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**study**

# Clinical benefits of systemic antibiotics may depend on periodontitis stage and grade

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## Background

The EFP S3-level clinical practice guideline for treating stages I to III periodontitis highlights the importance of weighing the benefits and possible adverse effects before prescribing systemic antibiotics adjunctive to subgingival instrumentation. The guideline concludes that adjunctive systemic antibiotics may be considered in specific cases, such as stage III and IV generalised periodontitis in young adults.

Previous studies that have explored diagnostic criteria as a decision-making strategy for prescribing adjunctive systemic antibiotics were based on the 1999 Classification of Periodontal Disease and Conditions. Bearing this in mind, this exploratory analysis of a large multicentre trial aims to explore whether the staging, extent, and grading of periodontitis under the current (2018) classification may influence treatment outcomes when prescribing systemic antibiotics adjunctively to subgingival instrumentation.

The authors hypothesised that generalised periodontitis stage III and IV in combination with grade C would receive greater benefits from the adjunctive use of metronidazole and amoxicillin.

If clinically relevant benefits of adjunctive systemic antibiotics can be associated with a particular diagnosis of periodontitis in accordance to the 2018 Classification of Periodontal and Peri-implant Diseases and Conditions, this could aid clinicians in deciding on the need for prescribing adjunctive systemic antibiotics based on the periodontal diagnosis.

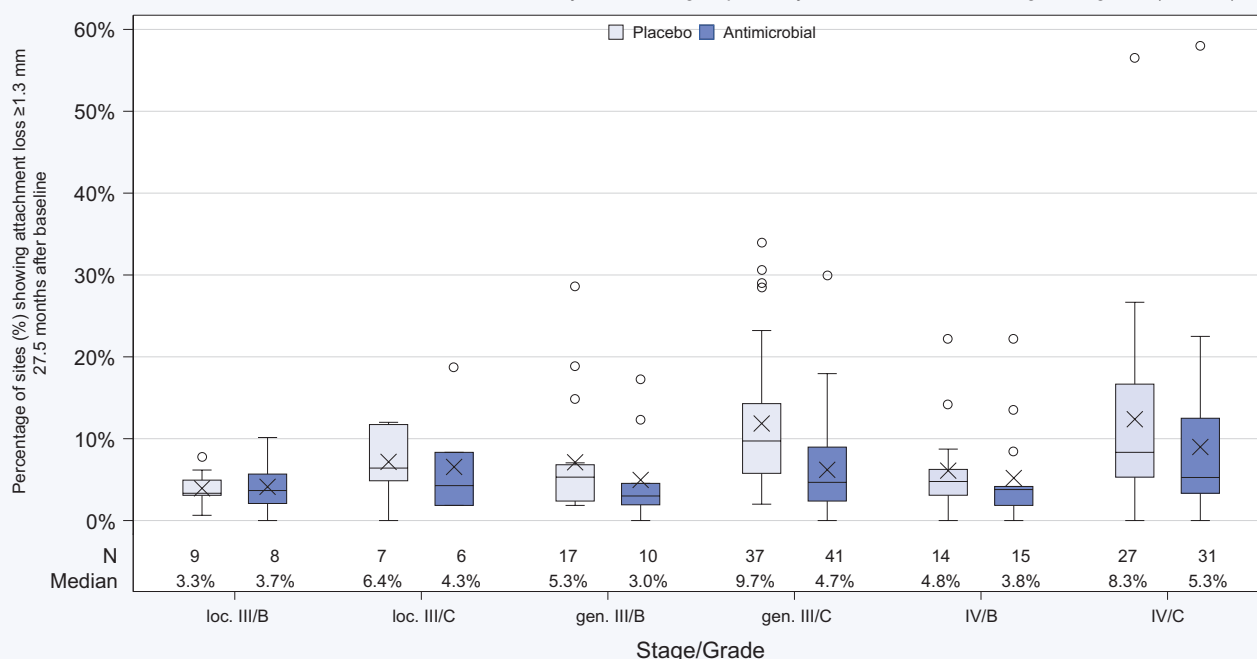
## Aim

This study aims to explore whether the staging, extent, and grading of periodontitis may influence treatment outcomes when prescribing systemic antibiotics adjunctively to subgingival instrumentation.

## Materials & methods

- An exploratory re-analysis was carried out of the ABPARO trial, a 27.5-month prospective, randomised, stratified, double-blind, multicentre trial that included 18- to 75-year-old patients diagnosed with severe chronic and aggressive periodontitis.
- Block randomisation, stratified in four strata based on periodontitis severity and smoking status, was carried out to assign patients in each centre in a 1:1 ratio to the antimicrobial treatment group (ANTI) or the placebo group (PLAC).
- At baseline (randomisation visit), smoking status was self-reported, and non-fasting blood samples were taken for the determination of HbA1c levels. Relative attachment-level measurements using the Florida Probe system were performed by blinded and calibrated examiners at six sites for each tooth. Other measurements included probing pocket depth (PPD), attachment level, bleeding on probing, and furcation involvement.
- After receiving supra and subgingival instrumentation (SI), systemic amoxicillin 500mg and metronidazole 400mg, three times daily for seven days, were prescribed to the ANTI group, while placebo pills were given to the PLAC group.
- Re-evaluation was carried out at least two months after debridement and all patients received their maintenance therapy at three-month intervals.
- Reclassification according to the 2018 classification of periodontitis was done by one calibrated author, using data obtained at baseline or  $\leq 12$  months earlier. The primary criterion for grade assignment was the indirect evidence of bone loss/age index using the most affected tooth, with smoking and diabetes status also considered.
- Treatment effect was evaluated by the per-patient percentage of sites with new clinical attachment loss (PSAL)  $\geq 1.3$ mm comparing baseline measurement/randomisation and 27.5 months as the main outcome.

**Figure:** Boxplots of the percentage of sites per patient showing new relative attachment loss  $\geq 1.3$  mm between baseline/randomization and 27.5-month visit by treatment group and by the combination of stage and grade (n = 222)



**Note:** The box represents the interquartile range (IQR), with the median indicated by a horizontal line inside the box. The whiskers extend to the most extreme data points within 1.5 times the IQR. Outliers, defined as data points beyond 1.5 times the IQR, are plotted as individual points. Marker X refers to the mean. The median and number (N) of each subgroup are reported below the boxplots.

## Results

- Patients with generalised stage III and IV periodontitis, when prescribed with adjunctive antibiotics, showed significantly lower PSAL  $\geq 1.3$  mm, when compared to the placebo group.
- These patients also showed greatest benefit from the use of systemic antibiotics in reduction of both mean PPD and percentage of sites with PPD  $\geq 5$  mm.
- Grade C periodontitis patients in the treatment group had lower PSAL  $\geq 1.3$  mm at 27.5 months, compared to those in the placebo group
- For patients with generalised periodontitis stage III and Grade C, the use of adjunctive systemic antibiotics led to a clinical benefit of lower incidence of new additional clinical attachment loss after 27.5 months ( $< 50\%$ ).
- Patients with localised periodontitis stage III did not receive any clinically significant benefit from the use of systemic antibiotics in reduction of either PPD or PSAL  $\geq 1.3$  mm after 27.5 months, compared to mechanical debridement alone.
- The use of systemic antibiotics did not result in significant difference for patients with grade B periodontitis in terms of PSAL  $\geq 1.3$  mm at 27.5 months after SI.
- Patients with generalised periodontitis stage III or IV and grade C showed significantly higher frequencies of achieving a 'treat-to-target' endpoint ( $\leq 4$  sites with PD  $\geq 5$  mm) when prescribed adjunctive systemic antibiotics.

## Limitations

- Not all the patients were given with a diagnosis under the 2018 classification.
- Radiographs were not available for all patients, therefore grading could not be assigned to all participants.
- The statistical analysis is of low power because of the small sample size in each diagnosis subgroup.
- It was presumed that all tooth loss resulted from periodontal reasons, which may lead to misclassification for the staging.
- Daily cigarette-pack intake was used in this study for the smoking assessment of grading, instead of the daily number of cigarettes intake used in the 2018 classification.
- HbA1c was only used to determine grading for patients with self-reported diabetes, which could exclude possible undiagnosed diabetic patients.

## Conclusions & impact

- Within the limitations of this study, a greater clinical benefit of less additional clinical attachment loss from systemic amoxicillin/metronidazole adjunctive to subgingival instrumentation can be achieved for patients diagnosed with generalised stage III, grade C periodontitis.
- Clinicians may refer to the identified diagnosis as one of the decision factors when considering whether to prescribe adjunctive systemic antibiotics.
- Future randomised controlled trials should be designed by incorporating the 2018 Classification of Periodontal and Peri-implant Diseases and Conditions from the start of the study.



JCP Digest 117 is a summary of "Clinical benefits of systemic amoxicillin/metronidazole may depend on periodontitis stage and grade: An exploratory sub-analysis of the ABPARO trial". *J Clin Periodontol.* 2023; 50(9):1239-1252. DOI: 10.1111/jcp.13838



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