

Mercury released from amalgam restorations does not give rise to toxic effects on the nervous system of children

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Clinical scenario

The director of a low-income paediatric clinic has decided to invest in dental materials for its dental service. He is aware of the lower costs of amalgam restorations, but has concerns about the possible toxic effects on children's nervous systems. He decides to do a bibliographic search to help him with his decision.

Clinical question

The PICO (see below) question developed was: in children of between 6 and 10 years of age (Population) do amalgam restorations (Intervention) compared with composite restorations (Comparison) increase the risk of neuropsychological disorders (Outcome)?

Search strategy

Four databases, namely PubMed, Lilacs (Latin American & Caribbean Health Sciences Literature), Cochrane Library and Trip Database (www.tripdatabase.com) were searched using the following terms:

“neurotoxicity syndromes” [mesh] and “dental amalgam” [mesh] and (“mercury” [mesh] or “mercury poisoning, nervous system” [mesh]). limited to English or Spanish, child: 6–12 years and randomised controlled trials (see Table 1).

No articles were found in Lilacs or the Cochrane Library, one systematic review was found via the Trip database, and six articles were found in PubMed. Of the latter six, three papers were considered relevant. These are summarised in Table 2.

Discussion

Silver–mercury restorations have been used since 1830 but the controversy about the material's safety and its adverse effects on general health still continues. It is a fact that vapour of mercury is released from dental amalgam restorations and it is absorbed by the patient. The issue is, does this situation cause neuropsychological damage, particularly in children, who could be more vulnerable to the toxic effects of mercury than adults?

There are some confounding variables, such as eating and toothbrushing habits, fish consumption, gum chewing habits, etc., which influence daily mercury release and absorption from amalgam restorations. In order to reduce bias because of the variability between subjects, the studies selected for consideration here are randomised controlled trials.

The results of both studies^{1,2} provide consistent evidence of no adverse effects on the nervous systems of the children who received amalgam restoration. Both clinical trials were well-designed, randomisation was correct and the tests were of sufficient power to detect clinically important neuro-cognitive effects.

Because of the nature of the intervention, blinding was not possible for dentist and patients but psychometrists were instructed to be blinded. The followup period for these studies could be insufficient for two reasons: amalgam restorations generally remain in place longer than the period followed in these trials (Kaplan-Meier median survival times were 12.8 years for amalgam restorations) and the delayed effects later in life, if they exist, are unknown.

Statistical considerations

The power of the test in New England Children's Amalgam Trial² (80%) could be considered not strong enough to detect

small effects. In fact, the researchers calculated the sample size to detect a 3-point difference between treatment groups based on the existing evidence^{3,4} which shows that, in children, a 10–15- $\mu\text{g}/\text{dl}$ increase in blood lead level is associated with a 3-point decline in intelligence quotient. Because analysis of exposure data using the intention-to-treat principle did not consider the varying amounts of amalgam restorations in the children of the treatment group, the authors analysed the data (in another paper),⁵ stratifying subjects by surface-years of amalgam or by urinary mercury excretion, adjusting for test score, randomisation stratum, age, sex, family socio-economic status, hair mercury concentration and blood lead level. In the Casa Pía trial¹, De Rouen and colleagues considered a power of 97% for the tests. The sample size for the study was selected to ensure adequate power for detecting a small but near-uniform effect of 0.3 standard deviations for the three neurobehavioral outcomes considered, while maintaining control of the overall type-I error. For the data analysis in this trial, they developed a new statistics procedure, which allows comparisons with longitudinal data on multiple outcome variables and facilitates the detection of differences between treatments at the earliest possible time.⁶ The results in the three papers found no

Table 1. Search strategy

Search	Search term	Result
1	mercury	27 042
2	mercury toxicity	3783
3	(“mercury”[mesh] or “mercury poisoning, nervous system”[mesh])	15 226
4	amalgam	8664
5	“dental amalgam”[mesh]	7289
6	2 or 3 and 4	594
7	3 and 5	19
8	limits: English or Spanish; child: 6-12 years; randomised controlled trials	6

Table 2. Summary of relevant papers

Paper, date and setting	Patient group	Study details	Outcome	Key results	Study weaknesses
DeRouen TA, Martin MD, Leroux BG, et al. ¹ Lisboa, Portugal Feb. 1997–July 2005 Casa Pía Trial	507 children. 8–10 years old. No previous exposure to amalgam	Randomised control trial. Followup: 7 years, 85% retention rate at 5 years declined to 70% through year 7. Withdrawn patients analysed using intent-to-treat principle	Neurobehavioral assessments of memory, attention/concentration and motor/ visuomotor domains, plus nerve conduction velocities	Multivariate statistical analysis found no significant statistical differences between intervention and control groups. Hotteling t ² test, 0.60 (P 0.66); O'Brien test, 0.21 (P 0.42)	Randomisation method not clear. Participants and dentists not blinded to treatment assignment. 5 years after initial treatment, need for additional treatment was ~50% higher in composite group
Bellinger DC, Trachtenberg F, Barregard L, et al. ² Boston and Farmington, USA Sept. 1997–Mar. 2005 NECAT	534 children. 6–10 years old. No prior amalgam restorations. No neuropsychological, immune-suppressive or renal disorders	RCT. Randomisation: permuted blocks stratified by geographical location (Boston vs Maine) and number of teeth with caries (2–4 vs ≥5). Followup: 5 years, 75% retention rate. Withdrawn patients analysed using intent-to-treat principle	Primary outcome: changes in full-scale IQ for children. Secondary outcomes: changes in GMI and VMC	Fisher exact test found no significant statistical differences between groups. IQ, 1.0 (95%CI, -0.6/2.5; P 0.21) GMI, 0.9 (5% CI, -0.9/2.7; P, 0.34) VMC, 0.1 (95% CI, -2.0/2.2; P 0.93)	Power of test (80%) may be insufficient to detect small effects. Participants and dentists not blinded to treatment assignment. Binary classification of exposure could underestimate size of effect
Bellinger DC, Trachtenberg F, Daniel D, et al. ⁵ Boston and Farmington, USA Sept. 1997–Mar. 2005 NECAT	Same trial as above. Of 534 children enrolled, 434 analysed, stratifying subjects by surface–years of amalgam or by urinary mercury excretion	Follow up: 5 years. Exposure considered continuously in four groups. 217 subjects: no surface years of amalgam. 217 subjects classified in three groups: low (1.00–19.99 surface–years; n =72), middle (20.00–36.99 surface–years; n=73) and high (37.00–95.00 surface–years; n=72)	Primary outcome: changes in full-scale IQ for children. Secondary outcomes: changes in GMI and VMC	From analysis of covariance, no significant statistical association with amalgam dose and test scores was found. Surface–years of amalgam vs urinary mercury excretion: IQ, 0.01 (SD, 0.02; P 0.48) vs 0.46 (SD, 0.53; P 0.38) GMI, 0.03 (SD, 0.03; P 0.20) vs 0.74 (SD, 0.55; P 0.18) VMC, -0.01 (SD, 0.03; P 0.67) vs 0.20 (SD, 0.65; P 0.76)	100 of 543 patients enrolled not included in analysis. Participants and dentists not blinded to treatment assignment

NECAT, New England Children's Amalgam Trial; RCT, randomised controlled trial; IQ, intelligence quotient; GMI, general memory index; VMC, visual motor composite; CI, Confidence interval; SD, standard deviation.

significant statistical association between amalgam restorations and nervous systems disorders in children.

Recommendations

As the release of mercury from an amalgam restoration is at its peak just subsequent to placement in the cavity, declining to a much lower, steady-state level by 10–15 days,^{7–9} the replacement of successful restorations is not advised. Composite resins, a commonly used option, also suffer from a lack

of research into adverse effects and so cannot be considered free of risk. Furthermore, amalgam is more a cost-effective restoration material: composite resins have been shown to be 1.7–3.5-fold more expensive than amalgam to generate one tooth year.¹⁰ These considerations are particularly important in making decisions in Public Health.

Recently, a preliminary report by the European Scientific Committees on Consumer Products, on Health and Environmental Risks, and on Emerging

and Newly Identified Health Risks http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_011.pdf, concluded that there are no increased risks of adverse systemic effects exist and that dental amalgam is a safe material to use in restorative dentistry. Future research should be directed towards analysing adverse effects of amalgam in the less than 1% of the population genetically vulnerable to mercury toxicity or allergic to mercury.⁶

Clinical bottom line

There is no significant statistical association between the changes in the neurobehavioral and neuropsychological scores considered and the exposure to amalgam restorations in children. Under conditions similar to these trials, there is no reason other than aesthetics to discard amalgam as a choice to restore posterior teeth in children.

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