

# Effect of Locally Administered 1% Metformin Gel in the Treatment of Chronic Periodontitis

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## Abstract

**Aim:** To investigate the effectiveness of metformin gel as an adjunct to scaling and root planning in the treatment of periodontitis.

**Materials and Methods :** The parallel design study comprised of 16 individuals diagnosed with chronic periodontitis. The subjects were divided into 2 groups: Group 1 consisted of 8 patients who underwent SRP and local drug delivery metformin administration and group 2 consisted of 8 patients who underwent SRP and placebo. Clinical parameters were evaluated at base line and 1month. They included gingival index, probing depth and clinical attachment loss. The results were tabulated and statistical analysis was done using SPSS software version 20.

**Results:** The results of this study proved that there was a significant decrease in the clinical parameters when compared to baseline and one month. When compared between placebo group and metformin group, no statistically significant differences were seen.

**Conclusion:** On conclusion, long term follow up after the surgical intervention might be required to establish a difference in the periodontal parameters between the two groups. However, within the limits of the study of less sample size and short term follow up, it was demonstrated that Metformin has an effect on the periodontal tissues but it was not significant when compared to a placebo.

**Key words:** metformin, local drug delivery, chronic periodontitis, non-surgical periodontal therapy

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## INTRODUCTION

Periodontal disease is a chronic inflammatory disease characterized by inflamed gingiva, bleeding on probing, resorption of alveolar bone, and attachment loss between the tooth and its surrounding alveolar bone. In the past decade, periodontal disease has been recognized as not merely a local infectious disease but also as a chronic, subclinical, inflammatory disease for the host [1]. As of now, there is no conventional periodontal and surgical treatment which can regenerate lost periodontal tissue to a significant clinical degree. Therefore, establishing new therapeutic procedures that enable the complete regeneration of periodontal tissue which was already destroyed due to the periodontal disease progression is an important task [2].

Diabetes mellitus is a clinically and genetically heterogeneous group of metabolic disorders manifested by abnormally high levels of glucose in the blood.[3]

Metformin was first developed in 1957. It is one of the most commonly used oral antihyperglycemic agents for the treatment of type II diabetes mellitus. The mechanism of action is mainly at the hepatocyte mitochondria in which metformin interferes with intracellular handling of calcium, decreasing gluconeogenesis and increasing the expression of glucose transporters.[4] In 1995, the Food and Drug Administration approved metformin for use in the United States, which led to a significant increase in clinical use.[5], It is currently recommended as first-line therapy in overweight or obese patients with this condition.[6] The United Kingdom Prospective Diabetes Study showed that treatment with metformin reduces the risk of life-threatening macrovascular complications compared to other antihyperglycemic agents.[7]

However, it does not only effectively lower blood glucose but also protects bone tissue and prevents bone loss in patients with diabetes. Numerous studies have reported the effects of this agent on bone turnover. The action of metformin on the development of osteoblast-like cell lines was first investigated by Cortizo et al., who found a direct osteogenic effect of metformin on osteoblasts in culture.[8] Previous experiments have showed the effect of the systemic administration of metformin on alveolar bone resorption. The periapical bone loss area in the metformin treated group significantly decreased. Metformin inhibits the periapical lesions by reducing the number of osteoclasts and bone resorption areas.[9] Studies on the local delivery of a locally-delivered simvastatin gel and alendronate gel have demonstrated an improved response to therapy in chronic periodontitis patients.[10,11] These recent studies support the concept that the local application of these agents significantly improves clinical parameters and leads to defect depth reduction. Therefore, the aim of the study was to investigate the effectiveness of metformin gel as an adjunct to scaling and root planning in the treatment of periodontitis.

## MATERIALS AND METHODS:

All subjects in this study were patients who visited Saveetha Dental college, Chennai. The parallel design study comprised of 16 individuals diagnosed with chronic periodontitis. All patients included in the study had probing depth of more than 3 mm atleast in 20 sites with a minimum of 20 teeth present. Patients who were pregnant, lactating, or with any systemic diseases, or who have underwent previous periodontal treatment for the last 6 month, or who are taking antibiotics were excluded from

the study. It was made clear to the potential patients that their participation was voluntary. Written informed consent was obtained from patients. The subjects were divided into 2 groups: Group 1 consisted of 8 patients who underwent SRP and local drug delivery metformin administration and group 2 consisted of 8 patients who underwent SRP and placebo. Clinical parameters were evaluated at base line and 1month. They included gingival index, probing depth and clinical attachment loss. The results were tabulated and statistical analysis was done using SPSS software version 20. Paired T Test was used to compare baseline and one month values and intergroup comparison was done by using Independent T test.

**Metformin gel formulation** Dry gellan gum powder was dispersed in distilled water maintained at 95°C. The dispersion was stirred at 95°C for 20 minutes using a stirrer 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. A weighed amount of MF was added with stirring. Then glycerine, sucralose, citric acid, and preservatives (methylparaben) were added with stirring. Finally, the required amount of sodium citrate was

dissolved in 10 mL distilled water and added to the mixture. The mixture was allowed to cool to room temperature to form gel.

Metformin gel was prepared and baseline periodontal parameters were measured. Metformin gel and placebo gel were applied subgingivally on the upper first molar teeth after SRP using a syringe. In case the upper first molars were missing, the gel was applied on the upper second molar teeth. Periodontal parameters are to be re-assessed after one month and compared with baseline parameters to obtain results.

## RESULTS

The results of this study proved that there was a significant decrease in the clinical parameters when compared to baseline and one month. When compared between placebo group and metformin group, no statistically significant differences were seen. Both the groups showed that gingival index, probing depth and clinical attachment level improved on non-surgical periodontal treatment after one month. However, on comparing the placebo and test group, both showed similar improvement and thereby a distinct difference could not be observed.

	Placebo					Metformin					Intergroup comparison
	Base line		One month		Paired t Test	Base line		One month			
	Mean	Std. dev	Mean	Std. dev			Mean	Std. dev	Mean	Std. dev	Paired t Test
Gingival index	1.5675	.35009	1.2450	0.29052	0.030*	1.7150	0.29179	1.3562	.21784	0.003*	0.431
Probing depth	4.3550	.43566	4.0838	0.64533	0.005*	4.5037	0.59978	4.0988	.64789	0.034*	0.957
Clinical attachment level	5.8525	.77680	5.6938	0.96980	0.001*	5.9338	0.70908	5.6400	.78834	0.007*	0.581

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## DISCUSSION

The use of metformin started from 1957. It is one of the most commonly used oral antihyperglycemic agents for the treatment of type II diabetes mellitus.<sup>12</sup> It is currently recommended as first-line therapy in overweight or obese patients with this condition.<sup>13</sup> However, the effects of metformin were not only limited to effectively lowering blood glucose levels but also protects bone tissue in patients with diabetes. Since metformin has an effect of protecting bone tissue, it could be used in the treatment of periodontal diseases and prevent disease progression. Previously, the effects of varying concentrations of metformin was studied by A R Pradeep et al. they proved that 1% metformin proved most effective in treatment of intrabony defects. Therefore, this study was aimed to investigate the effectiveness of 1% metformin gel as an adjunct to scaling and root planning in the treatment of periodontitis.

The parallel design study comprised of 16 individuals diagnosed with chronic periodontitis. All patients included

in the study were diagnosed with chronic periodontitis according to AAP classification having probing depth of more than 3 mm atleast in 20 sites with a minimum of 20 teeth present. Patients who were pregnant, lactating, or with any systemic diseases, or who have undergone periodontal treatment for the last 6 months, or who are taking antibiotics were excluded from the study. The subjects were divided into 2 groups: Group 1 consisted of 8 patients who underwent SRP and local drug delivery metformin administration and group 2 consisted of 8 patients who underwent SRP and placebo. Clinical parameters were evaluated at base line and 1month. They included gingival index, probing depth and clinical attachment loss. The results of this study proved that there was a significant decrease in the clinical parameters when compared to baseline and one month. When compared between placebo group and metformin group, no statistically significant differences were seen.

Previous studies have shown that the local route of drug delivery of an antimicrobial agent in subgingival sites has

greater efficacy when compared with a systemic drug regimen.<sup>14</sup> The advantages of local drug delivery, such as high concentrations at the target site with reduced dosage, fewer applications, and high patient acceptability, were considered in the current study as a technique of direct subgingival injection of MF into periodontal pockets of chronic periodontitis patients with intrabony defects.<sup>15</sup> According to Pradeep et al,<sup>2016</sup>, the local delivery of 1% MF gel into periodontal pocket in chronic periodontitis patients with intrabony defects stimulated a significant improvement in clinical parameters, such as PD and CAL, and improved IBD depth reduction in vertical bone defects as compared to a placebo gel as an adjunct to SRP. The 1% MF gel, along with SRP, was found to show improvement in clinical and radiological parameters. This can provide an alternative direction in the field of periodontal regeneration. [16] The present study failed to prove that there is a difference in the improvement of patients with chronic periodontitis who underwent non-surgical therapy with metformin as an adjunct to SRP when compared to placebo, thereby proving the null hypothesis. The possible reason for this results may be due to a smaller sample size and short term follow up of patients.

#### Limitations:

1. Small sample size
2. Patients with moderate periodontitis (according to AAP classification) were included in the study.
3. Short term follow up

#### CONCLUSION

On conclusion, long term follow up after the surgical intervention might be required to establish a difference in the periodontal parameters between the two groups. However, within the limits of the study of less sample size and short term follow up, it was demonstrated that Metformin has an effect on the periodontal tissues but it was not significant when compared to a placebo.

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