Do surgical prophylactic antibiotics reduce postoperative infection and early dental implant failure?

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A critical appraisal of meta-analysis: Chrcanovic BR, Albrektsson T, Wennerberg A. (2014) Prophylactic antibiotic regimen and dental implant failure: a meta-analysis. Journal of Oral Rehabilitation. Published online 8 July 2014, doi: 10.10.1111/joor.12211

Summary

Systematic review conclusion: Prophylactic use of antibiotics significantly decreases the risk of implant failure by 45%. The number needed to treat to prevent one patient having an implant failure was 50 (95% CI 33-100), based on an implant failure rate of 6.32% in patients not receiving antibiotics. Prophylactic antibiotics had no apparent significant effect on the occurrence of postoperative infections in healthy patients receiving implants.

Critical appraisal conclusion: Overall the quality of the evidence was weak and contributed no new knowledge. The results of the review however, supports current scientific evidence that in general, prophylactic antibiotics are beneficial for reducing failure of dental implants placed in ordinary conditions.

Implications for clinical practice: 2 g of Amoxicillin given orally in a single dose, one hour pre-operatively before implant placement, in general, is beneficial for reducing failure of dental implants placed in ordinary conditions. The purpose of this regimen is to attain elevated levels of antibiotic in serum during, and for some hours after the surgical procedure. Good surgical technique performed together with good asepsis and sterile surgical procedures remain the cornerstone for minimizing infection and successful outcome of implant surgery.

Clinical question

Do prophylactic antibiotic regimens have any positive effect on implant failure rates and post-operative infection when performing dental implant treatment in healthy individuals compared to those not receiving prophylactic antibiotic treatment?

Review methods

Search strategy and study selection

Three independent investigators searched the following electronic databases: [MEDLINE-Pubmed, Web of Science, and the Cochrane Oral Health Group Trials Register in March 2014 to identify articles on the topic in the clinical question. They also conducted a manual search of most dental implant-related journals. Reference lists of identified studies and reviews were also screened for studies. Online clinical trial databases were also checked for information about clinical trials in progress. They used no time or language restrictions. Disagreements on inclusion of a study were resolved by discussion between the authors. The investigators recorded all studies that were rejected as well as the reason for exclusion. This systematic review methodology and subsequent meta-analysis followed the guidelines of PRISMA statement.[1]

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Eligibility and exclusion criteria

The reviewers searched for randomised or non-randomised clinical trials in any group of patients receiving versus not receiving antibiotic prophylaxis regimen for the placement of implants in human subjects and comparing implant failure/survival rates. Subjects receiving grafts were also eligible for inclusion in the study. Case reports, technical reports, animal studies and review papers were excluded.

Outcome measures and data extraction

All patients receiving antibiotics were considered for quantitative analysis in the group 'use of antibiotics'. Variation of antibiotic regiment by type of antibiotic, dosage, and time of administration was not taken into consideration in the data analysis. Implant failure and post-operative infection were the outcomes that were measured. They contacted the authors of the primary studies to gain information on missing data.

Data analysis

Meta-analysis was done on studies that presented with similar comparisons reporting the same outcomes. Data from the selected studies were combined to estimate the treatment effect size. The estimate of relative effect was expressed by risk ratio (RR) with 95% confidence intervals. Heterogeneity of effect across the studies was formally assessed with the Cochran *Q* test and characterized with the I^2 statistic to describe the proportion of total variation in the estimated effect sizes due to heterogeneity among studies. Random effects models were utilized throughout to estimate the effect size of implant failure rate and the fixed-effects model was used to assess post-operative infection outcomes of the pooled data. Risk of bias of the included RCT's was assessed according the Cochrane Collaboration risk of bias assessment tool.[2] Potential publication bias for the studies was assessed using the funnel plot approach. A sensitivity analysis was also conducted by excluding the studies with high risk of bias.

Main results

The search process yielded 14 studies eligible for qualitative analysis, (8 RCTs, four controlled clinical trials (CCT's), and two retrospective studies. Seven studies were judged a high risk of bias, one study at moderate risk, and six studies were considered low risk of bias. A statistically significant heterogeneity was found when assessing implant failure (p= 0.004; I^2 = 58%) but not when assessing post-operative infection (p= 0.690; I^2 = 0%).

A total of 8603 implants were placed in patients receiving antibiotics with 304 failures (failure rate of 3.53%) and 6269 implants were placed in patients not receiving antibiotics with 396 failures (failure rate of 6.32%). Only 8 articles provided information on post-operative infection. Twenty-five (25) occurrences of post-operative infection were observed in 1000 patients receiving antibiotics (2.5%) and 29 episodes of post-operative infection in 770 patients not receiving antibiotics (3.8%).

The pooled data showed that use of antibiotics significantly affected the implant failure rates. A RR of 0.55 (95% CI 0.41 – 0.75) (p = 0.0002) for prophylactic use of antibiotics implies that implant failures in patients receiving prophylactic antibiotic treatment were 0.55 times likely to happen than implant failures in patients not receiving prophylactic antibiotic treatment. Excluding the studies with high risk of bias presented similar estimate of the overall treatment effect.

The meta-analysis showed that there were no apparent significant effects of prophylactic antibiotics on the occurrence of post-operative infections in health patients receiving implants (RR of 0.84, 95% CI 0.49 – 1.44; p = 0.52)

Conclusion

The authors concluded that the evidence suggests that a prophylactic antibiotic regimen significantly reduces failures of dental implants placed in ordinary conditions. They also concluded that there were no apparent significant effects of prophylactic antibiotics on the occurrence of post-operative infections in health patients receiving implants.

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Commentary

Background and importance

Fear of surgical site infection and the financial and legal repercussions of failure is generally the key motivation for the use of prophylactic antibiotics.[3] Preventing post-operative infection in implant related surgical sites are of great importance to both patient and clinician. The routine use of prophylactic antibiotics to prevent infection in implant dentistry is a controversial issue with conflicting evidence in the literature. Some studies have shown that antibiotic prophylaxis used prior to surgical placement of an implant can reduce the occurrence of post-operative infection, and increases the success rates of osseointegration.[4, 5] In comparison, other studies found no such effect.[6,7]

Making an incision and placing a dental implant causes a break in the tissue barrier, allowing invasion and contamination by microorganisms that can potentially lead to infection of the wound and risk of implant failure. Opening of the mucosa and hard tissues in the oral cavity is classified as a clean-contaminated wound and has a confirmed infection rate of 5-15%.[8] Factors that might be of great importance towards contributing to the risk of post-operative infection and early implant failures include the patients medical status, impaired healing ability, smoking, inadequate asepsis and sterile technique, poor surgical technique, degree of surgical trauma, and bacterial contamination during implant insertion.[9,10] Surgical trauma together with anatomical conditions are believed to be the most important etiological factor for early implant losses.[9]
The question of using prophylactic antibiotics to prevent post-operative infection is an important issue and a need exists to answer this question in order to improve the successful outcome of dental implants, whilst minimising biological complications, harms and adverse effects.

Are the results valid?

The studies included in this review had several basic limitations and weaknesses that affected the quality of the evidence presented. Firstly, the reviewers did not provide a precise statement of what range of patients and exposures they decided to include in the study. The review pooled results from a wide range of antibiotic regimens, for all types of patients (biologic and individual variation) and a variety of procedure and skill subsets to generate a single estimate of the effect of antibiotics on implant failure. From a biological perspective one would not expect the same treatment effect across the range of patients due to the wide range of target population risk variation (i.e. younger vs. older; smoking vs. non-smoking; healthy vs. sick) and variation in target bacteria present in individuals. Pooling of results across a wide range of type of antibiotics, dosages, timing and duration is also a concern. Therefore, it is reasonable to conclude that treatment effect is not likely to be similar across the range patients and exposures.

Based on this construct, the clinical question (or hypothesis in this case) may be too broad, to provide a valid estimate because there are many factors likely to lead to variation in treatment effect such as biologic and individual variation, differences in the intervention and different surgical and procedural skills.

Secondly, the investigators did not state whether their search included recently published abstracts presented at scientific meetings and databases held by pharmaceutical companies in their search strategy. Systematic reviews based on a number of small studies with limited total sample sizes are particularly susceptible to publication bias. The asymmetry observed by the funnel plots is indicative of potential publication bias.

Thirdly, eligibility of studies was not restricted to RCT's. Of the 14 trials included 8 were RCT's, 4 CCT's and 2 were retrospective studies. The less rigorous CCT and retrospective studies included in this review may tend to overestimate the effect of therapeutic and preventive interventions.[11]

Fourthly, two of the review authors decided whether potentially eligible trials met eligibility criteria, with disagreement resolved by consensus by third party adjudication. The reviewers reported no measures of agreement for either eligibility or quality rating decisions.

Overall, the methods of the systematic review and the methodological quality of the trials included in the systematic review were weak, thus resulting in poor quality of evidence.

What were the key findings?

Generally there was marked variability and inconsistencies between the studies included in the meta-analysis for all outcomes measured. This is likely due to differences in the sample population characteristics, interventions used, and outcome measurement.

For the outcome implant failure risk ratio (RR) point estimates were similar and confidence intervals overlapping supporting the reviewers decision to pool the results in a single estimate of effect (RR) = 0.55 95% CI [0.41, 0.75] p= 0.0002. However, the test for heterogeneity across studies was statistically significant (p= 0.004) and I^2 = 58%, thus representing substantial heterogeneity that raises serious concern about a single pooled estimate of effect. When studies judged as having a high risk of bias were excluded from the meta-analysis the trend still favoured use of antibiotics (P=0.003 statistically significant) RR = 0.37 95% CI [0.19, 0.72]; p =0.003. The test for heterogeneity in this subgroup of results was statistically non-significant (p = 0.38) and I^2 = 6%, thus representing minimal variability and therefore increasing our confidence in the overall estimate of the effect of favouring antibiotic use. However, using post hoc subgroup analysis also raises concerns in using these results.

For the outcome post-operative infection the point estimates for RR across studies showed no trend for either favouring use or non-use of antibiotics. Test for heterogeneity showed minimal variability (p= 0.66; I^2 = 0%), and therefore

increasing our confidence in the overall estimate of the effect of antibiotic use on post-operative infection. The estimate of the overall effect of antibiotic use or non-use on the outcome post-operative infection was statistically non-significant and clinically inconclusive RR = 0.84 95% CI [0.49, 1.44]; p= 0.52.

Irrespective of the limitations and weaknesses of review we can reasonably assume that in 95% of cases when an antibiotic is used the true effect of the RR = 0.55 95% CI [0.41, 0.75] for the outcome implant failure, will lie between the lower and upper level of the confidence interval as indicated.

The results of this review are in accordance with that reported in other meta-analysis on this question.[12, 13]

How are the results of this review applicability in clinical practice?

Post-operative complications and early implant failures are important patient outcomes because of health, inconvenience and cost implications thereof. As a general rule, antibiotic prophylaxis is always indicated when there is an important risk of infection, either because of the characteristics of the surgical procedure (i.e. type and duration of surgery), because of the patient's local or systemic infection risk (i.e. diabetes, immunodeficiency's, inflammatory arthropathies), or for patients with post-bacteraemia focal infection risk factors (i.e. infectious endocarditis, infection of joint prostheses).

Do the benefits outweigh the potential harm and costs?

Scientific evidence suggests, specifically that 2g of Amoxicillin given orally in a single dose, one hour pre-operatively before implant placement, in general, is beneficial for reducing failure of dental implants placed in ordinary conditions.[12] The Cochrane Oral Health Group authors also reported that no significant adverse events were found with this prophylaxis regimen.

The benefit of antibiotic prophylaxis is the prevention of infectious and biological complications subsequent to implant surgical procedures; however, their indiscriminate use may result in emergence of resistant pathogens, increased cost, adverse reactions, and a false sense of security.

The most common adverse effects of antibiotics are direct toxicity, hypersensitivity, allergic- or anaphylactic reactions. The ill-advised use of antibiotics has proven to be expensive as well as directly responsible for development of resistant microorganisms. This risk of adverse effects is minimal if prophylactic antibiotics are initiated just prior to start of surgery and if use is restricted to less than 24 hours post-operatively.[14] this finding is endorsed by the study of the Cochrane Oral Health Group.[12]

The clinician's criterion for using antibiotic prophylaxis or not, must be based on the benefit and the cost of risk. The economic cost of short-term surgical antibiotic prophylaxis is acceptable when compared with the total cost of managing biological complications and implant re-treatment due to infection.

The aim of antibiotic prophylaxis in dental implant surgery is to prevent possible peri-operative or post-operative infection in the surgical wound as this could compromise the osseointegration process thus resulting in biological complication and early implant failure. This is primarily achieved by attaining elevated levels of antibiotic in the serum during the surgical process, and for some hours after the implant is placed and surgical wound is closed.

Risk of contamination of the surgical site increases with exposure time (duration) and complexity of the procedure (i.e. grafts), and is minimized with proper sterile surgical technique and when the patient is in a healthy condition.[9, 10] It is widely accepted that the benefits of providing surgical antibiotic prophylaxis is worth the potential risks thereof. Meticulous surgery and careful pre-operative and post-operative care is still the mainstay in minimizing wound infection and risk of post-operative complications.

Clinical Resolution

The clinical question addressed in this review is of great importance to the patient and the clinician. Overall the quality of the evidence was weak and contributed no new knowledge. The results however supports the scientific evidence that, "in general antibiotics are beneficial for reducing failure of dental implants placed in ordinary conditions". Implant related surgery will always have a risk of infection, and as a general rule, prophylaxis is always indicated when there is an important risk of infection, either because of the characteristics of the operation or because of the patient's local or systemic health situation. It is still unknown whether post-operative antibiotics are beneficial, and which antibiotic works best.[12] Double blind randomized control trials remain elusive in this regard due to the ethical implications of such studies. Regardless of use or non-use of antibiotic prophylaxis, asepsis and good surgical technique still remain cornerstones in the prevention of wound infection and early implant failure.

Disclosure

Dr Johan Hartshorne is trained in clinical epidemiology, biostatistics, research methodology and critical appraisal of research evidence. This critical appraisal is not intended to, and do not, express, imply or summarize standards of care, but rather provide a concise reference point for dentists to aid in understanding and applying research evidence from referenced early view or pre-published articles in top ranking scientific publications and to facilitate clinically sound decisions as guided by their clinical judgement and by patient needs.

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