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study

Antibiotic prophylaxis when placing dental implants: What is the best protocol?

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Background

A Cochrane systematic review of randomised controlled trials (RCTs) highlighted the efficacy of prophylactic antibiotics in reducing early implant failures at dental-implant placement. Nonetheless, the 2015 consensus conference of the European Association for Osseointegration (EAO) stated that antibiotic prophylaxis should not be recommended in "straightforward" implant surgery in systemically healthy patients because of the possible adverse reactions and side effects, and the public-health threat from antibiotic resistance,

In cases where an antibiotic prophylaxis at implant placement is needed, it is still not clear which type of antibiotic, which dose, and which regimen are to be preferred.

A new type of meta-analysis named "network meta-analysis" (NMA) has recently been introduced into the dental literature. Compared to conventional meta-analysis ("pairwise meta-analysis"), NMA allows both direct comparison between more than two simultaneous interventions and indirect comparisons among interventions even when direct comparison studies have not been conducted. These two advantages are particularly relevant in the scientific context of antibiotic prophylaxis at implant placement, which is characterised by numerous proposed protocols (versus placebo/no antibiotic) but with few direct comparisons between them.

Aim

The primary aim of this systematic review with NMA of RCTs was to answer the following question: In patients undergoing dental-implant placement, what is the best antibiotic prophylaxis protocol to prevent early failures?

Materials & methods

The MEDLINE, SCOPUS, CENTRAL, and Web of Knowledge electronic databases were searched in duplicate for RCTs testing antibiotic prophylaxis protocols up to July 2017. Additional relevant literature was identified through (i) handsearching in relevant journals and reference lists, and (ii) database searching for "grey literature".

The titles and abstracts of all identified reports were screened independently by two authors. For studies that appeared to meet the inclusion criteria, or for which there were insufficient data in the title and the abstract to make a clear decision, the full report was obtained.

The selected full reports were assessed independently by two authors to establish whether the studies met the inclusion criteria. All studies meeting the inclusion criteria were then included in the systematic review and underwent duplicate data extraction and risk-of-bias assessment.

Any disagreement was discussed between the two authors and a third author was consulted if resolution was not possible.

In the presence of at least two studies with a direct comparison, a pairwise frequentist meta-analysis was concucted.

An NMA was also conducted in a frequentist framework, and the probability that each protocol was the "best" was estimated.

Figure

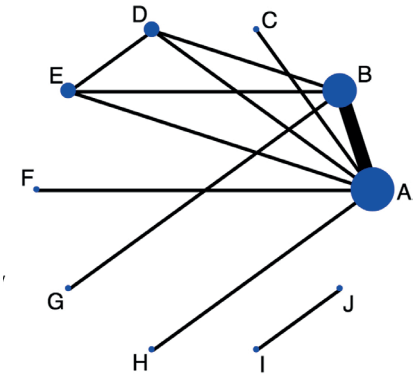
(a) List of antibiotic prophylaxis protocols found.

(b) Network diagram: network of the protocols in relation to early implant failures as outcome (protocols I and J were not connected to the network).

(a)

Protocol A1	No antibiotics;
Protocol A2	Placebo;
Protocol B	Amoxicilin 2g per os, 1 hr pre-operatively;
Protocol C	Amoxicilin 3g per os, 1 hr pre-operatively;
Protocol D	Amoxicilin 2g per os, 1 hr pre-operatively + 1g twice a day, for 7 days post-operatively;
Protocol E	Amoxicilin 1g per os, for 7 days post-operatively;
Protocol F	Amoxicilin 1g per os, 1 hr pre-operatively + 500mg four times per day, for 2 days post-operatively;
Protocol G	Amoxicilin 2g per os, 1 hr pre-operatively + 1g in the evening of the day of surgery + 1g twice a day, for 2 days post-operatively;
Protocol H	Amoxicilin 500mg per os started just after the surgery and continued every 8hr, for 7 days post-operatively (up to finish 21 capsules);
Protocol I	Amoxicilin 1g per os, 1 hr pre-operatively;
Protocol J	Amoxicilin 1g per os, 1 hr pre-operatively + 500mg three times per day post-operatively started 8hr after the pre-operative lose.

(b)



Results

- Nine RCTs (one from grey literature) were included, with a total of 1,693 participants.
- The antibiotic type used in all the trials, at different doses and timing, was amoxicillin alone (without clavulanic acid); there were no trials using alternative antibiotics.
- The implant failure rate was 5.6% in patients not receiving antibiotics and 1.8% in those receiving them. When a meta-analysis of direct comparisons was carried out, the use of antibiotic prophylaxis was protective in terms of implant loss (Odds Ratio = 0.28, 95% Confidence Interval: 0.14-0.55).
- Extremely few adverse events in people using antibiotics were reported: only four out of 947 patients receiving antibiotics, and three of these were related to prolonged courses.
- For both the outcomes considered, two trials had to be considered at low risk of bias and seven at high risk of bias.
- Because of the few events reported, it was not possible to conduct an NMA for adverse events; therefore, it was conducted only for implant failures (IF). The protocol with the highest probability (32.5%) of being the "best" one to prevent IF was the single dose of 3g of amoxicillin administered one hour pre-operatively. Although the single pre-operative dose of 2g of amoxicillin is the protocol most often used, it achieved only a probability of 0.2% of being the "best" one.

Limitations

Limitations of the primary studies:
- Only nine RCTs available (all underpowered, and seven at high risk of bias).
- The only antibiotic type tested was amoxicillin without clavulanic acid.
- Poor reporting of adverse events.

At the "systematic review" level, no important limitations could be observed.

Network meta-analysis limitations:
- It was not possible to carry out an NMA for adverse events because of the limited number of events.
- Large confidence intervals.
- The protocol with the highest probability of being the best one (single pre-operative dose of 3g of amoxicillin) was tested only in a single high-risk RCT with an unusually high implant failure rate in the control group.

Conclusions & impact

- All the proposed protocols tend to reduce early implant failures.
- The most frequent protocol (single pre-operative dose of 2g of amoxicillin) does not seem to be indicated by the available literature.
- The use of post-operative antibiotics does not seem to be justified, as prolonged courses were associated with a tendency towards more adverse events, but without an increased efficacy in reducing implant failures.
- While the use of antibiotic prophylaxis is protective against early implant failures, this is not enough to indicate its routine use in all clinical situations because of the risk of adverse reactions and bacterial resistance.
- When an antibiotic prophylaxis is needed, there is still insufficient evidence to confidently recommend a specific protocol.

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