.001	Significance
Baseline-3 months	-1.80±0.68 (-29.06%)	-4.07±0.41 (-65.13%)		
1 month-3 months	-0.93±0.50 (-17.62)	-2.41±0.85 (-51.19%)		

CAL: Clinical attachment level



Graph 3: Intragroup comparison of clinical attachment level scores between three interval for Groups I and II

the groups at all intervals, but the reduction is more significant in Group II (SRP+ 1% metformin). Thus, it shows that 1% metformin is more efficient in gaining the CAL.

DISCUSSION

Periodontitis is a multifactorial disease with the presence of pathogenic bacteria being necessary for initiation of inflammation, but the progression of periodontal disease depends equally on the host's response to various pathogenic bacterial products and components. The bacterial products initiate a local host response in gingiva that involves recruitment of inflammatory cells, generation of prostanoids and cytokines, elaboration of lytic enzymes, and activation of osteoclast.^[10]

Advances in understanding the etiology and pathogenesis of the periodontal disease have led to increasingly effective pharmacological intervention along with phase-I therapy. In this regard, safe and intrinsically efficacious medication can be delivered into periodontal pockets to suppress or eradicate the pathogenic microbiota or module the inflammatory response or thereby limit tissue destruction.

Delivery of therapeutic agents to the periodontium can be achieved through local or systemic administration. The success of the treatment is largely dependent on the environment in which the therapeutic agent is administered, the mode of administration, the length of time that the therapeutic agent remains in the periodontal pocket and the type of therapeutic agent administered.^[11,12]

Site-specific drug delivery leads to the administration of drugs through mucosal linings, namely nasal,

rectal, vaginal, ocular, and oral. The advantages of delivery through these transmucosal routes are that the dosage by-passes first-pass metabolism in the liver, avoids pre-systemic elimination, and directly delivers the drug to the systemic circulation.^[12,13]

The local delivery of therapeutic agents to periodontal pockets has the benefits of administering more drugs at the target site, thus achieving high intra-sulcular drug concentration over a predetermined period of time, avoiding its systemic side effects, and a better patient compliance.^[14]

Schwach-Abellaoui et al. (2000) recommended that a suitable delivery system intended for the treatment of periodontal diseases should meet the following criteria:

- The polymer must be free from impurities, additives, stabilizers, catalyst residues, and emulsifiers that may be eluted from the device.
- The physical, chemical, and mechanical properties of the polymer should not be changed by the biological environment from a non-degradable device.
- The device should be thermally and mechanically stable.
- The device must be easily processed into the intended form, i.e. film, fiber, gel, or multi-particulate.
- The device should not evoke an inflammatory, toxic, or carcinogenic response.
- The device should be prepared under sterile conditions or be sterilized afterward.^[15]

Addy and Fugit (1989) differentiated the local drug delivery to the oral cavity according to the vehicle used in the delivery devices based on the expected time which the therapeutic agent would remain in the mouth as follows:

- a. Short term (seconds to minutes): Examples are toothpastes, mouthwashes and irrigations.
- b. Medium term (hours): Examples are gels and ointments.
- c. Long term (days to weeks): Examples are degradable and non-degradable sustained delivery devices.^[16]

Short-to-medium term delivery vehicles are used mainly in supragingival plaque control and in the prevention of gingivitis. Addy (1994) noted that mouth rinsing did not penetrate periodontal pockets sufficiently, therefore limiting its use in subgingival applications.^[11]

Sustained drug delivery devices can be further subdivided into degradable and non-degradable devices. The

device generally consists of a matrix within which the drug is evenly distributed. In non-degradable devices, the drug diffuses from an insoluble non-degradable polymer which needs to be removed after treatment is completed, while degradable devices release the drug through diffusion and matrix erosion and therefore do not need to be removed from the periodontal pocket.^[17] Higher levels of drug in gingival fluid leads to improved clinical parameters which is evident with intrapocket delivery systems, which distribute the drug evenly throughout the periodontal pocket.^[18]

Site-specific drug delivery selectively targets the diseased site with superior treatment results (Research, Science, and Therapeutic Committee of the American Academy of Periodontology, 2001). Furthermore, degradable devices have the added advantage of improved patient compliance as there is no need to remove the device from the periodontal pocket.^[19]

Polymers frequently used in the formulation of drug delivery devices placed within the periodontal pocket.

In this study, 1% metformin gel is used to treat periodontal pocket in chronic periodontitis as an adjunct to SRP and compared to SRP alone.

Metformin HCl (1, 1-dimethyl biguanide HCl), a second-generation biguanide, has been used very commonly for type 2 diabetes mellitus treatment.

Recently, studies indicate that SRP with 1% MF was more effective than SRP with placebo in decreasing PD and mSBI and increasing CAL in patients with chronic periodontitis.^[22] The mechanism of action appears to be mainly at the hepatocyte mitochondria in which MF interferes with intracellular handling of calcium, decreasing gluconeogenesis and increasing expression of glucose transporters.^[3]

MF was shown to inhibit cytosolic and mitochondrial reactive oxygen species production induced by advanced glycation end products in endothelial and smooth muscle cells.^[19]

Considering aim and objectives, this study was designed in two treatment groups: Group A and Group B.

- Group A: Patients were treated with SRP alone
- Group B: Patients were treated with SRP along with subgingival application of 1% metformin gel.

Control of plaque and gingivitis is important in clinical studies because both vary in their association with periodontitis and both affect measured response to therapy. Since PD and loss of relative attachment are pathognomic for periodontitis, pocket probing is a crucial and mandatory procedure in diagnosing periodontitis and evaluating the success of periodontal therapy.^[21]

The patients selected were subjected to the assessment of mSBI, PD, and CAL.

At baseline, sites with pocket depth ≥ 5 mm were selected for both the groups. The PPD and CAL were recorded using UNC-15 probe and occlusal stent as a reference point (Clark *et al.* 1987).^[20]

Clinical Observations

- Group A: On observation, there was statistically significant reduction ($p < 0.05$) in mean mSBI, PD, and gain in CAL post-operatively at 1 and 3 months from baseline to SRP in treating chronic periodontitis.
- Group B: On observation, there was statistically significant reduction ($p < 0.05$) in mean mSBI, PD, and gain in CAL post-operatively at 1 and 3 months from baseline which is in accordance with the findings of the study by Pradeep *et al.*^[3] who observed the significant improvement in PI, PD, and CAL 6 months postoperatively on the use of varying concentrations of subgingivally delivered metformin gel as an adjunct to SRP in treating chronic periodontitis.

Another study by Pradeep *et al.*^[22] has shown similar results with reduction in PI, PD, and CAL ($P < 0.001$), 6 months postoperatively on the use of subgingivally delivered metformin gel in treating chronic periodontitis patients.

Comparison of Group A with Group B: Intergroup analysis shows that there is statistical significant differences in the reduction of mSBI, PD, and CAL scores among patients receiving SRP alone and patients receiving subgingivally delivered 1% metformin gel in adjunct to SRP.

At each patient's initial appointment, baseline data were obtained on mSBI and PD. CAL was measured with a UNC-15 periodontal probe for the same teeth. SRP was performed until the root surface is considered smooth and clean by the operator. SRP were performed in both the groups. Group I received SRP alone and Group II received 1% metformin gel. No antibiotics or anti-plaque and anti-inflammatory agents were prescribed after treatment. 1 month and 3 months later, these measurements (mSBI, PD, and CAL) were repeated. The results obtained were compiled and subjected to statistical analysis. The following conclusions were drawn from the results:

1. mSBI: The percentage of change in mSBI is significant in both the groups from baseline to 3 months.
2. PD: The percentage of change in PD index is significant in both the groups from baseline to 3 months.
3. CAL: The percentage of change in CAL is significant in both the groups from baseline to 3 months.

The conclusion drawn from this study is that there was a significant reduction in clinical parameters in

both the groups, but Group B, i.e., 1% metformin gel is more effective in reducing the clinical parameters (modified sulcular bleeding index and PD) and gain in CAL. This study indicated that clinical effects achieved with the agent may reduce the need for further advanced and surgical periodontal treatment which would limit morbidity for the subjects, the time of treatment, and cost of the therapy. The results obtained present a valid promise for further studies with a larger sample size.

CONCLUSION

In the present study, 30 subjects selected on the basis of inclusion criteria were categorized into two treatment groups. After subject selection, 15 patients were randomly assigned to each treatment group.

Group I ($n = 15$): Patients treated by SRP alone.

Group II ($n = 15$): Patients treated by SRP with subgingival 1% metformin gel.

Clinical Measurement

At each patient's initial appointment, baseline data were obtained on mSBI and PD. CAL (custom-made occlusal stent) was measured with a UNC-15 periodontal probe for the same teeth. These parameters were examined on the mesiobuccal surfaces of the same teeth. For each lower quadrant, SRP was performed until the root surface was considered smooth and clean. SRP were performed in both the groups. Group II received 1% metformin. No antibiotics or anti-plaque and anti-inflammatory agents were prescribed after treatment. 1 month and 3 months later, these measurements (mSBI, PD, and CAL) were repeated. The results obtained were compiled and subjected to statistical analysis. The following conclusions were drawn from the results:

1. mSBI: The percentage of change in mSBI is more significant in Group II from baseline to 3 months.
2. PD: The percentage of change in PD index is more significant in Group II from baseline to 3 months.
3. CAL: The percentage of change in CAL is more significant in Group II from baseline to 3 months.

The conclusion drawn from the study is as follows:

Metformin in adjunct with SRP is effective in reducing the clinical parameters (mSBI and PD) and gain in CAL.

Thus, results of the present study favor the use of locally delivered metformin gel in the treatment of chronic periodontitis. This study indicated that clinical effect achieved with the agent may reduce the need for further advanced and surgical periodontal treatment which would limit morbidity for the subject, the time of treatment, and the cost of therapy. The results obtained present a binding promise for further study with a larger sample size.

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