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study

Optimal dose and duration of amoxicillin-plus-metronidazole as an adjunct to non-surgical periodontal therapy: A systematic review and meta-analysis of randomised, placebo-controlled trials

Kelly McGowan, Troy McGowan, and Saso Ivanovski
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RELEVANT BACKGROUND

The discovery of antibiotics in the 1940s was a fundamental turning point in medicine, but their subsequent misuse and overuse have resulted in critical levels of antibiotic resistance.

There is reasonable evidence to suggest that the use of systemic antibiotics in the treatment of periodontitis as an adjunct to non-surgical therapy (NST) may provide modest improvements in clinical attachment gain and that this benefit is greater in deeper pockets and in patients suffering from severe (aggressive) forms of periodontitis.

The use of amoxicillin-plus-metronidazole features prominently in the literature and it has been reported that these two agents in combination can provide a synergistic activity against periodontal pathogens, Gram-negative anaerobes in particular.

AIMS

This review aims to determine the optimal dose and duration of amoxicillin-plus-metronidazole, when prescribed as an adjunct to non-surgical periodontal therapy.

MATERIALS AND METHODS

This systematic review and meta-analysis is reported in accordance with the PRISMA guidelines.

The review was conducted to answer the following question: "Does the dose or duration of amoxicillin-plus-metronidazole prescribed as an adjunct to non-surgical periodontal therapy have an effect on probing depths or clinical attachment levels at three months post-treatment in periodontitis patients?"

Participants: Adult patients (≥18 years old) with clinically diagnosed periodontal disease were eligible for inclusion.

Intervention: Trials comparing the benefit obtained from adjunctive amoxicillin-plus-metronidazole in NST (debridement and/or root planning) were selected. Studies that included surgical periodontal therapy or any other type of antibiotic therapy were excluded.

Outcomes: The primary outcome measures were periodontal pocket depth (PPD) and clinical attachment loss (CAL) at three months after completion of NST. Secondary outcome measures were adverse events and compliance.

An electronic search of Embase and MEDLINE databases was conducted on 23 April 2017. The Cochrane Central Register of Controlled Trials and the WHO International Clinical Trials Registry Platform were also searched for relevant clinical trials.

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results

15 studies were included in the meta-analysis.

Dosage:

- Because of variability, it was necessary to group the lower doses (250/200mg, 375/250mg, 375/500mg, or 500/250mg of amoxicillin and metronidazole, respectively) and higher doses (500/400mg or 500/500mg of amoxicillin and metronidazole, respectively).
- It was found that the lower-dose group showed a marginally greater effect on mean CAL, while results for PPD were comparable to the higher dose.

Duration:

- Variability limited the analysis to seven versus 14 days.
- This analysis showed that the seven- and 14-day groups reported the same mean CAL and very similar mean PDD.
- Three- and 10-day duration treatments were not included the meta-analysis, but were found to have a similar effect on PPD and CAL.

Additional meta-regression analyses:

- PPD: dose, duration, diagnosis, and timing did not have a significant relationship with mean PPD at three months.
- CAL: dose, duration, diagnosis, and timing also did not show a significant relationship with mean CAL at three months.

Adverse-event data:

- Neither dose nor duration were found to be significant.
- When calculated for all studies, there was a risk difference of 0.17, indicating a higher incidence of events in the antibiotic groups. When comparing doses and duration of antibiotics, there was a slightly higher rate of adverse events in the higher dose and longer duration groups.

LIMITATIONS

- Study variability necessitated the grouping of doses into lower and higher groups, rendering the dose-specific analysis less accurate.
- Study variability allowed comparison only between the seven- and the 14-day duration, relinquishing the three-day duration because of a lack of data.
- Inter-study variability in the definition of chronic periodontitis.
- Inter-study variability in treatment methods and post-treatment regimen.
- Three-month follow-up only.

CONCLUSIONS

- Longer (14-day) courses of antibiotics do not appear to provide any additional benefit with respect to CAL and PPD after three months.
- No clinically significant difference was found between the lower- and higher-dose groups with respect to CAL or PPD reduction.
- No decisive evidence was found to suggest that one regimen was superior to the others.
- Clinicians must take into consideration the risks of adverse events, non-compliance, and patterns of antibiotic resistance when prescribing antibiotics.
- The findings presented in this review are based mostly on the results of 15 studies that included a relatively small numbers of participants. Further research evaluating the treatment protocol and long-term effect is also needed to determine whether the clinical benefit of adjunctive systemic antibiotics is transient or long-lasting compared to placebo control.

IMPACT

- Different doses or duration of amoxicillin-plus-metronidazole have the same clinical periodontal effect three months post-treatment.
- Dentists and periodontists should take into consideration the risk of antibiotic resistance when prescribing antibiotics.

LINK TO ORIGINAL JCP ARTICLE:

https://www.onlinelibrary.wiley.com/doi/abs/10.1111/jcpe.12830
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