## ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION

**Silver diamine fluoride: A caries "silver-fluoride bullet."**
Rosenblatt A, Stamford TCM, Niederman R.
*J Dent Res 2009;88(2):116-25.*

## REVIEWER

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## PURPOSE/QUESTION

**The authors conducted a systematic review of clinical studies on the effectiveness of silver diamine fluoride to arrest and prevent dental caries at the cavitated level.**

## SOURCE OF FUNDING

**NIH Grant (DOI:10.1177/0022034508329406)**

## TYPE OF STUDY/DESIGN

**Systematic review**

## LEVEL OF EVIDENCE

**Level 2: Limited-quality patient-oriented evidence**

## STRENGTH OF THE RECOMMENDATION GRADE

**Grade B: Limited-quality patient-oriented evidence**

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# Silver Diamine Fluoride (SDF) may be Better than Fluoride Varnish and no Treatment in Arresting and Preventing Cavitated Carious Lesions

## SUMMARY


### Selection Criteria

Two investigators reviewed 5 databases (Medline, LILACS, EMBASE, Cochrane, and the Brazilian Dental Library) for articles written in English, Spanish, or Portuguese between 1966 and December 31, 2006, matching specific inclusion criteria (see below). One hundred forty-nine reports were compiled, and the first review of titles and abstracts identified 110 unique studies. A full review of the publications identified 12 relevant studies. Three additional reports were identified from the reference lists of these 12 studies, but none met the inclusion criteria. Upon closer examination, 10 of the original 12 studies did not meet inclusion criteria either. Two studies were selected: Chu et al[1] published in 2002 and Llodra et al[2] published in 2005. The former was designed as a cohort study (blinded, but without random allocation to treatment), whereas the latter was a randomized blinded study.

### Key Study Factor

The inclusion criteria included the following: studies on silver diamine fluoride (SDF) and caries; studies in humans; randomized controlled trials (RCTs), cohort, or case-control studies; person as the unit of measurement; and reporting variance estimates. Data were abstracted into an evidence table. A third investigator was used to resolve disagreements. Both studies compared SDF at 38%. The Chu et al study applied the experimental SDF to cavitated primary maxillary anterior teeth once a year, whereas the Llodra et al study applied SDF to cavitated primary cuspids and molars and permanent first molars 2 times a year. Comparison groups included children receiving fluoride varnish (5%) or water 4 times a year (Chu et al), or just water 4 times a year (Llodra et al). Trials lasted 2.5 years (Chu et al) and 3 years (Llodra et al).

### Main Outcome Measure

Both studies reported the prevalence of arrested and new cavitated lesions as outcomes and reported effectiveness by comparing intervention (SDF) versus controls (fluoride varnish or water). In addition, the authors of the review conducted the following quantitative analysis of the reported data:

a. *Prevented fraction* (PF). The fraction of the preventive effect that can be attributed to the preventive agent,[3] in this case the fluoride compounds tested (SDF and F varnish). *Preventive fraction* is calculated as the difference in caries increment between the control group ($Ic$) and the experimental group ($Ie$), divided by the increment in the control group ($Ic$):

$$PF = \frac{(Ic - Ie)}{Ic}$$

The higher the PF value, the more effective is the preventive intervention.

b. *Number needed to treat* (NNT). Defined as the number of persons who need to be treated in order to prevent one additional bad outcome. *Number needed to treat* is calculated by taking the inverse of the absolute risk reduction[4]:

$$NNT = \frac{1}{Ic * PF}$$

The ideal NNT value is 1, where everyone improves with the active intervention and no one improves in the control group. The higher the NNT, the less effective is the preventive intervention.

### Main Results

As reported by the authors of the systematic review,[5] the application of SDF once or twice per year "can significantly arrest active caries, reduce the incidence of new caries, and not substantially increase the risk of adverse events." Results are reported in the evidence table (Table 10 in the article), from which the authors highlighted the higher *prevented fractions* and lower *number needed to treat* values in the SDF groups in both studies (applied to both arrested and new lesions). Regarding adverse effects, the authors reported less than 1% of pulpal incidents and that 7% of participants in the Chu et al study were troubled by the staining produced by SDF; in addition, 3 of 153 participants in the Chu et al study reported 24-hour tissue sensitivity to SDF.

### Conclusions

The authors concluded that SDF at 38% applied once or twice per year could be used to arrest or prevent cavitated carious lesions with minimum local and reversible side effects.

## COMMENTARY AND ANALYSIS

The authors claim that SDF is a product with potential public health use because it allows treatment and prevention at the same time, is easy to apply, noninvasive, requires minimal training, and is inexpensive. The authors indicate its potential use in the World Health Organization (WHO) "Basic Package for Oral Health" (available from the Department of Global Oral Health at the Radboud University Niejmegen Medical Center and accessible at http://www.globaloralhealth-nijmegen.nl/bpoc_start.html). The systematic review, however, addresses only effectiveness on arresting and preventing dental caries.

Only 2 of around 150 studies matched the criteria for inclusion in this systematic review. An additional clinical study by Yee and associates,[6] which focuses only on caries arrest, was not included because it was published after 2006. Thus, there is a scarcity of well-conducted clinical studies to address this issue.

Technically, this is a well-conducted review. One item that is missing is an assessment of studies' reports on lesion clinical assessment and coding and examiner reliability. Because SDF has 2 potential effects—one arresting existing carious lesions and the other preventing new ones—case definitions for and clinical assessment of "caries activity" and "new lesions" are crucial. Both studies used different coding. For example, the examiner in Chu et al scored tooth surfaces as sound, caries-active, caries-arrested and black, caries-arrested but not black, filled, or missing. The Chu et al study defines "caries-arrested" as "dentine that cannot be penetrated with a sharp sickle-shaped probe with light force." The Llodra et al study used 2 examiners who scored tooth surfaces as healthy, with active caries, inactive caries, filled, or absent, where activity was decided based on softness of floor/walls at examination. Furthermore, it seems that only the central part of the lesion was probed during examination, leaving other parts of the lesion untouched. It is impossible to ascertain whether these differences between studies affect the results. Detection of new lesions appears to be at the cavitated level, missing the opportunity of assessing the preventive effect on noncavitated lesions.

In terms of reliability, both studies reported Cohen's kappa values, but they do not explain what each value represents in terms of the codes included and the prevalence among those receiving a second examination.

Tabulated results are depicted in Table 10 ("Evidence Table").[5] In abstracting data from the 2 reports, the authors choose the mean number of active lesions corresponding to the entire number of participants at baseline and not just those for which there were follow-up data. This, however, does not change the results because *preventive fractions* and *number needed to treat* were estimated from the mean number of arrested lesions at follow-up (labeled as "Inc" in Table 10). Results are in agreement with the hypothesis that both fluoride compounds are more effective in arresting carious lesions than nontreatment. SDF appears to have a greater effectiveness than fluoride varnish, but the latter was not designed to arrest cavitated dental caries. The data for effectiveness in permanent teeth is weaker than the data supporting effectiveness in primary teeth: the mean number of arrested lesions in the Llodra et al study (the only study addressing permanent teeth) was 0.1 surfaces in the SDF group and 0.2 in the control (water) group, which provides unreliable PF and NNT. New cavitated lesions in permanent teeth were dramatically different (mean of 0.4 in the SDF group and 1.1 in the control group), which suggest the expected preventive effect despite the lower number of arrested lesions.

A final issue is the handling of suspicious carious lesions in pit and fissures showing obvious undermining enamel in noncavitated lesions. Both studies do not report on the occurrence of these lesions, nor did they include a specific coding for these lesions. This, in turn, may imply that they were included as sound/healthy in the Llodra et al study (Chu et al reported excavation in 2 of the intervention arms, but using an excavator).

## Clinical Applicability

Although most clinicians will be appalled by an approach that focuses on inactivating an existing cavity and leaving it open versus providing a restorative treatment (or sealants), SDF and similar techniques to arrest carious lesions are potentially viable options when no other treatment is available. This is probably not an optimal clinical procedure but is a palliative and cheap alternative in situations where not even simplified techniques such as the atraumatic restorative treatment[7] are available. Thus, in theory, SDF and similar solutions have a niche in clinical dental care. The question, thus, is whether SDF is efficacious, effective, and, compared with other alternatives, cost effective. The authors of the systematic review provide a list of in vitro and in vivo studies supporting the efficacy of SDF to arrest carious lesions and explain potential modes of action for such effect. (Incidentally, some reactions need to be balanced and require a pK to explain levels of ionic disassociation.) The question remains whether a carious lesion can be arrested and what the survival of these arrested lesions is. In other words, will an arrested lesion remain arrested? For how long? Will these lesions require a follow-up with a more "permanent" treatment? For the primary teeth during the 2 to 3 years of follow-up, and assuming replacement by permanent teeth, the 2 reviewed studies suggest that the treatment is effective. The same inference cannot be made for permanent teeth.

The preventive effect of SDF against new carious lesions is more problematic. The hypothetical assumption is that the F in SDF may have the same preventive effects of other fluoride compounds. Under the hypothesis of effectiveness in preventing new lesions, F will have to be released from the painted cavity and be at sufficient level to promote remineralization between applications. This is not easy to visualize, but the same can be argued for most topical fluoride applications with high fluoride content such as gels and varnishes.

In conclusion, the systematic review suggests that SDF is effective in arresting cavitated lesions in primary teeth under the case definitions used in the 2 studies reviewed. The limitations of the data suggest the need for further well-controlled clinical trials, survival studies, and demonstration interventions on the applicability of SDF in arresting carious lesions when other alternatives are not available. The most recent report by Yee and associates[6] reports lower efficacy to arrest cavitated lesions of a 12% SDF formulation versus the 38% after 2 years of a single application in Nepalese children, and it is coauthored by the researchers who designed the WHO Basic Oral Health Package. It is my conclusion that despite the 2 positive studies in the medical literature, the existing evidence does not fully support SDF as the "silver-fluoride bullet" yet.

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