REVIEW ARTICLE

Dental Amalgam and Multiple Sclerosis: A Systematic Review and Meta-Analysis

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Abstract

***Objectives**: Amalgam restorations have long been controversial due to their mercury content. Allegations that the mercury may be linked to nervous disorders such as Alzheimer's, chronic fatigue syndrome, and multiple sclerosis (MS) have fueled the calls for the removal of amalgam restorations from dentists' armamentarium. To explore and quantify the association between amalgam restorations and MS we have conducted a systematic review and meta-analysis of the literature. **Methods**: A systematic search in Medline (from 1966 to April 2006), EMBASE (2006, Week 16), and the Cochrane library (Issue 2, 2006) for English-language articles meeting specific definitions of MS and amalgam exposure was conducted. Studies were also identified using the references of retrieved articles. Studies were independently reviewed by two authors and disagreements were resolved by consensus. Studies were selected based on an a priori of defined criteria. Odds ratios (ORs) or relative risks were pooled using the random effects model. Heterogeneity was assessed using Q statistics. **Results**: The pooled OR for the risk of MS among amalgam users was consistent, with a slight, nonstatistically significant increase between amalgam use and risk of MS. **Conclusion**: Future studies that take into consideration the amalgam restoration size and surface area along with the duration of exposure are needed in order to definitively rule out any link between amalgam and MS.*

Key Words: dental amalgam, amalgam, mercury, multiple sclerosis, meta-analysis

Introduction

Mercury amalgam restorations have been used in dentistry since 1818 (1). Although more esthetic dental materials are becoming readily available to the profession, amalgam retains its popularity due to its low cost, durability, and lower technique demand. Dental amalgam contains about 50 percent mercury. Due to its mercury content, the use of amalgam in dentistry has long been controversial. In the 1920s and 1930s mercury was identified as a health hazard (2), and in the1970s mercury from dental amalgams was found in different body tissues (3–6). In 1978 Craelius (7) reported a correlation between multiple sclerosis (MS) and dental caries, and in 1986 Ingalls (8) suggested that this correlation was due to the mercury in dental fillings and proposed its possible role in the etiology of MS. Several observational studies have shown an association between MS and dental amalgam fillings. While Bangsi et al. (9), Bates et al. (10), and Cassetta et al. (11) reported elevated relative risk (RR) for MS and amalgam fillings, McGrother et al. (12) found no such correlation. Presented with these discrepant results, we sought to explore and quantify the association between amalgam restorations and MS by conducting a systematic review and meta-analysis of the literature.

Methods

We systematically searched Medline (from 1966 to April 2006), EMBASE (2006, Week 16), and the Cochrane library (Issue 2, 2006) for all relevant articles entering terms including "dental amalgam," "amalgam," "mercury," and "multiple sclerosis." We also searched for potentially missed articles from reference lists of retrieved articles and from previous narrative reviews on this topic. We looked at human studies in the English language that had the following criteria: a) explicitly described the exposure status (amalgam fillings); b) defined method for determining MS diagnosis; c) presented odds ratios (ORs) or RRs or enough data to calculate the parameters; and d) adjusted for potential confounders through statistical regression modeling or matching. We initially found 18 potential articles, but only four met our inclusion criteria. The studies were independently reviewed by two authors and disagreements were resolved by consensus. A spreadsheet was constructed and information was extracted regarding the author name, number of cases/controls or cohort size, variables adjusted for, and the RR or OR for each study.

Exposure was defined as having any amalgam restorations during the study period. In the case where more than one amalgam restoration was reported or where amalgam presence was reported as a factor of tooth surface, the statistical average

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Table 1
Patient Characteristics in Studies of Dental Amalgam and Multiple Sclerosis

Author	Age	Cases/Controls	Variable adjusted or matched for:	OR and 95% CI
Case Control	Cases 36.9 ± 0.76	143/128	Age†, Sex†, Smoking,	2.05 (95% CI, 1.19–3.53)
Bangsi et al.	Controls 37.9 ± 0.84		Education, Income	
McGrother et al.	25–65	39/105	Age†, Sex†, General practitioner†, Oral hygiene status, Socioeconomic status, Education	0.96 (95% CI, 0.87–1.06)
Casetta et al.	Cases 38.4 ± 10.7 Controls 36.7 ± 10.7	132/423	Age†, Sex†, Study location, Sex, Oral hygiene status	1.35 (95% CI, 0.96–1.91)
Cohort	16–75	7/20,000*	Sex, Age, Army rank	1.24 (95% CI, 0.99–1.53)
Bates et al.				

* This number represents the number of cases divided by the total number of persons.
† Variables matched for.
OR, odds ratio; CI, confidence interval.

was used. The random effects model was used to pool RRs across the studies as this approach will account for between-study heterogeneity.ORs were considered an approximation of the RR. Heterogeneity was quantified by the bootstrap version of the Q statistic.

Results

Four observational studies that met our inclusion criteria (Table 1) (9, 12), three case-control (9, 11, 12) studies, and one cohort (10) study were found. The studies differ in methodologic qualities mainly in the manner by which MS was diagnosed. Most of the studies adjusted for some of the potential confounders. The pooled OR for the risk of MS among amalgam users was 1.24 (95 percent confidence interval, 0.96–1.61). There was significant statistical heterogeneity among the studies (Q statistics = 13.7, $P = 0.004$).

Discussion

Our results are supportive of a lack of an association with respect to amalgam restorations and the risk of MS. When the studies were pooled, significant heterogeneity was noted. A cause of this heterogeneity lies in the study design among the studies, as well as the lack of control for confounding. Bangsi et al. (9) looked at the number of amalgam restorations in the mouth, and the duration of exposure to the amalgam restorations. However, they did not consider the size of the amalgam restoration or the surfaces of the tooth that they covered. A large amalgam restoration of a molar covering the occlusal, buccal, and lingual surfaces would release more mercury than a small amalgam restoration on the biting surface of a premolar. McGrother et al. (12) followed a similar approach and did not consider restoration size. In McGrother's study (12), four patients had all their amalgam restorations removed upon being diagnosed with MS. These patients were not excluded by the investigators when calculating ORs for exposure to amalgam restorations. The authors also did not consider the duration of exposure to amalgam as a risk factor for MS. This was a relatively small study and did not have adequate power to find an association. The study by Casetta et al. (11) looked at patients' dental records. However, no examination was performed on patients to ascertain the exact number of amalgam restorations as well as their size. In the cohort study performed by Bates et al. (10), an effort was made to take into consideration the size of the amalgam restorations. The authors created an amalgam exposure index in which large restorations on molars received a greater weighting than smaller restorations. Although this system is an improvement over the others, it is still not an exact measurement of the amalgam surface area as an exposure variable. Finally, Bates et al. (10) report a relatively strong association between amalgam exposure and MS. However, they make that assertion from only seven cases of MS out of a cohort of 20,000.

Conclusion

This systematic review suggests a slight, nonstatistically significant increase between amalgam use and MS. However, this investigation was limited to four studies with significant heterogeneity. Future studies that take into consideration the amalgam restoration size and surface area along with the duration of exposure are needed in order to definitively rule out any link between amalgam and MS.

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