Which is the best antibiotic prophylaxis protocol to prevent early implant failures?

Iman Abd-Elwahab Radi[1] and Ahmed Hassaan[2]

A commentary on

Romandini M, Tullio I D, Congedi F et al.

Antibiotic prophylaxis at dental implant placement: which is the best protocol? A systematic review and network meta-analysis. *J Clin Periodontol* 2019; **46:** 382395. DOI: 10.1111/jcpe.130.

Practice point

For implant patients who are systemically well, and not allergic to antibiotics, the most beneficial antibiotic protocol is 3g of amoxicillin administered one hour prior to the surgical procedure.

Abstract

Selection criteria The inclusion criteria of this systematic review were patients undergoing dental implant placement. Only randomised clinical trials (RCTs) that compared placebo, no antibiotic and/or any type of antibiotics, administered pre-operatively, intra-operatively, post-operatively or combinations of these, at any dose and for any duration were considered eligible. Included RCTs were required to have a follow up period of at least three months with at least 20 patients per treatment arm. No restrictions on date of publication or language were applied.

Key study factor Four electronic databases (MEDLINE, SCOPUS, CENTRAL and Web of Knowledge) in addition to six related journals (*Journal of Clinical Periodontology, Clinical Oral Implants Research, Clinical Implant Dentistry and Related Research, Journal of Periodontology, European Journal of Oral Implantology, International Journal of Oral & Maxillofacial Implants*) were searched in duplicate for RCTs up to July 2017. Additional relevant literature was identified through hand-searching of reference lists, and through grey literature databases. Two independent reviewers screened the titles and abstracts . Data extraction and risk of bias assessment was performed simultaneously by two reviewers independently and in duplicate using the Cochrane tool for risk of bias assessment. A Network Meta-analysis (NMA) was conducted by integrating direct and indirect comparisons and the probability that each protocol was optimal was estimated. Subgroup and sensitivity analyses were planned to test the effect of risk of bias and of different variables on the results, but were not conducted due to the limited number of included studies.

Main outcome measure Outcomes analysed were adverse events and early implant failures, defined as removal of mobile or stable implants with progressive marginal bone loss or infection in the first year after placement.

Main results A total of 2248 RCTs were identified after removing duplicates, nine of which were finally included. Different protocols of antibiotic prophylaxis were compared with a total number of 1,693 participants. Seven of the included trials compared the use of one or more protocols of antibiotic prophylaxis with no prophylaxis or prophylaxis with a placebo, and two trials compared the use of different protocols, without the use of a no prophylaxis/placebo group. Amoxicillin was the only type used in all studies. Doses and timing varied among studies, although most of them used a single dose taken just before the implant placement. For the investigated outcomes, two trials were considered at low risk of bias and seven at high risk of bias.

All protocols were more effective in reducing implant failures compared to placebo/no antibiotic (mean OR 0.08 to 0.45). Meta-analysis of direct comparison was only possible for the four trials comparing 2 g amoxicillin one hour preoperatively (B) to no antibiotic or placebo (A), indicating B as more effective (pulled OR = 0.40; 95% CI: 0.19–0.88; heterogeneity chi-squared 1.40, P = 0.706). These results were consistent with NMA effect estimates (mean OR = 0.45; 95% CI: 0.0210.93). A single dose of 3 g of amoxicillin administered one hour pre-operatively (C) was statistically more effective in reducing implant failures if compared to no prophylaxis/placebo (OR = 0.41, 95% CI = 0.180.91) and was considered as the most effective protocol. The single dose of 2 g of amoxicillin administered one hour pre-operatively was less effective than protocol C. Adverse events could not be studied in a meta-analysis due to an insufficient number of trials reporting it.

Conlusions Implant patients are likely to benefit from antibiotis being administered one hour preoperatively in a dose of 3 g orally. The use of post-operative antibiotics does not seem, however, to be justified.

GRADE rating

Commentary and analysis

Efficacy of antibiotic prophylaxis for implant placement in reducing implant failure has been demonstrated by a Cochrane systematic review published in 2013.[1] It was claimed that antibiotic prophylaxis reduced the risk of implant failure by 67%. However, their use in systemically healthy patients, requiring straightforward implant surgeries, has been prohibited to decrease the risk of enhancing antibiotic resistant strains of bacteria. This decision was based on the 2015 consensus conference of the EAO.[2] Considering that the risk of antimicrobial resistance increases with longer regimens, it would be particularly important to determine, if shorter protocols are sufficient to prevent early implant failures, or if longer courses are preferred.[3] This systematic review aimed

to explore which dose, timing and type of antibiotic prophylaxis should be used at time of implant placement using network meta-analysis. The latter allows for direct and indirect comparisons among the different regimens. The quality of the review is very good, however, it might be at some risk of bias. It appears that the authors of the review were very thorough in finding RCTs covering the topic. Two authors worked in duplicate, searching four electronic databases, in addition to hand-searching of relevant journals, reference lists and grey literature with no restrictions on language or date of publication. They provided a detailed search strategy for all databases. However, they restricted the included RCTs to those treating ≥20 participants and those with a minimum of three month follow up period post-implant placement without justifications. The restrictions seem to be unnecessary, since early implant failure might happen before three months following implant placement. Besides, when intending to pool data in a meta-analysis, the number of participants included in each trial does not seem to be important, because the meta-analysis per se aims to increase the sample size, thereby decreasing the possibility of β error. The unnecessary restriction might place the review at a risk of selection bias. The review suggests that adverse events were insufficiently investigated or reported in the primary studies. Assessment of risk of bias seems to have been satisfactorily performed, since it was carried out by two reviewers independently within and across the studies at the outcome. Unfortunately, the review is based on seven RCTs which were of high risk of bias and only two which were of low risk of bias. Most of the included RCTs were underpowered or did not report a sample size calculation. The statistical methods used were appropriate. However, the network meta-analysis, which allowed for 18 indirect and ten direct pairwise comparisons, increased the heterogeneity and hence widened the confidence interval, thereby decreasing the precision and the reliability of the results. The risk of publication bias was not assessed in the review. This might be related to the insufficient number of RCTs involved in the direct comparisons. This should have been clarified in the review.

Accordingly, dose and duration of antibiotic prophylaxis are still debatable, however, the reviewers recommend a single dose of 3 g oral amoxicillin administered one hour before implant surgery but they do so with caution. Antibiotic cover is especially important, where a complex surgical procedure is expected, although the systemic condition of the patient should be considered along with whether he is allergic to penicillin or not.

Further RCTs with a calculated sample size, a follow up period not less than one year and a direct comparison among the different protocols, especially in complex cases as immediate implants, are still required. Besides, the added benefit of clavulanic acid in amoxicillin needs to be verified.

References

1. Esposito M, Grusovin M G, Worthington H V. Interventions for replacing missing teeth: Antibiotics at dental implant placement to prevent complications. *Cochrane Database Syst Rev* 2013; CD004152: DOI: 10.1002/14651858.CD004152.pub4.
2. Klinge B, Flemming T, Cosyn J *et al.* The patient undergoing implant therapy. Summary and consensus statements. The 4th eao consensus conference 2015. *Clin Oral Implants Res* 2015; **26 Suppl 11:** 64–67.
3. Harbarth S, Samore M H, Lichtenberg D, Carmeli Y. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 2000; **101:** 2916–2921.

Author affiliations

[1]Professor of Prosthodontics and Member of the Evidence Based Dentistry Centre, Faculty of Dentistry, Cairo University
email: iman.abdelwahab@dentistry.cu.edu.eg
[2]PhD candidate and Assistant Lecturer of Prosthodontics, Faculty of Dentistry, ElFayyoum University, Egypt

Evidence-Based Dentistry (2019) **20**, 105-106.
https://doi.org/10.1038/s41432-019-0056-z