The effect of different formulations of chlorhexidine in reducing levels of mutans streptococci in the oral cavity: a systematic review of the literature

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CRD summary
The authors concluded that chlorhexidine mouthwash had no lasting effect on mutans streptococci levels, but 1% gel worked for up to 26 weeks after intensive treatment or 10 to 14 daily applications. Results for varnish were inconsistent. The limited search, failure to conduct validity assessment and lack of conclusive randomised evidence mean that the findings may not be reliable.

Authors' objectives
To evaluate the duration of effect of chlorhexidine (CHX) solutions, gels and varnishes in reducing levels of mutans streptococci in the oral cavity.

Searching
PubMed and LILACS were searched to October 2005. Search terms were reported. Unpublished studies, theses and dissertations were excluded.

Study selection
Clinical studies that evaluated the effect of chlorhexidine solutions, gels or varnishes on mutans streptococci levels were eligible for inclusion. Studies that lacked data on reduction in mutans streptococci levels over time were excluded, as were those in which the intervention included other preventative methods (such as dental hygiene guidance, use of fluoride and intensive professional prophylaxis) or which involved no prior restorative treatment.

The review included studies of chlorhexidine solution (at concentrations of 0.025% to 0.2%, 4mL to 15mL used as a rinse for 30 to 60 seconds up to four times daily for up to six weeks), gel (at concentrations of 0.2% to 1%, applied daily by toothbrush for seven to 14 days or at 1% to 5% concentration applied by one or two intensive professional treatments) and varnish (at 1% to 40% concentrations, professionally applied two to four times over two to seven days or at intervals of 30 days or more).

Inclusion criteria for study populations varied widely (for example, dental students, mutans streptococci colonisation, presence of orthodontic appliance, eruption of first molars and good oral health). Participant ages ranged from 10 months to 98 years. The included studies reported reduction in decreased salivary or dental biofilm levels of mutans streptococci. Interventions were compared with different doses or formulations of chlorhexidine, placebo (such as saline, flavoured/coloured water) or no treatment.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Individual study results were described in tables. The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The data were combined in a narrative synthesis grouped by the type of intervention.

Results of the review
Forty-six studies were included (n=approximately 944): 17 studies described as randomised controlled trials (RCTs),
including four split-mouth and four crossover studies; 15 described as randomised uncontrolled trials; two described as non-randomised controlled trials (including one split-mouth); and 12 described as uncontrolled trials.

**Chlorhexidine solution (11 studies):** Two RCTs measured short-term effects; one found a significant benefit from chlorhexidine solution. Three RCTS measured long-term effects and found no significant benefit from CHX. Overall, 10 studies found a significant effect from chlorhexidine for up to 24 hours after rinsing.

**Chlorhexidine gel (13 studies):** Two RCTs found no significant difference between the groups in mutans streptococci when 0.2% or 0.5% chlorhexidine gel was applied with a toothbrush; mutans streptococci levels decreased in both groups. Professionally applied 1% gel (three sessions over one week) had a significant effect for two weeks compared with placebo (one RCT). Use of 5% gel produced no further improvement on outcomes (two RCTs). Results overall (13 studies) indicated that intensive two-day treatment or daily application for 10 to 14 days would significantly decrease mutans streptococci levels for four to 26 weeks.

**Chlorhexidine varnish (18 studies):** One parallel-group RCT reported that two applications of 1% varnish significantly decreased mutans streptococci compared to placebo. Effects persisted for at least one month after treatment. Three split-mouth RCTs reported variable findings associated with two to four applications of 1% chlorhexidine, with a decrease in mutans streptococci lasting three days, two to three weeks and three months. A single application of 40% varnish was significantly more effective than placebo for two months or (with increased treatment intensity) for up to four months (one RCT). Results overall for varnish (18 studies) were inconsistent.

**Chlorhexidine gel versus varnish (four studies):** Two RCTs found no significant difference between 1% gel and varnish (single application of 40% or two applications of 1%); one reported that gel was longer lasting. One uncontrolled study reported superior results in the varnish group and a second reported no difference between the groups.

**Authors' conclusions**
Chlorhexidine mouthwash had no lasting effect on mutans streptococci levels. One per cent gel decreased levels for up to 26 weeks after intensive treatment or 10 to 14 daily applications. Results for varnish were inconsistent, but 40% varnish appeared to have a longer lasting effect than 1%.

**CRD commentary**
The objective of the review was clear and the inclusion criteria appeared adequate, but the rationale for some criteria was not explained (for example, the exclusion of studies that did not involve prior restorative treatment). The search involved only two databases and was restricted to published articles, which meant that some studies may have been missed and that the review was prone to publication bias. No formal test for publication bias was conducted.

It was not stated whether steps were taken to minimise bias and error in the processes of study selection and data extraction by having more than one reviewer make decisions independently. Study validity did not appear to be systematically assessed. The design of some of the included studies was unclear from the information given (for example, randomised but not controlled). In the absence of detailed information about the design of primary studies or their quality (for example, blinding and follow up rates) it was hard to determine the reliability of the evidence. There were some inconsistencies between the table and text. It was unclear whether it was appropriate to combine the studies in a narrative synthesis, given the wide disparity of designs, populations, interventions and follow-up times. The variation in findings appeared to be attributed to individual variability in response to chlorhexidine; other sources of heterogeneity were not discussed in detail. The authors appropriately gave some precedence to randomised controlled trials in their discussion of study findings. In view of the limited search, failure to conduct validity assessment, absence of information on review processes and lack of conclusive randomised evidence, the authors' findings may not be reliable.

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

**Practice:** The authors stated that the effects of chlorhexidine treatment should be monitored.

**Research:** The authors stated that more research was needed in this area.
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