Original Article

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Dentistry Section

Exploring the Therapeutic Synergy of Quercetin Gel and Mechanical Debridement in Peri-implantitis Management: A Prospective Clinical Evaluation

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ABSTRACT

Introduction: Peri-implantitis is a chronic inflammatory disorder characterized by continuous bone loss around dental implants, endangering their stability and long-term function. While mechanical debridement remains the cornerstone of therapy, emerging evidence supports the enhancement of outcomes through adjunctive agents, including antibiotics, antiseptics, and antioxidants.

Aim: To evaluate the adjunctive efficacy of quercetin gel when applied locally alongside non-surgical mechanical debridement in peri-implantitis management.

Materials and Methods: The present prospective clinical study was conducted at the Department of Periodontology, Saveetha Dental College and Hospitals, Chennai,Tamil Nadu, India between August and December 2024. Fifty patients diagnosed with peri-implantitis were included and randomly divided into two groups (n=25 each). group 1 (Control) received mechanical debridement alone, while group 2 (Test) received mechanical debridement with subgingival application of 1.2% quercetin hydrogel. Demographic data such as age, and gender were recorded. Clinical parameters including Plaque Index (PI), Gingival Index (GI), Periimplant Probing Depth (PPD), and Clinical Attachment Level (CAL) were assessed at baseline and after three months. Statistical analysis included paired and independent t-tests, with significance set at $p<0.05$.

Results: At baseline, no significant differences were observed between the two groups in terms of age, gender, or clinical parameters ($p>0.05$). After three months, both groups showed statistically significant improvements in all clinical indices ($p<0.05$). However, group 2 demonstrated significantly greater reductions in PI (2.57±0.06 to 0.39±0.18), GI (2.55±0.16 to 0.66±0.19), PPD (5.84±0.19 mm to 3.01±0.02 mm), and CAL (6.47±0.11 mm to 3.13±0.12 mm) compared to group 1 ($p<0.05$ for all intergroup comparisons).

Conclusion: Incorporating quercetin gel into standard mechanical debridement protocols yielded enhanced periimplant health outcomes. These findings suggest that quercetin gel may serve as a valuable adjunct in the non-surgical management of Peri-implantitis.

Keywords: Antioxidant therapy, Local drug delivery, Polyphenols

INTRODUCTION

Modern implant dentistry has witnessed remarkable advancements, transforming the treatment of partial and complete edentulism. However, despite favourable long-term success rates, complications such as periimplant diseases continue to challenge clinicians. Chief among these are periimplant mucositis and peri-implantitis- both inflammatory in nature but differing in severity [1]. While the former involves inflammation limited to the surrounding soft tissue, the latter is more deleterious, involving progressive alveolar bone loss and jeopardising implant survival [2,3]. Prompt detection and meticulous intervention are crucial for preserving implant functionality.

Management strategies for periimplant diseases vary considerably among practitioners, yet the primary objective remains uniform: reduction of microbial burden and resolution of inflammation. Treatment modalities are categorised into surgical, non-surgical or a combination approach [4]. Non-surgical therapy is often initiated to cleanse the implant surface and curb the microbial load using various mechanical tools like titanium curettes, ultrasonic scalers, and air-polishing devices. Nevertheless, these methods sometimes yield transient improvements due to the resilient and complex microbial ecosystem associated with peri-implantitis [5]. To enhance therapeutic efficacy, the use of adjuncts has gained widespread acceptance. Among these, herbal therapy has emerged as a prominent adjunctive approach in dental therapeutics [6-9].

Quercetin, a dietary flavonoid abundantly present in fruits and vegetables, is well-regarded for its favourable safety profile and potent anti-inflammatory, antioxidant, and antimicrobial properties [10]. It has long been consumed as part of the human diet and has demonstrated multifaceted biological activity. Mechanistically, quercetin disrupts microbial integrity by damaging bacterial cell membranes, inhibiting adhesion and biofilm formation, and interfering with Deoxyribonucleic Acid (DNA) replication, thereby limiting the progression of microbial colonisation. It exerts anti-inflammatory effects by downregulating key proinflammatory cytokines such as Interleukin (IL)-1β, IL-6, and Tumour Necrosis Factor (TNF)-α, and by inhibiting cyclooxygenase and lipoxygenase pathways involved in the synthesis of inflammatory mediators. Its antioxidant potential is mediated through the scavenging of reactive oxygen species, suppression of lipid peroxidation, and upregulation of endogenous antioxidant enzymes like superoxide dismutase and glutathione peroxidase [11].

Peri-implantitis is characterised by microbial dysbiosis and an exaggerated host immune response leading to progressive periimplant tissue destruction. The rationale for the present study stems from the need to address both microbial and inflammatory components of peri-implantitis using a localised, biocompatible adjunct. Given quercetin's ability to modulate immune responses and control microbial load, its local delivery as a subgingival hydrogel may enhance the therapeutic outcomes of conventional

mechanical debridement. While preclinical evidence supports quercetin's pharmacological potential, clinical data on its use in peri-implantitis remain scarce. Hence, the present study was undertaken to evaluate the clinical efficacy of 1.2% quercetin gel as an adjunct to non-surgical therapy in the management of peri-implantitis.

MATERIALS AND METHODS

The present prospective clinical study was conducted at the Department of Periodontology, Saveetha Dental College and Hospitals, Chennai, Tamil Nadu, India between August and December 2024. Ethical clearance was obtained from the Institutional Ethical Committee (IHEC/SDC/PERIO-2303/24/026), and written informed consent was secured from all participants prior to their enrollment. A total of fifty systemically and periodontally healthy individuals, aged between 25 and 50 years, diagnosed with peri-implantitis as per the 2017 classification of the European Federation of Periodontology (EFP) and the American Academy of Periodontology (AAP) [12], were included in the study.

Sample size calculation: Sample size was estimated using G*Power software (Version 3.1.9.4), based on previously published data [13], using PPD value (3.66±1.03), to ensure adequate power and statistical reliability.

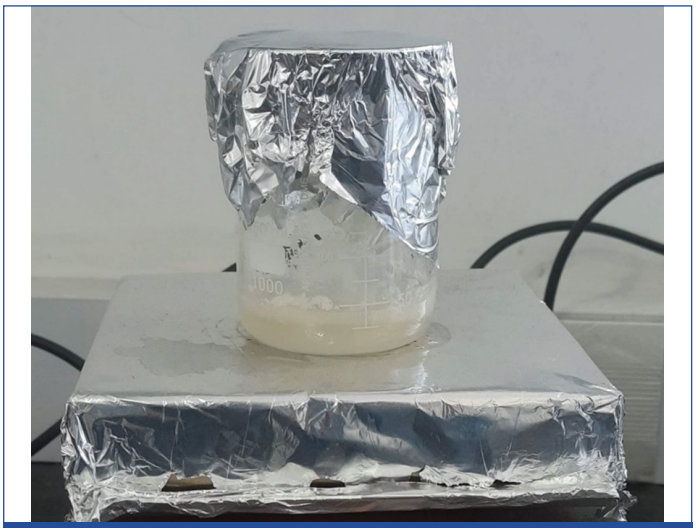
Participants were randomly assigned into two groups: group 1 (Control) received mechanical debridement alone (n=25), while group 2 (Test) underwent mechanical debridement along with subgingival application of 1.2% quercetin hydrogel (n=25).

Inclusion criteria: Inclusion criteria encompassed patients aged 25-50 years with at least one functional dental implant diagnosed with peri-implantitis. All participants were systemically and periodontally healthy.

Exclusion criteria: Exclusion criteria included tobacco use, pregnancy or lactation, ongoing medication or supplement intake within the last six months, systemic disorders, and current or past history of periodontitis.

Study Procedure

Formulation of 1.2% Quercetin Hydrogel: Quercetin extract, obtained from Biomed Ingredients (Goa, India), was utilised for gel preparation. To achieve a 1.2% concentration, 10 mg of powdered quercetin was initially dissolved in 4.87 mL distilled water. From this, 750 µL was mixed with three grams of sodium alginate, which served as the gelling agent. Distilled water was added to adjust the volume, and the mixture was thoroughly homogenised [Table/Fig-1]. Ionic cross-linking of sodium alginate facilitated the formation of a stable hydrogel matrix encapsulating quercetin. The formulation was prepared freshly under aseptic conditions and applied subgingivally on the same day of treatment, within one hour of preparation, to ensure maximum stability and therapeutic efficacy.



[Table/Fig-1]: Prepared 1.2% quercetin hydrogel treatment protocol.

Mechanical debridement was performed under local anaesthesia using a titanium curette (Titanium Imp Scaler Mini Five 11/12, Hu-Friedy®, Chicago, USA). In group 2, the prepared 1.2% quercetin gel was applied subgingivally into periimplant pockets using a 27-gauge needle-equipped syringe. A periodontal dressing (COE-PAK™, GC America Inc.) was placed over the treated areas in both groups. Participants were advised to refrain from using interdental aids or brushing the treated areas and to avoid consuming hard or sticky foods for a period of one week. After this interval, the dressing was removed, and all patients were recalled for clinical evaluation at three months. All procedures were performed by a single clinician (MT) to ensure consistency. No adverse reactions or hypersensitivity responses were reported following the subgingival application of 1.2% quercetin hydrogel in any participant throughout the study period.

Clinical Evaluation: Four primary parameters- PI, GI, PPD, and CAL- were recorded around the implant for each patient. PI was measured using the Silness and Loe index, while GI was determined using the Loe and Silness index [14]. Each index was recorded from four surfaces (distal, mesial, facial, lingual) and averaged. PPD and CAL measurements were obtained from six sites (mesio-buccal, mid-buccal, disto-buccal, mesiolingual/palatal, mid lingual/palatal, distolingual/palatal) using a periodontal probe (Hu-Friedy Colorvue®, USA). All clinical assessments were performed at baseline (T0) and three months (T1) by a single examiner (AR) who remained blinded to group allocation.

STATISTICAL ANALYSIS

Data analysis was executed using Statistical Package for Social Sciences (SPSS) version 23.0. Paired t-tests were employed for intragroup comparisons, while independent t-tests were used for inter-group analysis. Gender distribution between groups was evaluated using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Demographic and baseline clinical data are summarised in [Table/Fig-2]. In group 1 (mechanical debridement only), the average age was 40.32±4.15 years, with mean PI of 2.53±0.11, GI of 2.52±0.13, PPD of 5.76±0.22 mm, and CAL of 6.40±0.21 mm. group 2 (mechanical debridement + quercetin gel) presented with a mean age of 42.09±2.11 years, PI of 2.57±0.06, GI of 2.55±0.16, PPD of 5.84±0.19 mm, and CAL of 6.47±0.11 mm. Gender distribution was nearly equal in both groups. No statistically significant differences were found between groups at baseline (p>0.05). Independent t-test results, summarised in [Table/Fig-3], showed that after three months, all clinical indices improved significantly in group 2 compared to group 1 (p<0.05).

[Table/Fig-4] displays intragroup comparisons using paired t-tests. In group 1, PI significantly decreased from 2.53±0.11 at baseline to 1.12±0.08 at three months, GI declined from 2.52±0.13 to 1.32±0.22, PPD reduced from 5.76±0.22 mm to 3.88±0.51 mm, and CAL improved from 6.40±0.21 mm to 4.54±0.21 mm

Outcome Variables	Group 1	Group 2	T value	p-value
Age (years)	40.32±4.15	42.09±2.11	-1.90	0.07[a]
Gender (Male/ Female) (n)	13/12	12/13	-	1.00[b]
Plaque Index (PI)	2.53±0.11	2.57±0.06	-1.60	0.17[a]
Gingival Index (GI)	2.52±0.13	2.55±0.16	-0.73	0.47[a]
Periimplant Probing Depth (PPD) (mm)	5.76±0.22	5.84±0.19	-1.38	0.18[a]
Clinical Attachment Level (CAL) (mm)	6.40±0.21	6.47±0.11	-1.48	0.15[a]

[Table/Fig-2]: Comparison of baseline demographic and clinical data of participants across both groups.
[a]Independent t-test; [b]Chi-square test, Statistically significant at p-value <0.05

Parameters	Timeline	Group 1 (Mean±SD)	Group 2 (Mean±SD)	T value	p-value
Plaque Index (PI)	T0	2.53±0.11	2.57±0.06	-1.60	0.17
	T1	1.12±0.08	0.39±0.18	18.52	<0.05
Gingival Index (GI)	T0	2.52±0.13	2.55±0.16	-0.73	0.47
	T1	1.32±0.22	0.66±0.19	11.36	<0.05
Periimplant Probing Depth (mm) (PPD)	T0	5.76±0.22	5.84±0.19	-1.38	0.18
	T1	3.88±0.51	3.01±0.02	8.52	<0.05
Clinical Attachment Level (CAL) (mm)	T0	6.40±0.21	6.47±0.11	-1.48	0.15
	T1	4.54±0.21	3.13±0.12	29.13	<0.05

[Table/Fig-3]: Intergroup comparison of clinical parameters using independent t-test analysis.
*Statistically signific ant at p-value <0.05 (Independent t-test)

quercetin. The implants, with varying chitosan concentrations, demonstrated sustained quercetin release and enhanced bone regeneration. The group with 0.5% chitosan coating showed optimal healing outcomes, emphasising the utility of quercetin in postoperative recovery and tissue regeneration [22].

Further supporting its role in oxidative stress modulation, Catauro M et al., formulated a biomaterial consisting of an inorganic silica matrix grafted with poly-ε-caprolactone and quercetin. The hybrid material exhibited antioxidant activity dependent on quercetin concentration and retained bioactivity in simulated body fluid over time. Notably, it showed minimal cytotoxicity, making it a promising candidate for implant coatings [23]. Gomez-Florit M et al., further highlighted the antibacterial and regenerative potential of quercitrin- a rhamnosylated derivative of quercetin [24]. Also,

Parameters	Timeline	Group 1 (Mean±SD)	T value	p-value	Group 2 (Mean±SD)	T value	p-value
Plaque Index (PI)	T0	2.53±0.11	106.02	<0.05 *	2.57±0.06	79.56	<0.05*
	T1	1.12±0.08			0.39±0.18		
Gingival Index (GI)	T0	2.52±0.13	43.01	<0.05*	2.55±0.16	82.63	<0.05*
	T1	1.32±0.22			0.66±0.19		
Periimplant Probing Depth (mm) (PPD)	T0	5.76±0.22	26.19	<0.05*	5.84±0.19	81.09	<0.05*
	T1	3.88±0.51			3.01±0.02		
Clinical Attachment Level (CAL) (mm)	T0	6.40±0.21	69.92	<0.05*	6.47±0.11	227.21	<0.05*
	T1	4.54±0.21			3.13±0.12		

[Table/Fig-4]: Intragroup comparison of clinical parameters using paired t-test analysis.
*Statistically significant at p-value <0.05 (Paired t-test)

(p=0.00). In group 2, PI showed a significant reduction from 2.57±0.06 to 0.39±0.18, GI from 2.55±0.16 to 0.66±0.19, PPD from 5.84±0.19 mm to 3.01±0.02 mm, and CAL from 6.47±0.11 mm to 3.13±0.12 mm (p=0.00). Notably, all clinical parameters demonstrated a more pronounced improvement in group 2 compared to group 1.

DISCUSSION

The current investigation was designed to assess the clinical performance of 1.2% quercetin gel as an adjunctive treatment modality to non-surgical mechanical debridement in patients with peri-implantitis. The results revealed that the group receiving the quercetin gel exhibited more improvements in clinical indices compared to the control group, underscoring the potential of quercetin in periimplant therapy.

These findings corroborate existing literature on the multifaceted properties of quercetin in oral health management. Previous studies have underscored its antimicrobial and anti-inflammatory capabilities, which are especially valuable in treating chronic inflammatory oral conditions such as periodontitis and peri-implantitis [15-18]. Much like periodontitis, peri-implantitis is characterised by microbial colonisation, pocket formation, and progressive loss of attachment and bone [19]. Quercetin, due to its antioxidant and anti-inflammatory nature, may help suppress the local immune response, inhibit microbial proliferation, and enhance the healing of soft and hard-tissues surrounding implants [20].

Yang N et al., explored the role of quercetin in mitigating implant loss by targeting senescent cells in a rat model of peri-implantitis. The study demonstrated that quercetin administration resulted in decreased expression of senescence markers (p19, p21, and p16), preventing implant detachment within 24 days. These findings indicate that cellular senescence may play a critical role in periimplant disease progression and that quercetin's senolytic activity may prove beneficial in combating such mechanisms [21]. In another study, Mohan L et al., developed drug-eluting titanium dioxide nanotube-based dental implants coated with chitosan and when applied as a nanocoating on titanium surfaces, it significantly reduced the expression of osteoclast-related genes both in vitro and in-vivo [25]. Similarly, Liu N et al., investigated quercetin-functionalised 3D-printed titanium alloy implants. Their study found that quercetin coatings improved osseointegration, encouraged osteoblast differentiation, and downregulated proinflammatory cytokines, highlighting its immunomodulatory and osteogenic benefits [26]. The positive outcomes of the present study align well with these experimental findings, reinforcing the hypothesis that quercetin could serve as a bioactive molecule capable of improving periimplant healing. Well-structured randomised controlled trials with larger sample sizes and extended observation periods are essential to better understand quercetin's therapeutic range.

Limitation(s)

This study had certain limitations. Notably, it lacked a long-term follow-up to determine the durability and stability of the observed clinical improvements. Additionally, biomarker and microbiological analyses were not performed, which may have provided valuable insights into the underlying biological mechanisms. The investigation also did not examine the effects of varying concentrations or application frequencies of quercetin gel. Future clinical trials are warranted to address these gaps. Investigating its systemic absorption, pharmacokinetics, and local tissue interactions will further elucidate the mechanisms behind its clinical efficacy. Moreover, assessing the gel's role in altering the local microbiome or inflammatory biomarkers may provide deeper insight into its clinical behaviour.

CONCLUSION(S)

In this prospective clinical evaluation, quercetin hydrogel emerged as an effective adjunct to mechanical debridement in managing peri-implantitis. The notable improvement in clinical parameters following its use underscores its potential in routine non-surgical periimplant treatment strategies. Long-term studies are essential to validate these preliminary findings and expand upon its clinical utility.

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