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Original Research Article

Efficacy of Periodontal Therapy on the Anemic Status of Chronic Periodontitis Patients: A Systematic Review

Dr. Raveena Naveen Bhanushali, BDS (MDS)[1*], Dr. Anita Kulloli, MDS[1], Dr. Sharath Shetty, MDS, DNB (PhD)[1], Dr. Santosh Martande MDS[1]

[1]Deptartment of Periodontology, Dr. D. Y. Patil Vidyapeeth, Pune India

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***Corresponding author:** Dr. Raveena Naveen Bhanushali, BDS (MDS)

Abstract

Aim: To systematically examine the published findings on the clinical effectiveness of periodontal therapy on anemic status of patients with chronic periodontitis. ***Method:*** A systematic search was conducted using MEDLINE, Cochrane Central Register of Controlled Trials, Google Scholar, Google, Clinical trials registry and manual search using DPU Vidyapeeth library resources were searched up to 31st October 2019 to identify appropriate studies. All cross reference lists of the chosen studies were also screened. Two reviewers assessed the eligibility of studies. ***Results:*** The electronic and manual search identified a total of 138 articles. A final screen consisted of 21 articles out of which 16 articles were selected for full-text assessment. Finally, 5 articles were selected for detailed evaluation for the systematic review which evaluated the efficacy of effect of periodontal therapy on anemic patients with chronic periodontitis. ***Conclusions:*** Chronic periodontitis may cause to anemia and provides evidence that non-surgical periodontal therapy can improve the anemic status of patients with chronic periodontitis.

Keywords: Chronic periodontitis, Anemia, Periodontal therapy.

INTRODUCTION

Periodontitis is an inflammatory condition of the supporting tissues of the tooth caused by specific microorganisms in a susceptible host. Gram‐ negative anaerobic bacteria are most commonly associated in the initiation of periodontitis [1]. The bacteria and their products evoke an immune-inflammatory reaction in the host tissue. Although this process is intended to eliminate the microbial challenge, it often results in damage to the host tissue [2].

The sulcular epithelium acts as a protective barrier and prevents entry of microorganisms and other irritants into the systemic circulation. The host-microbial interaction in periodontitis results in the ulceration of sulcular epithelium. The ulcerated epithelium acts as a portal of entry for the bacteria to enter into the systemic circulation via the connective tissue. Bacteremia has been observed in patients with periodontitis and has been directly associated with the severity of inflammation. The subgingival microbiota in patients with periodontitis poses a significant and persistent Gram-negative bacterial challenge to the host [2].

The host response may offer explanatory mechanisms for the interaction between periodontitis and a variety of systemic disorders [3]. Infections, malignant cells, and autoimmune dysregulation all lead to the activation of the immune system and production of cytokines most notably tumor necrosis factor‐ alpha (TNF‐ α) and interleukin‐ 1 (IL‐ 1) and IL‐ 6 [4] Such inflammatory cytokines can depress erythropoietin (Epo) production leading to the development of anemia[5].

Anemia is defined as haemoglobin (Hb) concentration in blood below the lower limit of the normal range for the age and sex of the individual [1]. In India, anemia is a common and serious health disorder among both sexes and all age groups, although it has a higher prevalence among women than men [6].

The association between anemia and periodontal disease has been explored since 20th century [7]. Available literature indicates a 2–way relationship with some reports suggesting anemia to be a cause of destructive periodontal disease, whereas others suggest it is a consequence of it [8]. Siegel et al.1945 [9], reported depression in the number of

erythrocytes apparently secondary to the presence of periodontal disease. Lainson et al. [10], implicated anemia as a systemic cause of periodontitis.

Mechanical debridement has been the cornerstone for professional plaque control and prevention of periodontal disease for centuries. It aims not only to preserve periodontal tissues, but also aims at limiting the source of inflammation contributing to overall systemic well–being.

MATERIAL AND METHOD

Reporting format

This systematic analysis was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement.

Population (P), Intervention (I), Comparison (C) and Outcomes (O) – PICO

- Population: Patients that presented with chronic periodontits and were suffering from anemia.
- Intervention: periodontal therapy.
- Comparison: Not applicable.
- Outcome: Improvement in anemic status of patients with chronic periodontitis.

Focused question

To what extent does periodontal therapy affect the haemoglobin concentration in chronic periodontitis patients?

Protocol development

A comprehensive search convention was created and followed as indicated by the PRISMA (Preferred Reporting Items for Systematic review and Meta-analysis).

Eligibility criteria

Articles were screened considering the inclusion and exclusion criteria

Inclusion Criteria

1. Eligible studies included longitudinal, interventional and randomized controlled trial with essential data on chronic periodontitis, anemia and periodontal therapy
2. Patients with at least 30% or more of the teeth having greater than or equal to 4 mm probing depth and hemoglobin levels less than or equal to 12.5 mg/dl
3. Pubmed search which includes articles published from the earliest available data upto 31stOctober 2019.
4. Only papers written in English were accepted.

Exclusion Criteria

1. Unpublished and grey literaturewere excluded.
2. Studies including medically compromised patients, smokers and pregnant women.
3. Studies including animal models.

INFORMATION SOURCES

Search strategies were performed using electronic database like PubMed, Scopus, Cochrane and manual search using university library resources. Articles in English were preferred. These databases were searched up to October 2019 utilizing the search strategies. All cross-references list of the chosen articles were screened for extra literature.

Study selection

Preliminary screening was done after entering the search strategy. The initial screening comprised cumulative of 138 articles, of which 21 articles were distinguished through the title and after the removal of duplicates. The articles were screened. Of these, 16 articles were excluded because of the non-availability of the articles or by reading abstracts as they did not meet the inclusion criteria. Finally 5 articles were considered appropriate for the review (Figure1).

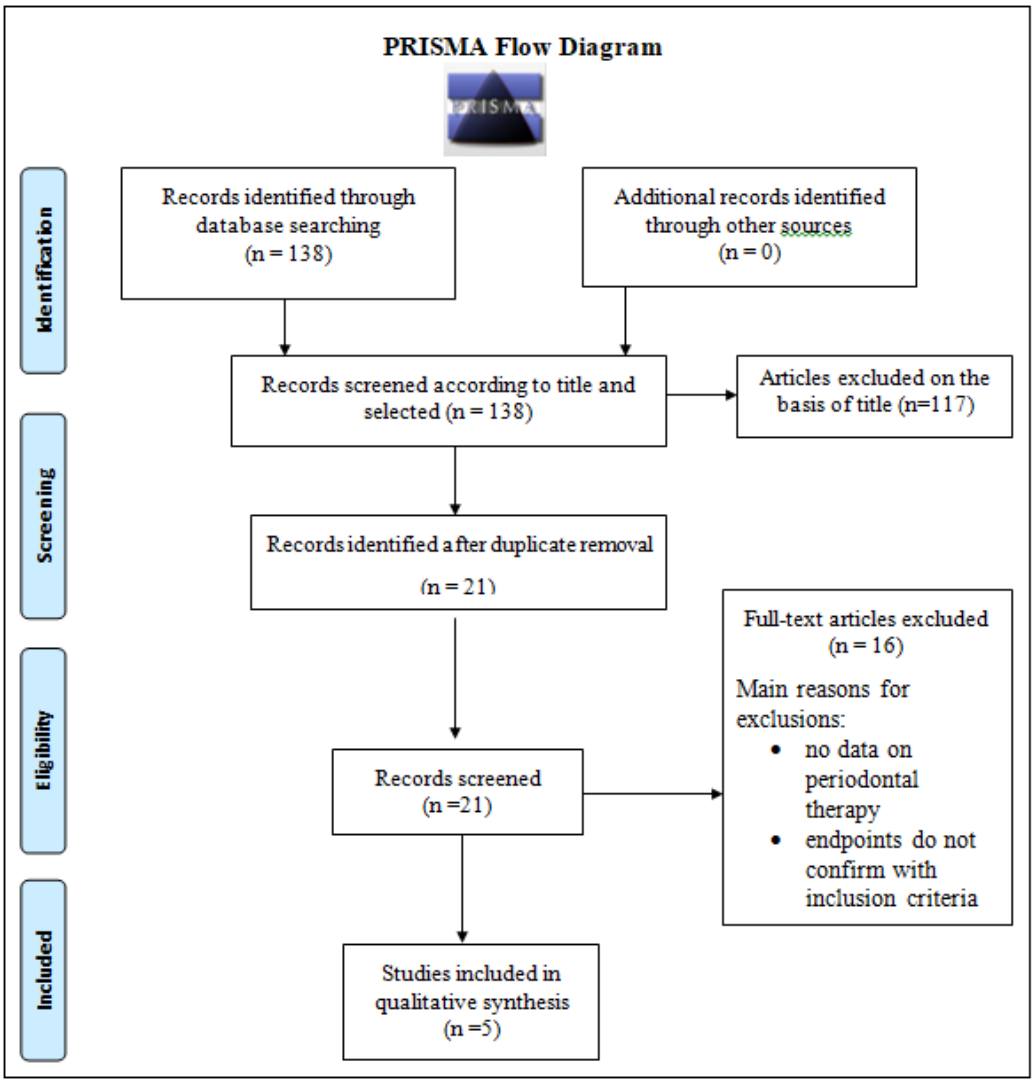

Fig-1: Study Selection

DATA COLLECTION METHOD

A standard trial form in Excel sheet was prepared and all the irrelevant headings were excluded by the reviewer. Data extraction was completed for one article, and this frame was finalized by an expert.

Data items

Study design, sample size, condition, intervention/exposure, evaluation time, Hb, RBC, ESR, MCV, MCH, MCHC, plaque index, gingival index, probing pocket depth, clinical attachment level and the result were evaluated from the articles.

Outcome measurement

The accompanying result measures were considered as follows:

Main outcome

1. Increase in hemoglobin

Secondary outcomes

1. Increase in RBC count, MCV, MCH,MCHC and clinical attachment level
2. Decrease in plaque index, gingival index, probing pocket depth.

RESULTS

Data regarding the increased values of haemoglobin, RBC count, MCV, MCH and MCHC are mentioned in Table 1.

There was a significant increase in Hb levels starting from 12.86 g/dl to 16.55 g/dl in studies where periodontal therapy was performed in anemic patients with chronic periodontitis. The increase in RBC levels ranged from $4.88x10^6$ to $5.0x10^6$. The decrease in probing depth ranged from 2.10mm to 2.82mm. The decrease in clinical attachment level ranged from 2.38mm to 3.94mm. The decrease in plaque index ranged from 0.51 to 0.84. The decrease in gingival index ranged from 0.56 to 1.86.

Change in parameters

There was significant increase in Hb levels from 14.38±0.48 to 15.33±0.5397 [8], 11.92±0.78 to 12.97±0.70 [11], 14.29±0.65 to 14.60±0.81 [12], 11.93±1.42 to 12.86±1.16 [7], 12.63 to 14.09 [6] which was low at baseline due to the presence of pathogenic bacteria or their products, which stimulate the release of inflammatory cytokines resulting in depression of erythropoiesis and a blunted erythropoietin response. The rise in Hb postoperatively was due to removal of bacterial etiology by periodontal therapy which results in decrease of cytokines [7].

An increase in RBC count was seen from 4.777±0.441 to 4.996±0.4343 [8], .46±0.23 to 4.68±0.23 [11], 4.60±0.42 to 4.70±0.40 [12], 4.68±0.40 to 4.88±0.42[7], 4.1972 to 4.786 [6]. The RBC count at baseline was low at baseline due the down regulation of the erythropoiesis in bone marrow by pro‑inflammatory cytokines such as IL‑1, IL‑6 and tumour necrosis factor which could be responsible for a decrease in number of erythrocytes. There was significant increase in RBC count postoperatively due to the effect of nonsurgical therapy, which caused resolution of inflammation [7].

A significant increase in MCV from 90.8433±5.7549 to 91.546±5.4629 [8], 89.32±1.32 to 89.84±1.32 [11], 92.99±7.37 to 92.46±7.14 [12], 88.41±1.67 to 88.68±2.32 [7] , 87.250 to 87.748 [6] MCV levels are the important determinants of certain anemias. A depressed level of MCV (microcytosis) relates anemia to iron deficiency and elevated level of MCV (macrocytosis) relates anemia to vitamin deficiency or mineral deficiencies.

MCH from 30.257±2.100 to 30.8610±2.0150 [8], 29.36±0.85 to 29.90±0.88 [11], 31.38±2.22 to 31.09±3.20 [12], 27.41±1.67 to 27.66±2.32 [7]. A decrease in the MCH value is seen in microcytic anemia caused due to iron deficiency, whereas an increase in MCH value is seen in macrocytic anemia caused due to vitamin deficiency.

MCHC from 33.31±0.82 to 33.7073±0.9393 [8], 32.56±1.64 to 33.15±1.64 [11], 31.61±1.67 to 32.06±2.32 [7] and 34.48 to 34.488 [6]. The small increment of change in MCHC values compared with increase in Hb levels implied that anemia associated with periodontitis is of normochromic type.

Clinical parameters showed a significant reduction in plaque index, gingival index, probing pocket depth and an increase in the clinical attachement level after periodontal therapy due to effective mechanical debridement, which helps in reducing the bacterial load by decreasing the local inflammation post-operatively.

DISCUSSION

This systematic review evaluated the effect of periodontal therapy on the haematological parameters of patients with chronic periodontitis. From a total of 138 articles retrieved from 3 electronic databases 21 studies were identified for full-text analysis. Finally, 5 studies were analyzed for methodological quality and the results were presented descriptively. Four interventional and one randomised controlled trial were included reporting 387 patients with haemoglobin less than average concentration of 12.5mg/dl. Data were highly heterogeneous regarding follow-up duration.

Population

The population sampled in this systematic review is quite heterogeneous. This applies to the reported follow-up periods. Out of the 5 studies included, the study by Malhotra et al. [12] reported the least follow up period of 3 months. 40 systemically healthy non–smoker male subjects in the age group of 25 to 50 years suffering with chronic periodontal disease were selected and categorized into 2 groups. Group A was categorized as chronic generalized gingivitis, and Group B was categorized as chronic generalized periodontitis on the basis of clinical findings. Three studies, Pradeep et al. [11], Musalaiah et al. [7] and Patel el al. [6] evaluated the patients for a period of 6 months. Pradeep et al. [11] evaluated 187 patients in the age group of 30-50 years and Sixty-three (33.6%) subjects had Hb% below normal reference values. The group comprised of 37 male and 26 female patients. In total 3 patients failed to follow up. The selected population group entered the second phase of the study where they underwent non-surgical periodontal therapy. Musalaiah et al. [7] evaluated 30 subjects with anemia and chronic periodontitis within age group of 33-55 years blood samples were obtained from all patients for RBC analyses and hs‑CRP was done and the patients were followed after 6 months. Patel et al. [6] conducted a 6-month follow-up randomized controlled double-blind study including only male patients of age between 20 and 50 years. They were divided into 2 groups including 50 patients having healthy periodontium and 50 patients had chronic periodontitis. A maximum follow up period was seen in the study by Agarwal et al. [8]. Thirty chronic generalized periodontitis male patients with hemoglobin levels below 15 mg/dl and serum ferritin values above 30 mg/ml were selected for the study. Thus, a substantial amount of heterogeneity exists with regard to observation periods.

Intervention

In all studies included in this systematic review, patients received oral hygiene instructions and nonsurgical periodontal treatment was performed. Periodontal treatment including surgery was performed only in one study given by Agarwal et al. [8]. In all the studies venous blood was drawn from ante-cubital fossa

under aseptic conditions and sent for the hematological investigations. Blood parameters estimated included number of erythrocytes, hemoglobin concentration, erythrocyte sedimentation rate, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular hemoglobin concentration.

Observation: Synthesis of results

Due to the observed heterogeneity between the studies a statistical meta-analysis was not appropriate, and therefore, was not performed. However, a descriptive synthesis of data was performed. It is observed that inflammation might affect erythropoiesis. The downregulation of the erythropoiesis in bone marrow by pro-inflammatory cytokines such as interleukin (IL)-1 and -6 and tumor necrosis factor-alpha could be responsible for a decreased number of erythrocytes resulting in anemia. Periodontal inflammation often results in bleeding from the gingiva. Therefore, the direct loss of blood might be responsible for the reduction in the number of erythrocytes, but the explanation was not proved. Anemic state might be a risk factor for periodontal disease. The reduction of erythrocytes might decrease oxygen in gingival tissue. Confounding factors might be involved in the relation between reduced erythrocytes and the progression of periodontitis.

LIMITATIONS

A larger sample size with larger duration of follow-up period is required for successful predilection.

CONCLUSIONS

The results indicated that non- surgical periodontal therapy showed an increase in Hb levels and RBC counts, reduction in probing pocket depth, gain in clinical attachment level. Based on the results obtained from the present systematic review, it can be concluded that chronic periodontitis may lead to anemia and provides evidence that the anemic status of patients with chronic periodontitis is improved after periodontal therapy.

FUTURE IMPLICATIONS

Future studies with more patients and experimental animal studies should be conducted to analyze the maximum potential of non- surgical periodontal therapy for improving the anemic status of patients with chronic periodontitis.

CLINICAL RELEVANCE

Scientific Rationale

Haematological parameters in chronic periodontal disease are inevitably affected after the provision of periodontal therapy. The present systematic review aimed at summarizing the scientific evidence available concerning effect of periodontal therapy on anemia.

Principal Findings

Periodontal therapy leads to significant reduction in inflammatory cytokines which lead to further decreased depression of erythropoiesis and a blunted erythropoietin response.

Practical Implications

There is consistent evidence showing that periodontal therapy lead to an improvement in the hematological parameters of patients with chronic periodontitis.

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