Do adjunctive statins improve periodontal treatment outcomes in patients with chronic periodontitis?

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A Commentary on

Muniz FWMG, Taminski K, Cavagni J, Celeste RK, Weidlich P, Rösing CK.

The effect of statins on periodontal treatment-a systematic review with meta-analyses and meta-regression. *Clin Oral Investig* 2018; **22:** 671-687. doi: 10.1007/s00784-018-2354-9. Epub 2018 Feb 2. Review. PubMed PMID: 29396642.

Practice point

- A small benefit was suggested with the adjunctive use of statins, however the available evidence is of low quality and should be interpreted cautiously

Abstract

Data sources Medline-PubMed, Scopus and Embase databases.

Study selection Controlled clinical trials studies with at least one month follow-up that utilised locally or systemically delivered statins as a sole adjunctive treatment to mechanical periodontal therapy in patients diagnosed with chronic or aggressive periodontitis were included. Selection was carried out independently by two reviewers.

Data extraction and synthesis Data were extracted to a spreadsheet with authors being contacted for missing data. Risk of bias for randomised controlled trials was assessed using the Cochrane tool with the ROBINS-I tool being used for non-randomised studies. Weighted mean differences between baseline and six months after periodontal treatment for clinical attachment level (CAL), probing pocket depth (PPD) and intrabony defect (IBD) were calculated.

Results Fifteen studies were incorporated in the systematic review, with ten investigations included in the meta-analysis. In the meta-regression, the additional use of simvastatin, rosuvastatin and atorvastatin decreased pocket depth in contrast with mechanical periodontal treatment and a placebo gel ($p < 0.05$). Simvastatin and rosuvastatin significantly reduced the development of intrabony defect in contrast with control group ($p < 0.05$). Statins failed to provide a statistically significant difference between the adjunct therapy for both periodontal pocket depth and intrabony defect ($p < 0.05$). Simvastatin provided a statistically significant improvement in clinical attachment level gain, as compared to the control group (2.02 ± 0.79 mm; $p = 0.043$).

Conclusions Improvements in periodontal parameters were observed with the use of statins as adjunct to mechanical periodontal therapy. Simvastatin was the main medication that demonstrated additional advantages in all assessed parameters. The use of statins in relationship with non-surgical scaling and root planing provided better clinical periodontal outcomes.

Commentary

Statins are hyperlipidemia medications, which have antioxidant and anti-inflammatory properties. These latter properties may control inflammatory mediators and increase bone production. This systematic review was undertaken to assess the effects of statins on periodontal treatment.

The reviewers focused on understanding how effective statins are when used as an adjunct to mechanical periodontal treatment, in comparison to the same treatment without statins or with adjunctive use of placebo medication, in patients with aggressive or chronic periodontitis. The outcomes to be measured were defined as probing pocket depth, clinical attachment level and intrabony defect alterations six months after treatment.

The study is a systematic review of papers utilising meta-analyses and meta-regression. The number of papers in the review, and their inclusion and exclusion criteria were well addressed. The authors included studies of all languages and publication dates. Clinical trials of at least one month were included. Relevant important studies were included using a precise methodology. The quality of the included studies was assessed carefully using a risk of bias tool. There were two reviewers working, and if they did not agree, a third author was used to resolve any disagreement on the eligibility of the included studies. At the point when essential information was missing in the original reports a contact with the authors was made twice by email, with no response. The review excluded any observational or experimental studies, case reports, letters and reviews. The authors excluded studies that have not performed any mechanical periodontal therapy or studies that used statins with other concomitant medication.

Limitations of the included studies were also well described including their clinical relevance. In spite of the effort expended there are several shortcomings that are important to note. For instance, in the studies analysed, three clinical trials were included that were not randomised. Within the overall combined patient groups there were patients with hyperlipidemia and diabetes, and smokers. Diabetes is a systemic contributing factor for periodontal disease Alotaibi *et al.* showed that there was an increased risk of tooth loss associated with diabetes ($p=0.01$).[1] Smoking is a periodontology risk factor. Cutler *et al.* showed a significant association between periodontitis and hyperlipidemia, in relation to the triglycerides and total cholesterol levels.[2,3] As these factors are all confounding variables, the reviewers should have discussed these and accounted for them.

Unfortunately, nine out of fifteen studies were from the same research group, which reduced the original number of valid original

GRADE rating 

studies. Moreover, there was a difference in the follow-up periods and similarly in the number of sites for treatment application.

The review authors failed to report relevant details of how the medication was used. For instance at times it was not mentioned how deep were the pockets selected for treatment with the medication, what were the sites selected for medication application, and how many times the medication was administered, what dose at each specific site and/or how much reduction was achieved at those sites.

There was a range of doses used across the reviewed studies, ranging from 1.2% to 2% concentration in the form of: simvastatin, atorvastatin, rosuvastatin. The different concentration and different route of administration may have added to study heterogeneity.

More information on the participant characteristics could have been provided if available. These participant characteristics include gender, culture, ethnicity and age. Gender is a significant factor to consider, as for instance Shiau *et al*. concluded that men appear at greater risk for destructive periodontal disease than women;[4] the lack of this detail makes it difficult to apply the result of the study to a local population. Culture and ethnicity: information on country eg Mexico, Turkey, India, Chile was provided within the tables, but not ethnic groups. The cultural or ethnic differences may result in variability that make interpretation of the results challenging due to possible differences in the prevalence of periodontal disease among these different groups. Age: even though information was provided on age, it was not sufficiently detailed to draw strong conclusions of the relationship between intervention use and its outcome in specific age groups. Severity and extent of disease: other details that were not discussed are the severity of disease (mild moderate or severe), and its extent, localised or generalised. Furthermore, the diagnostic criteria by which chronic and aggressive cases were diagnosed were not defined. The authors also did not elaborate on local factors such as number of teeth. Blinding: there was no discussion as to whether the studies included blinding or allocation concealment. The researchers did not outline all the side effects of local statins although they mentioned adverse effects related to muscle loss and rhabdomyolysis. There was also no discussion of the cost-effectiveness of this use of statins.

Overall the current study provides low quality of evidence due to the high heterogeneity of the studies which were meta-analysed. Authors should be careful to perform meta-analysis on similar studies to avoid these concerns.

References

1. Alotaibi A, Modesto A, Vieira AR. Non-surgical periodontal therapy impact on progression of chronic periodontitis and prevention of further tooth loss. *J Oral Med* 2018; Vol.2 No.1: 3
2. Cutler CW, Shinedling EA, Nunn M, *et al.* Association between periodontitis and hyperlipidemia: cause or effect? *J Periodontol* 1999; **70:** 1429-1434.
3. Machado ACP, Quirino MR de S, Nascimento LFC. Relation between chronic periodontal disease and plasmatic levels of triglycerides, total cholesterol and fractions. *Braz Oral Res* 2005; **19:** 284-289.
4. Shiau HJ, Reynolds MA. Sex differences in destructive periodontal disease: a systematic review. *J Periodontol* 2010; **81:** 1379-1389.

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