Do viruses play a role in peri-implantitis?

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Critical Appraisal Commentary

Title/Question
Do viruses play a role in peri-implantitis?

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A Commentary on:
Akram Z, Al-Aali KA, Alrabiah M, Alonaizan FA, Abduljabbar T, AlAhmari F, Javed F, Vohra F. Current weight of evidence of viruses associated with peri-implantitis and peri-implant health: A systematic review and meta-analysis. Rev Med Virol. 2019 May;29(3): e2042. doi: 10.1002/rmv.2042. Epub 2019 Mar 22. PubMed PMID: 30901504.

Data Sources
A search of electronic databases (EMBASE, MEDLINE, Cochrane Oral Group Trials Register and the Cochrane Central Register of Controlled Trials) along with a manual search of various Science Citation Indexed Journals.

Study Selection
Four cross-sectional studies and one case-control study were included where percentage levels of Herpes Simplex Virus Type 1 (HSV1), Epstein-Barr Virus (EBV) and Cytomegalovirus (CMV) were sampled for in both peri-implantitis affected and healthy implant sites, with the latter used as the control. Studies were excluded that investigated any other infective agent, had fewer than ten participants, was performed in vitro or involved subjects with only periodontal disease.

Data Extraction and Synthesis
Data extraction followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guideline process. Two examiners used the Newcastle Ottawa Scale to determine overall study quality while the key information was extracted and tabulated for comparison. The data was analysed using Chi-Squared test and I^2 test for heterogenicity with a random effects or fixed affect models applied as appropriate. Risk difference of outcomes was displayed via a forest plot with 95% confidence intervals. Funnel plots were generated to evaluate publication bias.

Results
All four cross-sectional studies found searched for EBV, while three also looked for CMV. The case-control study included investigated for HSV1 presence only. EBV presence in peri-implantitis sites was found to be statistically significant in three of the four studies despite obvious heterogeneity. CMV presence at peri-implantitis sites was statistically significant in all relevant studies, but the data displayed notable heterogeneity so as to render it insignificant. HSV1 exhibited similar percentage frequency in both healthy and diseased implant sites.

Conclusions
Virus prevalence was found to be increased in patients with peri-implantitis when compared to healthy sites but this assertion must be treated with caution as the data supporting it is weak due to the limited number of studies involved and the significant inherent heterogeneity they displayed.

Grade rating
Very Low

Commentary
Prevalence studies estimate 10% of dental implants placed will develop peri-implantitis and with over 12 million implants placed annually worldwide, this represents a huge potential disease burden (1). Understanding the pathogenesis of any disease is vital to develop accurate diagnostic classifications and effective treatment strategies. Our understanding of the aetiology of periodontal disease and peri-implantitis has evolved significantly, moving from viewing plaque bacteria as the sole concern, to appreciating it is a complex multi-factorial inflammatory interaction involving a wide range of genetically determined immune-modifying factors, underlying systemic inflammatory disorders and systemic diseases (2). This evolution of our understanding is highlighted by the regular and significant changes to periodontal disease classification systems over the years (1986, 1989, 1993, 1999 and 2017).

It has been theorised that the role of Human Herpes Viruses (HHVs) in peri-implantitis is through stimulation of toll-like receptors expressed in susceptible periodontal tissue cells leading to up-regulation of genes expressing interferons and pro-inflammatory cytokines (3). This systematic review compared the prevalence at diseased and healthy implant sites of the three most commonly implicated HHVs- HSV1, EBV and CMV- as a means of assessing this premise. The study question was explicitly stated using the PECO model but we must highlight the risk of solely using correlation of presence of HHVs in disease sites to infer causality. The study design followed the PRISMA protocol resulting in only five studies from 45 search returns included for final assessment, but limiting the search to only journals published in English may have meant relevant data was missed from other important research countries. A further quality critique using the Newcastle-Ottawa scale determined only two studies were of a high standard.

The authors highlighted important shortcomings in the studies assessed. This included the use of the more inaccurate paper point sampling technique in two papers, the lack of reporting the pocket depth the samples were taken from and the significant publication bias observed from the funnel plots for the studies investigating EBV and CMV.

The analysis determined the only statistically significant virus presence in a diseased versus healthy implant site with an acceptable confidence interval was with the EBV. From this, the authors cautiously concluded that there is a link between peri-implantitis and HHVs, however we must disagree that this can be asserted from data extracted from so few studies of acceptable quality and in defiance of the obvious heterogeneity of the data. Further primary research of a more academically rigorous standard needs to be performed before asserting with certainty that viruses play a role in peri-implantitis development.

Practice point
The evidence outlined above is insufficient to show a causal role of viruses in peri-implantitis. The mainstay of periodontal treatment remains effective biofilm disruption.

References:

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