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Original Article

Gingival Recession Post Periodontal Treatment in Diabetic Patients with or without Topical Antibiotics

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ABSTRACT

Objective: To assess the recession following Scaling and Root Planning (SRP), and to compare the efficacy of Metronidazole (MTZ), Minocycline (MC) gels, and their combination in terms of recession for the management of diabetic periodontitis patients.

Study Design: Randomized Single Blind Clinical Study. (clinicaltrials.gov: NCT06027151)

Place and Duration of the Study: Pharmacology, Biochemistry, and Periodontology Department, Dental College, HITEC-IMS HIT Taxila Cantt, Pakistan, from Sep 22 to Aug 23.

Methodology: In this clinical study, 380 diabetic chronic periodontitis patients were randomly grouped into 4 categories: scaling and root planing (SRP) alone (Group-I), SRP plus Metronidazole Gel (Group-II), SRP plus Minocycline Gel (Group-III), and SRP plus both Metronidazole and Minocycline Gels (Group-IV). The effectiveness of four treatment regimens was assessed by checking the difference in periodontal measurements, i.e., recession at baseline, after 15 days, and 45 days of the treatment, and the percentage was measured.

Results: There was a notable reduction in recession after the treatment. The overall efficacy was most pronounced in Group-IV patients managed with the combination regimen, demonstrating an Improvement rate of 19%. Groups I, II, and III achieved similar efficacy rates of approximately 3.12%, 4.21%, and 4.40% respectively.

Conclusion: Metronidazole gel has similar effectiveness to Minocycline gel, and their combination has exhibited synergistic effects in treating diabetic periodontitis patients and should be used as an adjunct to SRP for enhanced clinical outcomes.

Keywords: Chronic Periodontitis, Diabetes Mellitus, Metronidazole Gel, Minocycline Gel, Recession, Scaling and Root Planning.

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INTRODUCTION

Diabetes mellitus and periodontitis are prevalent chronic inflammatory disorders that greatly reduce quality of life and pose a significant global public health concern. In Pakistan, their prevalence rates are alarmingly high at 26.7% and 56.62% respectively.[1] Periodontitis, characterized by anaerobic bacterial infection affecting dental tissues, leads to irreparable breakdown of periodontal collagen fibers and development of periodontal pockets between the gingiva and tooth, gingival recession, and finally, tooth loss. It represents the sixth most prevalent disease worldwide.[2] A relapsing–remitting nature influenced by fluctuations in local microflora dysbiosis and host inflammatory response plays a key role in the initiation of periodontitis. Manifestations of this ailment include redness or gum bleeding during tooth brushing, recurring gum swelling, halitosis, gingival recession, and loosened teeth.[3] Gingival recession (GR) is a multifactorial, frequent clinical characteristic of periodontitis and an unwanted state that escalates with age progression and in males, smokers, and buccal sites, particularly the canine tooth, and in areas with supra and subgingival calculus.[4] Periodontitis is linked to nearly 60 extra-oral conditions, including cardiovascular diseases like hypertension, obesity, atherosclerosis, diabetes, and stroke. Diabetes accelerates periodontitis progression, with inflammation marking the link between diabetes and periodontal disease through vascular and tissue changes.[5] Among those contending with periodontitis, a noteworthy 39% concurrently faced the complexities associated with diabetes mellitus, underscoring an intersection between these health challenges.[6]

Periodontitis treatments include SRP and local or systemic antibiotics application to eliminate dental plaques and manage infections. Broad-spectrum antibiotics like Amoxicillin, Metronidazole, Minocycline, or Doxycycline are used adjunctively after SRP to halt disease progression. Metronidazole, a synthetic nitroimidazole, has bactericidal action,

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causing destruction of bacterial DNA as well as an anti-inflammatory effect due to suppression of cytokine production.[7] Minocycline, a semi-synthetic derivative of tetracycline, has a bacteriostatic effect by impeding protein synthesis, as well as possesses notable substantivity, gradual-release, anti-collagenase activity, and excellent lipophilicity.[8]

The effectiveness of local metronidazole and minocycline in chronic periodontitis, evaluated through periodontal pocket depth, clinical attachment level, and bleeding on probing, is established. However, gingival recession post non-surgical periodontal treatment, especially with local antibiotics, is unexplored, particularly in diabetic patients. The potential synergistic effects of these antibiotics on recession have not been investigated. This study aims to ascertain the clinical efficacy of locally administered Metronidazole and Minocycline in reducing gingival recession in diabetic periodontitis patients, offering an alternative to systemic medications and enhancing patient compliance by mitigating potential adverse effects.

METHODOLOGY

A randomized single blind clinical study was conducted in the Pharmacology, Biochemistry and Periodontology departments of Dental College, HITEC-IMS HIT Taxila Cantt, Pakistan. The study is approved by the Institutional Review Board (IRB) of HITEC-IMS Dental College with Ref. No. Dental/HITEC/IRB/34. The study is registered with clinicaltrials.gov with the registration number NCT06027151. Data collection took place from Sep 22 till Aug 23. The sample size, calculated using the Cochran formula, with a 39% prevalence of diabetic periodontitis,[6] z-score=1.96, and 5% margin of error, was 380. A consecutive sampling technique was used using a randomization software to generate codes for the allotment of patients to groups.

Inclusion Criteria: Patients of either gender aged 18 to 50 years, presenting in the Outpatient Department with mild to moderate chronic periodontitis and previously diagnosed diabetes mellitus, having HbA1c levels from 6% to 9% on either oral hypoglycaemics or insulin treatment, were included in the study. Each participant provided written informed consent (both in English and Urdu).

Exclusion Criteria: Pregnant females or lactating mothers, patients with gestational diabetes, patients with a history of alcoholism or smoking, recent use of anti-inflammatory or antibiotic medications within the past two months before the study, known allergy to minocycline or metronidazole, and patients who had periodontal surgeries in the past were excluded from the study.

Initially, a comprehensive periodontal examination of the entire oral cavity was conducted, and participants who met the inclusion criteria were evaluated for gingival recession during the baseline visit (before the SRP and local drug delivery) by the periodontologist. The subjects who were enrolled were allocated randomly to four groups, with each group comprising ninety-five patients. Group-I was treated with SRP alone at baseline till a smooth, clean, and hard texture was achieved, as assumed by the examiner with the help of an ultrasonic scaler. Patients in Group-II were treated with SRP followed by 1ml of 1% metronidazole benzoate gel (Revomet gel, Kaizen Pharmaceuticals) applied once subgingivally with the help of a disposable plastic tip. The needle was inserted into the base of the pocket, and the gel was then carefully dispensed from the syringe. Subsequently, the needle was slowly removed from the periodontal pockets. The patients were advised to refrain from drinking or eating for 30 mins following gel injection. SRP followed by 1ml of 2% Minocycline Hydrochloride Gel (Periocline gel, Sun Star) was applied once subgingivally in Group-III patients with the same method as used for Group-II patients. Patients in Group-IV received a combination of treatments, starting with SRP, followed by subgingival application of 1ml of Metronidazole Gel and Minocycline Gel, followed by the same procedure.

The outcome was measured by evaluating the gingival recession on the baseline visit according to the classification of marginal tissue recession by Miller.

CLASS-I: Marginal tissue recession limited to the mucogingival junction. There is no bone or soft tissue loss in the interdental area. It can vary in width.

CLASS-II: Marginal tissue recession extending to or beyond the mucogingival junction. There is no bone or soft tissue loss in the interdental area. Width may vary.

CLASS-III: Marginal tissue recession extending to or beyond the mucogingival junction, often accompanied by loss of bone and/or soft tissue in the interdental area or tooth malalignment.

CLASS-IV: Significant marginal tissue recession reaching or surpassing the mucogingival junction,

accompanied by severe bone and soft tissue loss interdentally and/or severe tooth malalignment.[9]

They were recalled for follow-ups after 15 and 45 days, and gingival recession was rerecorded at both follow-ups. Improvement as a result of treatment in diabetic chronic periodontitis patients was determined by considering the changes in gingival recession during 1st, 2nd, and 3rd visits for all the groups. (Figure–1). The difference among groups was analyzed by the Chi-Square test. The relationship between age and clinical parameter (gingival recession) was determined using One-way ANOVA and Post-hoc Tukey. The Chi-square test was applied to analyze the relationship between gender and clinical parameter i.e., recession. A *p*-value of <0.05 was deemed statistically significant. Categorical variables were presented as counts and percentages.

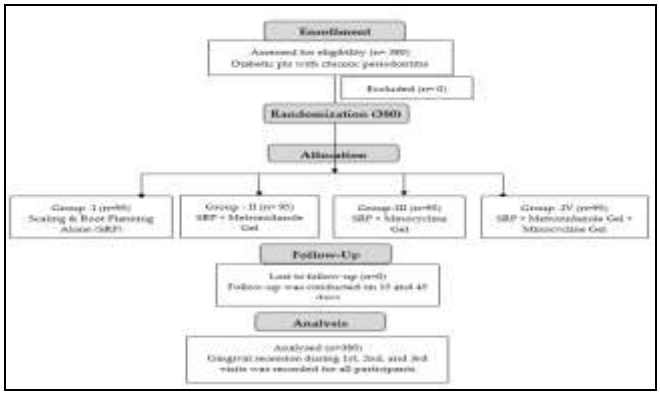

Figure-1: Patient Flow Diagram Showing Comparison Of Treatment For Chronic Periodontitis In Diabetic Patients

RESULTS

In this study, out of 380 patients, 221 patients i.e., 58.2% were males, and 159 patients i.e., 41.8% were females, with the mean age of 58.09±8.63. 56-70 years was the predominant age bracket, which included most of the patients from all the groups i.e., 49.5%, 44.2%, 55.7% and 62.1% patients from Group-I, II, III, and IV, respectively.

Results for recession during the third visit for all the groups is summarized in Figure-2.

The difference between groups for recession was evaluated, and highly significant results with a *p*-value<0.001 were observed. Notably, patients in Group-IV exhibited 44.7% class 1 recession patients by the third visit. Similarly, Group-I, II, and III displayed effectiveness, with 18.9%, 20.1%, and 16.4% of patients, respectively, experiencing recovery.

The assessment of treatment efficacy on each Class of recession was calculated. In the second visit, the treatment with SRP alone (Group-I) exhibited efficacy in patients with both Class II and Class III recession, with a modest improvement rate of 6.25%. The adjunctive use of Metronidazole Gel after SRP (Group-II) and Minocycline Gel following SRP (Group-III) demonstrated effectiveness primarily in Class II recession cases, with the efficacy rates of 19.23% and 19.35% respectively.

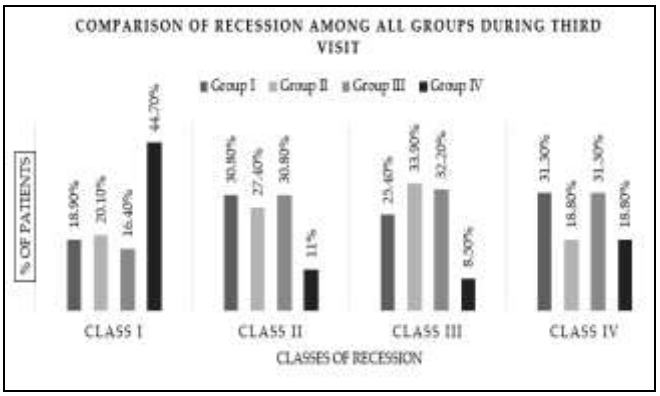

Figure-2: The Comparison of Recession Among All Groups During Third Visit (n=380)

Remarkably, Group-IV, which received a combination therapy of Metronidazole and Minocycline after SRP, displayed the most significant efficacy. This combination regimen was notably effective in Class II recession patients, achieving a recovery rate of 44.29%, and also exhibited effectiveness in Class IV recession patients with a rate of 25%.

By the third visit, incremental improvements were observed across the groups. Group-I, II, and III had improvements of 6.25%, 4.76%, and 10% respectively in patients with Class II recession. Strikingly, Group-IV exhibited a marked improvement of 50.54% in class II recession patients and 25% in Class IV recession patients.

In summary, the overall efficacy was most pronounced in patients managed with the combination regimen (Group-IV), demonstrating a notable Improvement rate of 19%. Groups I, II, and III achieved similar efficacy rates of approximately 3.12%, 4.21%, and 4.40% respectively as shown in Table-I.

Consequently, the adjunctive application of locally administered antibiotics demonstrated heightened efficacy in reducing recession. This contrasts favorably with outcomes of SRP in isolation,

underscoring the additional benefits conferred by the adjunctive antibiotic therapy.

Table-I: The Comparison of Efficacy Among all Groups (n=380)

Groups	Efficacy during 2nd visit	Efficacy during 3rd visit	Overall Efficacy
Group-I	3.12%	1.56%	3.12%
Group-II	4.80%	1.19%	4.20%
Group-III	4.83%	2.50%	4.40%
Group-IV	17.32%	14.74%	19.00%

Table-II: The Relationship Between Recession and Age (n=380)

Parameters	Recession				*p*-value
	Class I	Class II	Class III	Class IV	
Mean age (years)	58.72±9.02	57.88±8.14	61.36±8.23	61.63±6.88	0.002*

The relationship between age and clinical parameter (recession) was found to be highly significant, indicating the increase in the severity of recession with older age. A highly significant mean age difference was found between Class I and III, and Class II and III (Table-II). Post-Hoc Tukey test showing comparison of mean age difference between each class shown in Table-III.

Table-III: Post-Hoc Tukey Test Showing Comparison of Mean Age Difference Between Each Class (n=380)

Group comparison	Class I vs Class II	Class I vs Class III	Class I vs Class IV	Class II vs Class III	Class II vs Class IV	Class III vs Class IV
Mean age	0.63	0.002*	0.125	0.04*	0.34	0.999

DISCUSSION

Scaling and root planning (SRP) significantly enhanced periodontal health in patients with diabetes mellitus, with adjunct antibiotic treatment yielding superior clinical outcomes ($p<0.05$). Metronidazole gel showed comparable efficacy to Minocycline gel in improving gingival recession in diabetic chronic periodontitis patients, with no statistically significant difference between the two ($p>0.05$). Importantly, the combination of Metronidazole and Minocycline gels demonstrated a synergistic effect, producing significantly greater improvement in gingival recession than either agent alone ($p<0.01$), supporting their combined use as a more effective adjunct to SRP in this patient population. Metronidazole,[10] and minocycline,[11] were chosen for this study because both have antibiotic as well as anti-inflammatory effects. Minocycline also has anti-collagenase properties to reduce tissue destruction and bone resorption.[12]

Gingival recession is a multifactorial, common, and undesirable clinical feature of periodontal disease. As defined by the American Academy of Periodontology, gingival recession involves the shifting of marginal periodontal tissues below the cemento–enamel junction (CEJ). From the clinical perspective, recession is measured as the distance from CEJ to the lowest point of the gingival margin. Recession can impact patients due to aesthetic concerns, discomfort, root sensitivity, increased risks of dental issues like root cavities and abrasion, plaque retention, bleeding gums, and/or a fear of tooth loss, affecting their overall quality of life. Miller's classification used in this study provided the expected clinical success rate for root coverage and also emphasized the importance of interproximal bone support in ensuring treatment success.[4]

In our research, out of the total 380 patients, 221(58.2%) were males, and 159(41.8%) were females. This predisposition of chronic periodontitis in diabetes mellitus patients towards the male gender was also mentioned in another study performed in Pakistan by Ayesha et al., where it was 55% males and 45% females.6 In a study conducted by Ying *et al*., results showed a higher percentage of the sample.[13] However, in the clinical trial done by Qureshi *et al*., in Pakistan, reported 44.2% males and 55.8% females.[14]

It's intriguing to note that a significant reduction in recession, particularly within Group-IV, was observed. In concurrence with our investigation, Brinar et al., also concluded in their randomized single-blinded controlled clinical trial, analogous findings. They studied the effects of concomitant antimicrobial photodynamic therapy (aPTD) on periodontal disease in type 2 diabetes mellitus patients and found a statistically significant reduction in bleeding on probing only. Both the test and control groups showed improvement for gingival recession, but no statistically significant difference was found between the groups.[15]

Literature has also reported findings diverging from this study outcomes like Yusri *et al*., who revealed a non-significant difference regarding recession depth changes in their systematic review and meta-analysis, determining the effects of locally delivered antibiotics during periodontal surgery compared to periodontal surgery alone.[16] Interestingly, our findings also diverged from studies of Kaufmann *et al*., who observed a counterintuitive increase in recession after treatment. They ventured into a different landscape, employing systemic Amoxicillin and Metronidazole as complementary agents to SRP within the antibiotic group. They calculated recession

from available pocket depth and clinical attachment level values, while we used Miller's classification for the evaluation of recession.[17] Ramos *et al.*, in their randomized controlled clinical trial, documented an increase in gingival recession in all groups i.e., control group, antibiotic group(Amoxicillin and Metronidazole), and probiotic group(Lactobacillus reuteri) after undergoing periodontal debridement. In intergroup comparisons, the probiotic group showed lower gingival recession than the antibiotic group at 30 days and lower than both therapies at 90 days.[18]

The enhanced tolerability and safety profile of these medications render them a practical and effective choice for diabetic periodontitis patients. Given that Metronidazole proves comparably effective to Minocycline in our study's periodontitis patients, promoting their usage is prudent to mitigate unnecessary systemic antibiotic risks. In cases where monotherapy falls short, combining Minocycline and Metronidazole demonstrates a synergistic effect in treating diabetic periodontitis. A single application by the dentist will ensure the patient's compliance as well. Our study was single-centered and lacked a clinical comparison of antibiotic adverse effects; the omission of plaque and gingival index calculations was due to cost and time constraints.

Future recommendations include conducting a multicenter study to enable a more extensive investigation and validation. A comprehensive assessment, including plaque and gingival index calculations, would enhance our understanding. Endorsing locally applied antibiotic gels emerges as a valuable strategy in treating chronic periodontitis. With a judicious approach, it is imperative to discourage excessive and unwarranted systemic antibiotic use.

CONCLUSION

Scaling and Root Planning enhanced the periodontal health in diabetes mellitus patients, but superior outcomes were achieved in patients undergoing SRP and adjunct antibiotic treatment. Metronidazole gel exhibited comparable efficacy to Minocycline Gel for treating gingival recession in diabetic chronic periodontitis patients. A synergistic effect was observed between Metronidazole and Minocycline in treating gingival recession in chronic periodontitis patients with diabetes mellitus. This combination proved significantly more effective than using metronidazole alone or minocycline alone.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AC & SR: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AG & NZ: Data acquisition, data analysis, approval of the final version to be published.

WJ & UF: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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