Maternal xylitol and mutans streptococci transmission

Abstracted from

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Effect of maternal use of chewing gums containing xylitol on transmission of mutans streptococci in children: a meta-analysis of randomized controlled trials.
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Question: Does maternal use of xylitol gum reduce transmission of Mutans streptococci and prevent caries in children?

Data sources PubMed, EMBASE, SCOPUS, Cochrane Central Register of Controlled Trials databases and the ClinicalTrials.gov registry were searched with 'related articles'. Experts were contacted and a manual search of reference lists was undertaken.

Study selection Randomised or quasi-randomised controlled trials that evaluated the maternal use of xylitol gum on Mutans Streptococci (MS) colonisation in infants.

Data extraction and synthesis Two independent reviewers performed data extraction with a third reviewer asked to resolve any disagreements. Cochrane risk of bias tool was used to assess the quality of studies. Two reviewers independently appraised the methodological quality. The primary outcome measure was presence of MS in the saliva or plaque of infants, with the secondary outcome measure being occurrence of dental decay.

Results 11 studies published between 2000 and 2012 involving a total of 601 patients were included. Sample sizes ranged from 60 to 195 and the daily dose of xylitol consumption ranged from 1.95g to 5.28g. Follow-up ranged from six months to 120 months. There was a significant difference between the two groups, with infants in the control group experiencing greater incidences of MS in their plaque or saliva. Risk ratios were 0.44 (95% CI: 0.08-2.40) at 6-9 months, 0.54 (95% CI: 0.39-0.73) at 12-18 months, 0.60 (95% CI: 0.34-1.08) at 24 months, 0.56 (95% CI: 0.40-0.79) at 36 months and 0.61 (95% CI: 0.48-0.76) at 60 months. Caries data could not be pooled.

Conclusions Xylitol consumption by mothers with high MS levels was associated with a significant reduction in the mother-to-child transmission of salivary MS. These findings are based on evidence that may have suffered from biases.

Commentary

This review examined the effect of maternal use of xylitol gum on Mutans Streptococci reduction in infants and evaluated the role of xylitol gum in caries prevention strategies. The meta-analysis is well conducted with some limitations. The paper identifies itself as a meta-analysis and has a structured summary although it does not include objectives, study eligibility criteria, participants or interventions. In addition there is no discussion of any limitations or implications of the findings.

The rationale for the study is well described and there is detailed background information provided. While there is a clear statement of the question being asked in the introduction, it would have been useful to have had a PICOS search strategy given at this stage, as later in the document there is some confusion over inclusion criteria eg the age of participants included in the review.

In another planned Cochrane review,[1] the authors lay out a structured strategy with clear indication of age of participants at the outset. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) advises that having a pre-specified protocol is important because it can help reduce the likelihood of biased changes to a protocol as the review progresses. Protocols may need to be modified as a review progresses and the lack of a pre-specified protocol does not automatically make a review biased but it is important that these changes are transparent.[2] In this paper there is no mention of any review registration.

There is limited information on the search strategy. It would have been useful to have had a full search strategy either in a table or in an online appendix that could be referred to. The authors should have considered widening their search to include contacting researchers. The clinical trials database was searched but there does not seem to be have been contact with authors of registered trials and no attempt was made to contact one of the authors of a trial that was registered on the Clinical Trials Database (2015).

The process of selecting the studies and data collection were clearly described making the process clear to follow. The flow chart describing the reasons for exclusion was helpful in understanding the methodology. The length of follow-up for each study was clearly identified and risk of bias was assessed for all the studies. Tests for heterogeneity were performed and allocation concealment and blinding were recorded for all studies. There was no mention however of reporting bias and it is unclear whether the authors considered this. Publication bias occurs where trials with positive or interesting results are published but those with no statistical differences or negative results may not be published or available as

widely. To try to avoid publication bias, it is important to consider more than just those studies that have published results. [3]

Although 11 studies were used, the publications originated from five actual research teams and while all the studies were reported to be randomised or quasi-randomised controlled trials, the authors state there is only clear randomisation with respect to allocation generation described by two of the research teams.[4,5] It would have perhaps been useful for the review authors to contact the trial authors to obtain fuller information on this. Fontana[6] for example used a random numbers table to randomly assign participants to one of their four groups. The inclusion of quasi-randomised controlled trials such as those by Söderling[7-9] may have introduced bias into these results as they included women with a history of xylitol consumption into the xylitol group.

Blinding or masking, as it is sometimes referred to, is important in studies because it reduces the risk of knowledge of the intervention received rather than the intervention itself affecting the outcome. It is important to consider, where possible, blinding or masking participants, personnel and outcome assessors to reduce performance and detection bias.[10] It is difficult to blind participants in xylitol studies especially if one wishes to compare xylitol with a control that is simply not xylitol. In Söderling's studies[7-9] it would have been impossible to blind the participants in the various groups. In the Thorild[11-14] and Fontana[6] studies blinding was possible only because there were three groups all chewing some form of gum. Readers need to consider the influence of blinding on results of studies of this type.

Attrition bias is where there can be systematic differences between groups with respect to withdrawals from a study.[10] The loss to follow-up was variable between the two groups but was quite high in a number of these trials eg in Fontana's study, attrition was between 20% and 46% and Alamoudi was between 20% and 60%.[15] The small sample sizes and potential for attrition bias in the majority of studies indicates that caution should be exercised when interpreting findings from this meta-analysis.

There is some contradiction about the studies which were included. The review authors state that studies were chosen where mothers were recruited who had infants less than five months old, without teeth at the start of the study, or mothers who were pregnant or had just given birth (end of 3rd trimester or 3rd to 5th month). However, the Alamoudi study included infants with a minimum of eight primary teeth and considering usual eruption times this would make the child at least nine months old when they were enrolled into the study.

The authors undertook a meta-analysis on the primary outcome of presence of MS in saliva or plaque of infants. A meta-analysis can be useful to increase the power of studies, or to gain an improvement in the precision of studies. However, meta-analyses have the potential to mislead if there is not careful consideration of the variation between the studies (heterogeneity of the data). This heterogeneity is made up of clinical heterogeneity, the differences between participants, interventions and outcomes between studies, and also methodological heterogeneity, which is variation between the study design and risk of bias between studies. This heterogeneity can be statistically assessed to understand whether the probability of the observed pattern of results may have occurred simply through chance.[10] When one considers the xylitol studies there are considerable differences in xylitol dosage and controls used. Any analyst considering a meta-analysis needs to consider the implications of these differences before commencing this process. The heterogeneity of the data was variable across the different follow-up times and so some of these results must be accepted with caution. The inclusion criteria for most of the studies were that mothers had high salivary levels of MS. This makes wider application of findings more difficult as this effect may only be relevant in mothers with high MS levels.

The primary outcome showed a pooled significant difference in MS transmission from mothers to infants in the xylitol group. In the meta-analysis, the authors compared similar groups of comparisons. This showed an understanding of the need to group similar data in a meta-analysis. The authors also grouped the data into follow-up time allowing the authors to assess how maternal consumption of xylitol effects MS transmission over time.

The secondary outcome of the role of xylitol in caries prevention strategies only included three studies and no meta-analysis was performed. Results were inconclusive for this outcome.

Overall this review was well conducted but could have had more clarity in areas including PICOS, review protocol and search strategy. The final conclusion of the review authors is statistically significant (6-9mths p=0.34, 12-18mths p<0.0001, 24mths p=0.09, 36mths p=0.0008, 60mths p<0.0001) but this conclusion needs to be considered in line with the possibility of bias within the results. This review highlights the lack of good quality evidence available when trying to assess any link between caries experience and xylitol use.

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