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CLINICAL AND IMMUNOLOGICAL RATIONALE FOR COMPLEX TREATMENT OF CHRONIC GENERALIZED PERIODONTITIS IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE

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https://doi.org/10.5281/zenodo.23696862

Relevance. Chronic periodontitis affects about half of adults worldwide [1], and fatty liver disease has an estimated global prevalence of about 24% [2]. Both are chronic inflammatory conditions that frequently coexist in the setting of metabolic syndrome. In 2023 a multisociety consensus replaced the term NAFLD with metabolic dysfunction-associated steatotic liver disease (MASLD), which requires hepatic steatosis plus at least one of five cardiometabolic risk factors [3]. Because periodontitis is a modifiable factor and its treatment may improve liver parameters [4], a clinical and immunological rationale for a combined approach is needed.

Aim. To substantiate, from clinical and immunological standpoints, a complex approach to the treatment of chronic generalized periodontitis in patients with metabolic fatty liver disease.

Materials and methods. An analytical review of publications in PubMed/MEDLINE, PubMed Central and Google Scholar was performed. Systematic reviews, meta-analyses and randomized controlled trials (RCTs) were given priority. Most cited studies used the NAFLD definition, whose criteria overlap with, but are not identical to, those of MASLD [3].

Results and discussion. Epidemiological association. A meta-analysis of five studies (27,703 participants) found that periodontitis defined by pocket depth > 3.5–4 mm was associated with fatty liver disease (unadjusted pooled OR 1.48; 95% CI 1.15–1.89; I^2 = 92%), but the association lost significance after adjustment for metabolic parameters (OR 1.13; 95% CI 0.95–1.35) (Fig. 1). With a clinical attachment level criterion (≥ 3 mm) the unadjusted OR was 1.13 and the adjusted OR 1.08 (0.94–1.24) [5]. A later meta-analysis of seven studies (192,815 participants) reported no overall association (OR 1.04; 95% CI 0.97–1.12; I^2 = 58%) [1]. These data suggest that shared metabolic factors, rather than periodontitis alone, explain much of the link.

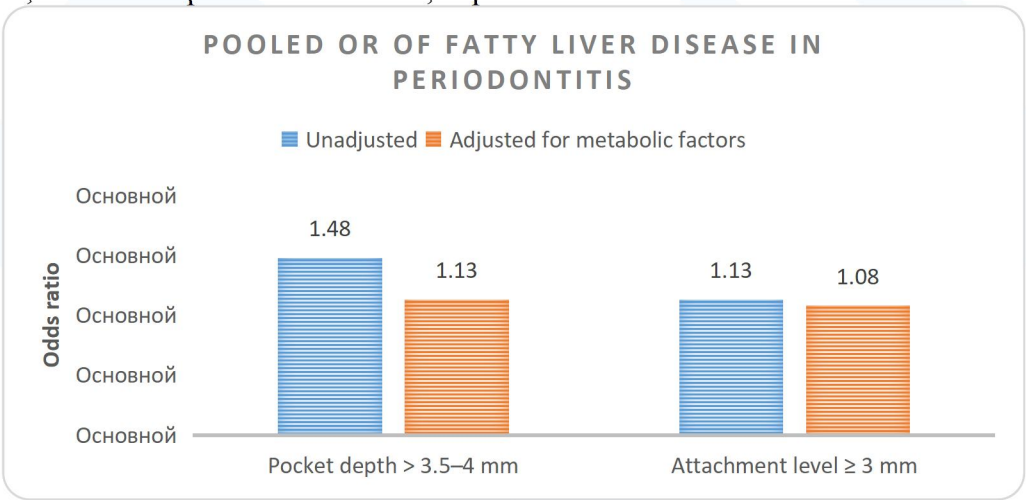


Fig. 1. Pooled odds ratios before and after adjustment (data from [5])

Immunological mechanisms. The oral–gut–liver axis links the two diseases. Porphyromonas gingivalis lipopolysaccharide (LPS) induces proinflammatory cytokines [4] and caused excessive hepatic lipid accumulation via NF-κB and JNK in experiments [9]. Swallowed pathobionts alter gut microbiota, downregulate tight-junction proteins and raise portal LPS, which activates TLR4 in

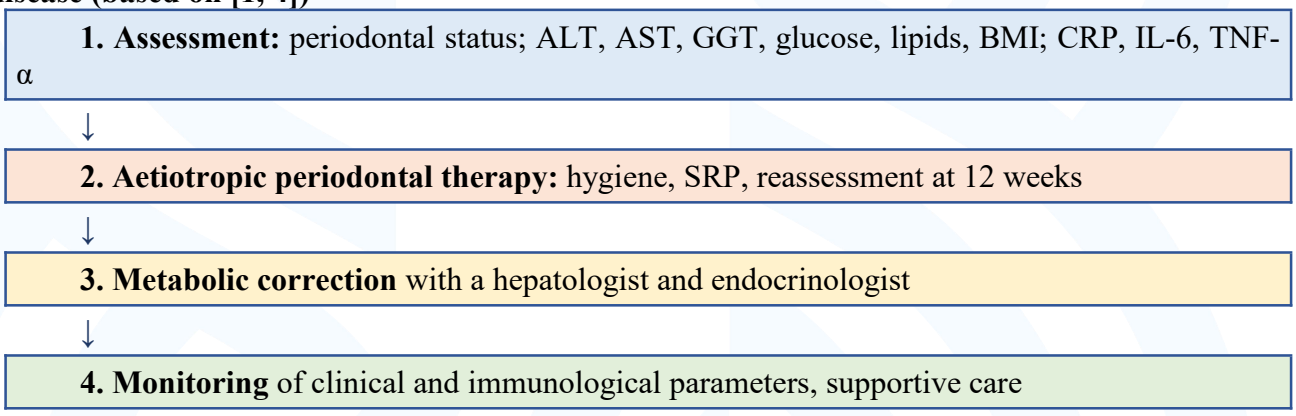
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Kupffer cells, hepatocytes and stellate cells, releasing IL-6, IL-1β and TNF-α [1, 10]. In periodontitis, CRP is higher than in controls [11], plasma IL-6, IL-1β and TNF-α are elevated [1], and the IL-23R^{+} Th17 subset is increased in blood [12], indicating a systemic immune skew that may amplify hepatic inflammation.

Effect of periodontal treatment. In the PERION RCT, 40 patients with NAFLD and periodontitis (ALT ≥ 40 U/L) were randomized to scaling and root planing (SRP, n = 20) or tooth-brushing instruction (n = 20) [4]. At 12 weeks ALT fell by 12 U/L in the SRP group and rose by 1 U/L in the control group (difference –12; 95% CI –20 to –5; p = 0.002); AST, GGT and MRI liver fat content (–2.2 vs +0.08%; p = 0.001), P. gingivalis IgG titres and endotoxin activity (p = 0.002) also decreased more with SRP (Table 2). The enzyme effect persisted to week 60, and no serious adverse events occurred [4]. Importantly, TNF-α, IL-6 and high-sensitivity CRP did not change significantly (p = 0.94, 0.51 and 0.11), so the benefit is more plausibly related to a lower bacterial and endotoxin burden than to changes in systemic cytokines.

Complex treatment model. The data justify a four-stage model (Fig. 2): (1) assessment of periodontal, hepatic, metabolic and inflammatory status; (2) aetiotropic periodontal therapy (oral hygiene, SRP) with reassessment at 12 weeks; (3) correction of metabolic factors together with a hepatologist and endocrinologist; (4) monitoring and supportive care. Only interventions with proven or generally accepted justification are included; drug therapy of fatty liver disease belongs to the hepatologist.

Fig. 2. Proposed model of complex management in chronic periodontitis with fatty liver disease (based on [1, 4])



Clinical assessment. In the PERION trial steatosis was diagnosed by B-mode ultrasound confirmed with elastography and MRI, while pocket depth and bleeding on probing were the periodontal parameters [4]. In practice, standard periodontal indices can be combined with liver enzymes (ALT, AST, GGT), glucose and lipid profiles and markers of inflammation, whereas in-depth liver assessment should be performed together with a hepatologist. Reassessment at 12 weeks corresponds to the time point at which the effect was demonstrated in the RCT [4].

Practical implications. First, periodontitis in a patient with fatty liver disease is a reason for obligatory periodontal care, because it may reduce liver enzymes and endotoxin burden [4]. Second, the effect of treatment should be judged not only by periodontal indices but also by liver parameters. Third, immunological data should be interpreted cautiously: systemic cytokines and CRP did not change in the RCT, so local or later changes in immune response may require other markers [4]. Fourth, the metabolic background, which best explains the association, must be managed in parallel [5].

Directions for research. Multicentre RCTs with larger samples and follow-up of at least one year using MASLD criteria are needed, together with an extended immunological assessment (Th17/Treg

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balance, antibody titres and bacterial load of P. gingivalis), stratification by degree of liver fibrosis, and interdisciplinary care models involving a dentist, hepatologist and endocrinologist [1].

Limitations. The benefit of SRP in fatty liver disease is shown in a single small open-label RCT without liver biopsy or a control group without periodontitis [4]; meta-analyses are heterogeneous (I^2 58–92%) [1, 5]; and most studies used the NAFLD rather than the MASLD definition [3]. The model requires validation in clinical studies.

Conclusions:

1. The link between periodontitis and fatty liver disease is explained largely by shared metabolic factors and the oral–gut–liver axis (P. gingivalis, LPS, TLR4/NF-κB, IL-6, TNF-α, Th17 skew); epidemiologically it weakens after metabolic adjustment.
2. Periodontal therapy improves liver enzymes and reduces endotoxin burden but did not change systemic cytokines within 12 weeks.
3. A complex approach combining periodontal therapy, metabolic correction and clinical–immunological monitoring is justified; larger RCTs are required.

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