Periodontitis and Rheumatoid Arthritis: Correlation and Identification of a Therapeutic Approach for Oral and Systemic Health

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ABSTRACT

Introduction: Oral health conditions can have repercussions on systemic health. The aim of this study is to evaluate the effectiveness of periodontal therapy (scaling and root planing, SRP) combined with pharmacological treatment in periodontal patients affected by rheumatoid arthritis (RA) in reducing clinical periodontal parameters.
Material and Methods: In this clinical study, patients underwent baseline periodontal parameter assessments, which were recorded in the periodontal chart (University of Bern). The patients were divided into three groups:
- Test group: patients with rheumatoid arthritis and periodontal disease treated with non-surgical mechanical therapy and pharmacological therapy;
- Control group I: patients with rheumatoid arthritis and periodontal disease treated with pharmacological therapy only;
- Control group II: patients with rheumatoid arthritis and periodontal disease treated with non-surgical mechanical therapy only.

Results: The findings indicate a significant improvement in clinical parameters in the group of patients treated with both therapies, with a p-value of 0.001 compared to Control Groups I and II (p-value 0.005).
Conclusions: The presence of periodontitis may contribute to the progression of RA, whereas RA may have little effect on accelerating the development of periodontitis.

Keywords: Oral Health, Rheumatoid Arthritis, Periodontitis

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INTRODUCTION

Recent studies have focused on the bidirectional relationship between oral and systemic diseases, reintroducing the hypothesis that oral health conditions can have systemic implications. Epidemiological studies indicate that more than 15% of the population in Western countries is affected by severe periodontitis. Periodontitis represents a risk factor for the progression of several systemic diseases, such as:
- Cardiovascular diseases;
- Diabetes mellitus;
- Metabolic syndrome;
- Obesity;
- Rheumatoid arthritis.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease (Fig. 1) characterized by widespread inflammatory alterations of connective tissue, particularly affecting the joints, leading to pain, swelling, and impaired mobility. Fortunately, with current pharmacological options, joint deformities have become rare.

The disease primarily affects women and can occur at any age, although it is most common between 30 and 50 years. The immune system—which normally defends the body against external aggression—mistakenly attacks healthy tissues. The primary target of the antibodies in this case is the synovial membrane, the inner lining of the articular capsule that extends to cover the articular bone surfaces. This membrane responds to inflammation by proliferating and forming a pannus, which expands and gradually destroys the cartilage. In severe cases, the proliferative process may extend to bone and surrounding tissues (subchondral bone, capsule, tendons, ligaments), resulting in disability in long-term sufferers. Possible environmental triggering factors include certain viral infections (Human Herpes Virus 6 and Epstein-Barr Virus), stress, tobacco smoking, and poor oral hygiene (periodontal disease associated with proliferation of *Porphyromonas gingivalis*). It is still unclear whether low vitamin D levels represent a potential risk factor or merely a consequence of the disease.

Diagnosis

RA can be difficult to diagnose because its onset may be

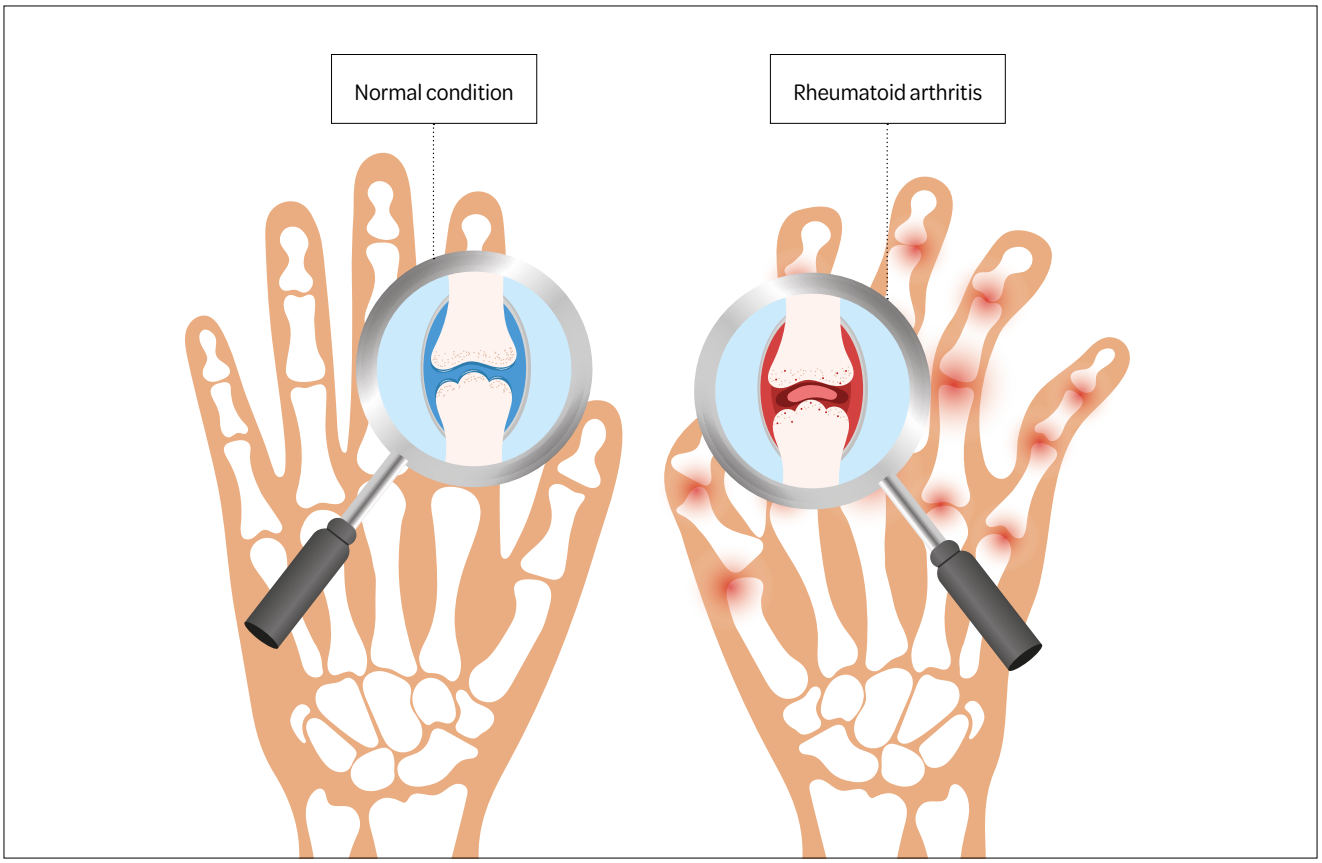

Fig. 1 Rheumatoid arthritis.

gradual and accompanied by nonspecific symptoms; indeed, many diseases, particularly in their early stages, can resemble RA.

The diagnosis of RA is based on the symptoms reported by the patient and on a rheumatological examination, which allows detection of pain, swelling, and warmth at the joint level. In addition, several laboratory tests assist in the diagnosis, including:

- Anemia;
- Rheumatoid factor;
- Anti-citrullinated peptide antibodies (anti-CCP antibodies, which are highly specific for RA);
- Elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels.

It is important to note that no single test can definitively diagnose RA. Only a rheumatologist, by integrating the patient's symptoms, physical findings, laboratory results, and imaging (radiographs or joint ultrasounds), can establish the correct diagnosis.

Prognosis

The course of rheumatoid arthritis is unpredictable. It tends to progress more rapidly during the first six years—particularly in the first year—and 80% of untreated individuals develop permanent joint damage within ten years. RA reduces life expectancy by approximately three to seven years. Spontaneous remission of rheumatoid arthritis is rare. Treatment relieves symptoms in approximately three out of four patients; however, in at least 10% of individuals, the disease remains severely disabling despite comprehensive therapy.

Factors associated with a poorer prognosis include:

- Female sex, white race, or both;
- Presence of rheumatoid nodules;
- Older age at disease onset;
- Involvement of 20 or more inflamed joints;
- Tobacco use;
- Obesity;
- Elevated ESR;
- High levels of rheumatoid factor or anti-CCP antibodies.

Treatment

With appropriate treatment aimed at reducing inflammation—and consequently pain—patients can live with the disease and maintain a good quality of life. Therapeutic options include conservative and pharmacological measures as well as surgical treatments. The simplest measures aim to relieve symptoms and include rest, an appropriate diet, and physiotherapeutic interventions. A diet rich in fish (omega-3 fatty acids) and vegetable oils but low in red meat may partially alleviate symptoms in some patients.

Physiotherapy

Along with pharmacological therapy to reduce joint inflammation, the management plan for rheumatoid

arthritis should include non-pharmacological treatments such as physical activity, physiotherapy (including massage, traction, and deep-heat treatments), and occupational therapy (including self-assistance tools).
Inflamed joints should undergo moderate stretching movements to prevent "freezing" in a fixed position.
Thermotherapy can be highly beneficial, as it improves muscle function while reducing stiffness and spasm.
When inflammation subsides, regular exercise can also be helpful.

Correlation Between Periodontitis and Rheumatoid Arthritis

The relationship between RA and periodontitis was proposed more than 200 years ago, as noted by Rutger et al. (2012). Rheumatoid arthritis (RA) and periodontitis (PD) are complex multifactorial diseases characterized by common pathogenic mechanisms involving chronic inflammation and bone destruction. Furthermore, these two prevalent diseases share several risk factors, particularly smoking. Observational studies based on clinical cohorts have suggested that the prevalence of RA is higher among patients with periodontitis than among those without it, and vice versa. This indicates that patients with RA may have a higher frequency of moderate-to-severe periodontitis compared to healthy controls. Recognizing the association between RA and PD and understanding the potential biological mechanisms involved in their pathogenesis are crucial for managing patients who require both periodontal and arthritic treatment. This implies that the clinical management protocol for RA patients may need to be modified to include periodontal examination, and, in cases of confirmed PD diagnosis, the treatment protocol may incorporate resolution of periodontal inflammation through non-surgical periodontal therapy (NSPT). Conversely, periodontal patients diagnosed with RA may experience improved periodontal status due to medications prescribed for arthritis, such as biologic disease-modifying antirheumatic drugs (DMARDs) or nonsteroidal anti-inflammatory drugs (NSAIDs), owing to their immunomodulatory effects on both diseases.

Pathological and Clinical Similarities

The relationship between periodontal disease (PD) and rheumatoid arthritis (RA) has been emphasized in numerous clinical studies.
Both diseases are described as chronic, destructive inflammatory conditions that share significant pathological and clinical similarities at cellular and molecular levels.
Among their pathological and immunological features are:

- Increased infiltration of inflammatory and immune cells, including neutrophils, monocytes, and T and B lymphocytes;
- Elevated release of proinflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), and matrix-degrading enzymes (MMPs, cathepsins);
- Upregulation of the receptor activator of nuclear factor kappa-B ligand (RANKL) pathway induced by soluble mediators released from immune cells, leading to osteoclast differentiation and maturation.

Patients with rheumatoid arthritis are more likely to exhibit severe periodontitis or missing teeth than healthy controls.
Similarly, individuals with periodontal disease have been shown to be more susceptible to RA than healthy individuals. A dose-dependent association model has been demonstrated between periodontitis severity and RA disease activity. Moreover, non-surgical periodontal therapy has been shown to have a positive effect on rheumatic disorders, and conversely, RA treatment has demonstrated a beneficial impact on periodontal status.
The chronic inflammation characteristic of both RA and PD is similar in terms of the predominant adaptive immune phenotype, the imbalance between pro- and anti-inflammatory cytokines, and the influence of smoking and genetic background as shared risk factors.
Despite the distinct etiologies of RA (autoimmune) and PD (dysbiotic microbial biofilm), similar biological processes are involved—such as citrullination, autoantibody response, and the role of bacterial dysbiosis—which may represent a direct link between the two conditions.
The common onset of periodontal dysbiosis in RA suggests that oral pathogens may trigger the production of disease-specific autoantibodies and arthritis in susceptible individuals. Periodontitis is characterized by the presence of citrullinated autoantigens, which serve as primary immune targets in RA. Citrullination patterns in periodontitis mirror those observed in rheumatoid joints, implicating the oral mucosa as a potential site involved in RA pathogenesis. Proteomic signatures of multiple microbial species have been detected in hypercitrullinated periodontitis samples. Among these, *Aggregatibacter actinomycetemcomitans* (Aa)—but not other candidate pathogens—was shown to induce hypercitrullination in host neutrophils. Special attention has been directed toward the periodontal pathogen P*orphyromonas gingivalis*, which has been implicated in the generation of anti-citrullinated protein antibodies (ACPAs) in RA patients, suggesting a direct biological intersection between PD and RA. However, further studies are warranted to confirm this association, elucidate the underlying mechanisms, and clarify the temporal relationships between RA and PD. Consequently, recent evidence has strengthened the hypothesis that PD is a potential risk factor for the development of RA. Researchers have shown that individuals at high risk of developing RA exhibit an increased prevalence of PD and periodontopathogenic bacteria (*P. gingivalis*), suggesting that PD is associated with disease onset and may represent a potential target for preventive interventions in RA.

Bacterial Connection

A study conducted by researchers at Johns Hopkins University provided new evidence of the link between these two diseases. Published in Science Translational Medicine, the study identified a bacterial connection

between the two pathologies: *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*.
The indirect involvement of *P. gingivalis* in RA pathogenesis—through the expression of peptidylarginine deiminase (PAD) and the process of citrullination—was first described in 2004. Citrullination is a post-translational modification process in which the amino acid arginine is converted into citrulline by PAD, an enzyme present in immune cells such as T and B lymphocytes, neutrophils, monocytes, and macrophages. This process leads to the production of anti-cyclic citrullinated peptide (anti-CCP) antibodies. When citrullinated proteins are overproduced, they may act as autoantigens, triggering the formation of autoantibodies that contribute to the pathogenesis of rheumatic diseases. P. gingivalis induces the production of proinflammatory cytokines (e.g., IL-6 and IL-1β) by immune cells. In this context, oral infection with *P. gingivalis* prior to RA onset may enhance immune reactivity by stimulating Th17 cell responses, potentially accelerating arthritis development. Furthermore, *P. gingivalis* has demonstrated the ability to invade primary human chondrocytes in vitro, influencing cellular responses that may contribute to tissue damage during RA pathogenesis.
These characteristics of *P. gingivalis* suggest that periodontal disease, particularly when associated with increased colonization by this microorganism, may influence RA development through citrullination processes and Th17-related immune pathways.
Although *P. gingivalis* is the most extensively studied periodontal microorganism in RA pathogenesis, recent research has identified another pathogen, *A. actinomycetemcomitans*, a Gram-negative coccobacillus, as a potential trigger for RA pathogenesis, providing a new microbial connection between PD and RA.

Effects of Periodontal Disease Treatment on Rheumatoid Arthritis

Several studies have demonstrated that treatment of PD improves clinical and pathological RA parameters (e.g., DAS28 score, CRP levels) and, conversely, that RA treatment can reduce periodontal inflammation. This evidence strongly suggests that PD and RA are interrelated and that their association involves reciprocal biological influences. zRA management includes various pharmacological approaches. Nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids (GCs), and both synthetic and biologic disease-modifying antirheumatic drugs (DMARDs)—including TNF-α inhibitors, interleukin-1 receptor antagonists (anakinra), and Janus kinase (JAK) inhibitors—are currently the most commonly prescribed medications for RA treatment.
These drug classes reduce pain, inflammation, and joint destruction, thereby improving clinical outcomes and overall quality of life. Long-term use of GCs and NSAIDs in RA patients, however, is associated with immunosuppression, which can result in oral alterations such as xerostomia and candidiasis. Although evidence from preclinical and clinical studies indicates that transient drug-induced immunosuppression may attenuate PD, prolonged immunosuppression is also associated with worsening periodontal conditions. Most studies investigating the influence of RA treatment on PD severity have focused on agents targeting specific molecular factors within the inflammatory cascade, such as biologic DMARDs. TNF-blocking agents used for RA treatment have been shown to significantly reduce biochemical markers of PD, including IL-1β and IL-8, in the gingival crevicular fluid (GCF) of patients with periodontitis. Similarly, anti–TNF-α therapy reduces both periodontal indices and TNF-α levels in the GCF of patients affected by autoimmune disease and periodontitis. These findings suggest that TNF-α inhibition in RA therapy may also benefit periodontal health. A systematic review confirmed that periodontal status was better in RA patients receiving antirheumatic medication than in untreated RA patients. These results support the beneficial effects of pharmacological therapy on clinical periodontal parameters, as evidenced by the reduction in gingival index (GI), bleeding on probing (BOP), and clinical attachment loss (CAL). Treatment of RA patients with DMARDs and anti–TNF-α agents reduced CAL severity compared with untreated patients.

Effects of Rheumatoid Arthritis Treatment on Periodontal Disease

The impact of rheumatoid arthritis (RA) treatment on periodontal disease (PD) remains a topic of great scientific interest. RA pharmacotherapy may indirectly affect periodontal tissues by modulating the systemic inflammatory response and immune cell activity. Methotrexate (MTX), one of the most commonly prescribed synthetic disease-modifying antirheumatic drugs (DMARDs), exerts anti-inflammatory and immunomodulatory effects by inhibiting purine synthesis and reducing cytokine production, particularly TNF-α and IL-6.Clinical studies have demonstrated that MTX therapy in RA patients can reduce gingival inflammation and probing depth when compared with untreated controls. Similarly, biological DMARDs—especially TNF-α inhibitors such as infliximab, etanercept, and adalimumab—have shown positive effects on periodontal parameters. These agents reduce both systemic and local inflammation, decreasing levels of proinflammatory cytokines within periodontal tissues and gingival crevicular fluid. A number of studies have also explored the effects of tocilizumab (an IL-6 receptor antagonist) and abatacept (a T-cell costimulation modulator), demonstrating improvement in periodontal indices such as bleeding on probing (BOP) and clinical attachment level (CAL). However, the immunosuppressive effect of RA pharmacotherapy—especially when prolonged—can increase susceptibility to opportunistic oral infections, including candidiasis and herpes simplex reactivation, and may lead to oral mucosal atrophy. Therefore, periodontal monitoring is recommended for RA patients under long-term immunomodulatory therapy.

Experimental Study

Objective

The objective of this study was to evaluate the effective-

ness of periodontal therapy (scaling and root planing, SRP) combined with pharmacological therapy in achieving clinical attachment gain in periodontal pockets of patients affected by rheumatoid arthritis (RA), compared with the results obtained in patients treated either with pharmacological therapy alone or with non-surgical mechanical therapy alone.

MATERIALS AND METHODS

Study Design

The study was designed as a prospective clinical trial.

Primary Outcome

The primary variable of this prospective study was probing depth (PD).

Secondary Variables

- Full Mouth Bleeding Score (FMBS);
- Full Mouth Plaque Score (FMPS);
- Gingival recession (REC);
- Tooth mobility;
- Clinical Attachment Level (CAL).

Inclusion and Exclusion Criteria

From a pool of patients attending the Department of Periodontology, University of Naples "Federico II," 30 patients were selected according to the following inclusion criteria:

- both sexes;
- diagnosis of periodontitis and rheumatoid arthritis;
- presence of at least one periodontal pocket greater than 5 mm in each quadrant.

Exclusion criteria:

- presence of systemic diseases other than rheumatoid arthritis;
- pregnancy or breastfeeding.

Protocol

During the first visit, after thorough anamnesis to verify inclusion and exclusion criteria, patients were informed about the clinical procedures to be performed and signed informed consent.
Patients were divided into three groups:

- Test group: patients with rheumatoid arthritis and periodontal disease treated with non-surgical mechanical therapy combined with pharmacological therapy;
- Control Group I: patients with rheumatoid arthritis and periodontal disease treated with pharmacological therapy only;
- Control Group II: patients with rheumatoid arthritis and periodontal disease treated with non-surgical mechanical therapy only.

A baseline periodontal charting was performed, including the evaluation of PD, FMPS, FMBS, bleeding on probing (BOP), gingival recession (REC), and tooth mobility. All collected data were recorded in the periodontal chart, providing an overview of the patient's periodontal status before treatment.
Patients in the test group underwent non-surgical periodontal therapy (SRP), consisting of one session of supragingival scaling and four sessions of root planing, each lasting approximately 30 minutes, in association with pharmacological treatment for rheumatoid arthritis. Patients in Control Group I continued their pharmacological therapy for RA but did not receive mechanical periodontal treatment. Patients in Control Group II received non-surgical mechanical therapy without pharmacological treatment for RA. A follow-up was performed at 3, 6, and 12 months to reassess the same clinical parameters recorded at baseline and to evaluate treatment outcomes over time.

Clinical Cases

Figures from 2 to 7.

RESULTS

Probing depth (PD) was measured at baseline and at 3, 6, and 12 months after treatment. Differences in parameters

Fig. 2 Control group II mechanical therapy baseline.

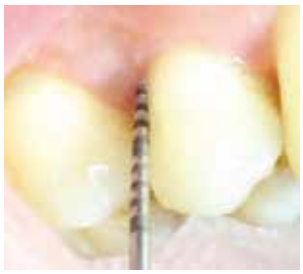

Fig. 3 Control group II mechanical therapy follow up.

Fig. 4 Control group I baseline drug therapy.

Fig. 5 Control group I drug therapy follow up.

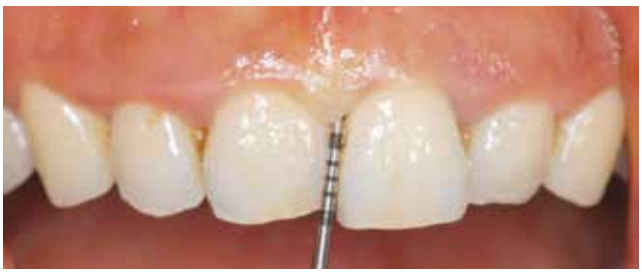

Fig. 6 Mechanical therapy test group combined with baseline pharmacological therapy.

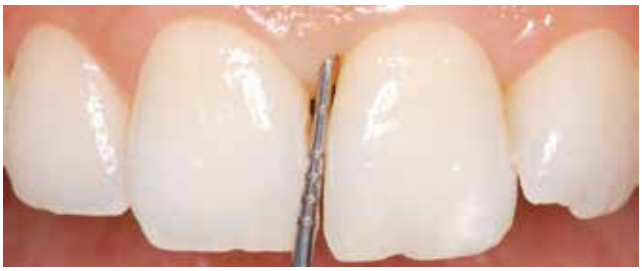

Fig. 7 Mechanical therapy test group associated with pharmacological therapy follow up.

between baseline and the three post-treatment evaluations are illustrated in Table 1. Comparisons across the follow-up periods revealed significant differences in clinical parameters after treatment.

DISCUSSION

In the present study, the clinical parameters PD and CAL were measured at baseline and 3, 6, and 12 months after treatment. The results indicate a significant improvement in these parameters in the group of patients treated with both periodontal and pharmacological therapies, with a p-value of 0.001, compared with patients treated either with pharmacological therapy alone or with non-surgical mechanical therapy alone (p-value 0.005). These findings suggest that the combined therapeutic approach produces superior clinical outcomes in the management of periodontal disease in patients affected by rheumatoid arthritis.

CONCLUSIONS

The presence of periodontitis may contribute to the progression of rheumatoid arthritis, whereas rheumatoid arthritis appears to have limited influence on the acceleration of periodontal disease. This study demonstrates that periodontal patients with rheumatoid arthritis receiving non-surgical periodontal treatment (NSPT) in addition to their pharmacological therapy experience a remarkable improvement in oral health, with reductions in both inflammation and pocket depth. The treatment protocol for RA patients could therefore be modified to include routine periodontal examination, and—if periodontitis is diagnosed—non-surgical periodontal therapy should be incorporated into the management plan to resolve local inflammation. Conversely, periodontal patients diagnosed with RA may experience improvement in their periodontal condition due to the immunomodulatory effects of RA medications, such as biologic DMARDs or nonsteroidal anti-inflammatory drugs (NSAIDs), which can exert beneficial effects on both diseases.

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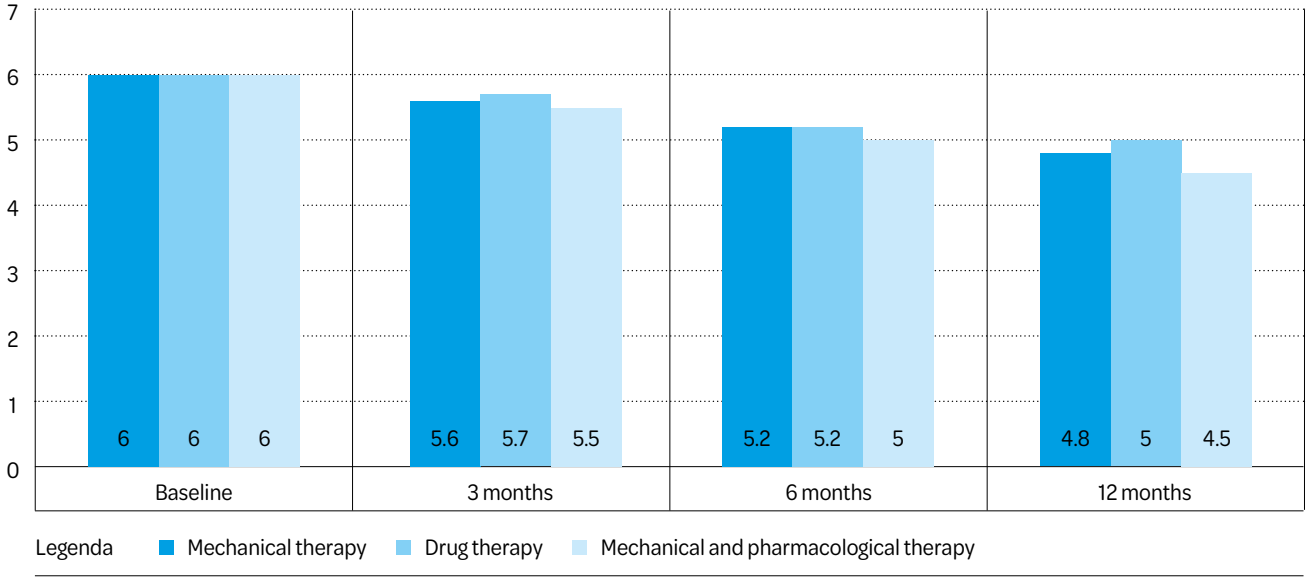

Tab. 1 The graph compares PD values over time (3, 6, and 12 months) following different therapies administered to patients with rheumatoid arthritis and periodontitis. The graph shows a significant final reduction in PD, especially when combining non-surgical mechanical therapy with pharmacological therapy.

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