The impact of polyol-containing chewing gums on dental caries: a systematic review of original randomized controlled trials and observational studies

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CRD summary
The authors concluded that there was consistent evidence to support use of xylitol- and sorbitol-containing chewing gum to prevent dental caries. This was a well-conducted review and the results are likely to be reliable for the population group evaluated (schoolchildren).

Authors’ objectives
To assess the effect polyol-containing chewing gum compared with no chewing gum on dental caries.

Searching
MEDLINE (from 1950), The Cochrane Library (May 2008) databases and Google Scholar (May 2008, first 200 hits) were searched. Search terms were indicated. Only studies published in English in a peer-reviewed journal were considered.

Study selection
Studies were eligible if they were experimental or observational studies that compared the effect of one or more chewing gums that contained at least one polyol (xylitol, sorbitol, mannitol or maltitol) against no treatment (defined as recommended or conventional oral hygiene, which included flossing and regular brushing with a fluoride or non-fluoride containing toothpaste) on caries development.

All of the included trials were randomised controlled trials (RCTs) or controlled clinical trials (CCTs); some follow-up data were presented as cohort studies. Trials originated from USA and Europe; one study came from China. About half the studies documented an industrial sponsor. A few studies included multiple intervention arms that compared different polyols. Interventions assessed included xylitol-containing chewing gum, xylitol-sorbitol blend, sorbitol and sorbitol-mannitol blend. Doses of xylitol and sorbitol ranged from 2.9g/day to 10.67g/day. The xylitol-sorbitol blend had a ratio of xylitol to sorbitol of between 3:40 and 1.27:1. All studies assessed the effect of chewing gum in school age children. Chewing gum was consumed either during school days or daily and generally associated with meal times. Original trials lasted between 24 and 40 months.

Two reviewers independently selected the studies. Any discrepancies were resolved by discussion or if necessary by consulting a third reviewer.

Assessment of study quality
Two reviewers independently assessed the quality of all included studies. RCTs were assessed using the five-point Jadad scale. Studies that scoring 3 or more were judged to be of high quality. US Preventive Services Task Force criteria were used to assess the internal validity of non-randomised studies.

Data extraction
Two reviewers independently extracted data. Outcome data reported on surface level (for all surfaces combined) were extracted instead of data reported on tooth level. Values were imputed for studies with missing or partially missing data. Where data were reported separately for clinical and radiological examinations, results for combined data were chosen.

Methods of synthesis
A meta-analysis was conducted, where incremental dental caries outcomes were converted to prevented fraction (PF): the proportional reduction in dental caries between the intervention and the control group relative to the control group expressed as a percentage, with 95% confidence intervals.

Studies were grouped by type of polyol (xylitol only, xylitol-sorbitol, sorbitol only, sorbitol-mannitol). Preventive
fractions of individual studies were weighted by the inverse variance of the mean. Data were pooled using both a random-effect and a fixed-effects model. Statistical heterogeneity was assessed with the $I^2$ statistic. Clinical heterogeneity in study characteristics was also considered. Sensitivity analyses were carried out to investigate various sources of heterogeneity. Specifically, analyses for RCTs and CCTs only were compared and analyses were carried out that excluded studies with imputed standard deviations and included studies with highest or lowest prevented fraction. Rosenthal's fail-safe N was calculated to address publication bias. A simple linear regression analysis was carried out to assess the effect of polyol dose on prevented fraction; this used polyol load (taking into account total daily dose and duration of exposure) as a covariate.

**Results of the review**
Fourteen studies (19 articles) that provided outcome data for 8,600 participants were included. Six studies were RCTs and eight were CCTs. Four of the eight CCTs were considered fair quality, three were good quality and one was poor quality. One of the six RCTs received a Jadad score of 5, one a score of 3, one a score of 2 and three a score of 1.

Based on random-effects models, dental caries was significantly reduced with xylitol-containing chewing gum versus no chewing gum (prevented fraction 58.66%, 95% CI 35.42 to 81.90, $p<0.00001$; six studies), with xylitol-sorbitol-containing chewing gum (prevented fraction 52.82%, 95% CI 39.64 to 66.00, $p<0.00001$; five studies) and with sorbitol-containing chewing gum (prevented fraction 20.01%, 95% CI 12.74 to 27.27, $p<0.00001$; five studies), but not with sorbitol-mannitol-containing chewing gum (prevented fraction 10.71%, 95% CI -20.50 to 41.93, $p=$not significant; three studies).

There was significant heterogeneity in all meta-analyses. None of the sensitivity analyses for the xylitol or xylitol-sorbitol studies resulted in the intervention effect becoming non-significant. The effect became non-significant for the sorbitol studies when only RCTs were considered.

The regression analysis for xylitol suggested that larger doses were associated with a greater effect (R$^2=49\%$). For sorbitol the correlation was smaller (R$^2=34\%$).

Results for Rosenthal's fail-safe N suggested that a large number of unpublished trials with a null-effect (between 89 and 565) would be required to offset the effects seen.

**Authors’ conclusions**
There was consistent evidence to support use of xylitol- and sorbitol-containing chewing gum to prevent dental caries.

**CRD commentary**
This systematic review addressed a clear research question and was supported by appropriate inclusion criteria. Measures were taken to avoid reviewer bias and error in the review process. The literature search included relevant databases and search terms were indicated. However, only studies in English were included and so some relevant studies may have been omitted. Methodological quality was assessed and sensitivity analyses were carried out based on study type, outcomes and method of analysis. Information on participants included in the trials was somewhat limited, but more information was provided online. All studies were in school children, so the effect in other populations was uncertain. The authors’ conclusions followed from the data presented and are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors made no specific recommendations for practice.

**Research:** The authors stated that research gaps existed with respect to dose-response relationships and the relative efficacy of different polyols. Future research should use more rigorous study designs, head-to-head comparisons of all polyols at optimal doses and higher methodological quality.

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