Int. J. Hyg. Environ. Health 204, 223–229 (2001)

http://www.urbanfischer.de/journals/intjhyg

International Journal of Hygiene and Environmental Health

"Amalgam disease" – poisoning, allergy, or psychic disorder?

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Received: January 31, 2001 · Revision received: August 1, 2001 · Accepted: August 22, 2001

Abstract

Frequently, patients in environmental health out-patient units relate various complaints to their amalgam fillings. However, an association between the toxic exposure and the reported complaints appears plausible only in few cases. We investigated toxicological, allergological and psychological parameters in patients with amalgam-associated complaints and compared them to controls with similar numbers of amalgam fillings.

Forty patients with health disturbances related to amalgam were compared to a control group without amalgam-associated complaints (n = 40), carefully matched for age, sex, and dental status. Mercury concentrations were analyzed in blood, saliva, and 24-h-urine. Atopic predisposition, determination of IgE, patch testing with amalgam and amalgam-associated metals and a psychometric assessment were performed in all participants.

Mercury concentrations in blood or urine were similar in patients and controls. Atopic predisposition was markedly enhanced in patients (11/40) as compared to controls (5/40). Only one patient with a lichen ruber of the oral mucosa showed a contact sensitization to amalgam. Patients reported more psychic strain and higher depression scores than controls. Somatization disorders were found in 10 patients (25%) and in one control. Eighteen patients (45 %) neither showed an atopic predisposition nor an influence of psychosocial factors.

Toxic exposure to mercury does not appear to play a role in "amalgam disease". Since many of these patients are atopic without an "amalgam allergy", but with more psychic strain and notably more depression, the treatment should be focused on allergologic and psychological factors.

Key words: Mercury – amalgam-related complaints – atopic – psychosomatic

Introduction

Patients with subjective physical complaints are abundantly seen in environmental health and allergy out-patient units. Often they relate their discomfort to their amalgam fillings and they fear to suffer from "amalgam poisoning" or "amalgam allergy." These patients complain about nonspecific symptoms like fatigue, dizziness, dry mouth, tachycardia, or headache with a long list of visits to many specialists.

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1438-4639/01/204-223 $ 15.00/0

They often demand mercury detoxification with chelating agents, thorough allergy diagnosis or dental treatment even including complete tooth extraction.

Amalgam fillings contribute to the inner exposure of the organism with mercury (Zander et al., 1990; Skare and Engqvist, 1994; Eley, 1997). Individuals with amalgam fillings have a two- to fourfold higher mercury concentration in urine (HgU) than people without amalgam. The mercury concentration in urine increases significantly with an increasing number of amalgam surfaces (Kingman et al., 1998). In Germany, persons without amalgam fillings show an average HgU concentration of 0.3 μg/l, as compared to those with more than 10 amalgam fillings with an average HgU concentration of 1.5 μg/l (Krause et al., 1996). Nonspecific toxic symptoms such as tiredness, difficulties to concentrate or nervousness are found only at HgU concentrations above 50 μg/l even in particularly sensitive individuals (WHO, 1991).

Patients who relate their complaints to amalgam are often referred to an allergist for "amalgam allergy". However, the prevalence of contact sensitization to amalgam is low (McGivern et al., 2000). Less than 2% of the German population show a positive reaction to amalgam in the patch test (von Mayenburg et al., 1991). Amalgam allergies with systemic reactions and symptoms such as erythema, tachycardia, or respiratory distress are very rare. Since 1900, only 50 cases have been documented world-wide (US Department of Health and Human Services, 1993).

The prevalence of psychosomatic and psychiatric disorders in patients with amalgam-associated disturbances is 40–60% higher than in the general population (Herrström and Högstedt, 1993; Malt et al., 1997, Bailer et al., 2001). Anxiety disorders, depression and somatization disorders have been primarily diagnosed but a relationship with Hg exposure has not been confirmed (Bratel et al., 1997; Osborne and Albino, 2001).

In this report toxicological, allergologic, dental and psychometric examinations were carried out in a group of patients and compared to a control group without amalgam-related complaints to check the following hypotheses:

- Patients with amalgam-associated complaints do not have elevated levels of Hg in blood, saliva, and urine im comparison to controls with similar numbers of amalgam fillings.
- These patients do not have "amalgam allergies" (contact sensitization to amalgam) more often than controls.
- They report higher psychic strain than the control group.

In addition we wanted to look for other possible psychological aspects and compared somatization and depression in patients and controls. The findings of the study reveal the parameters that were different between patients with amalgam anxiety and controls with the same amalgam exposure. Likewise, the outcome of the study was helpful referring the patients to the adequate treatment.

Materials and methods

Patients of the Allergy Out-Patient Unit of the Department of Dermatology, University of Giessen, who related amalgam to their health disturbances, were asked to participate in this study dealing with health complaints due to dental materials. Controls with similar numbers of amalgam fillings but without amalgam-associated complaints were recruited by the Department of Dentistry, University of Giessen. Only individuals were accepted into the control group who stated that they were not impaired by their fillings. Exclusion criteria in both groups was a mercury mobilization test during the last 4 weeks. The two groups were matched with respect to sex, age, and number of amalgam fillings. The participation in the study was voluntary and could be refused or discontinued at any time. The study was approved by the local ethic committee and informed consent was obtained from all participants.

We asked all 55 patients who went to the Department of Dermatology because of amalgam-associated problems in 1997. Nine of these patients did not fix a date after the first contact, six patients had all their amalgam fillings taken out in the meantime. Forty patients (73%) finally took part in the study, one of them did not appear for the second recording of the patch test. Forty-nine controls were recruited in the Department of Dentistry. Six of them did not come to the first appointment, three of them attributed various disturbances to palladium or to amalgam and were therefore excluded. All 40 controls (82%) who finally participated in the study appeared on all three arranged dates.

The age of the participants ranged from 22 to 67 years. The mean age of the patients was 42.8 (SD 11.4) and of the controls 39.9 years (SD 10.4). In both groups were 17 men (42%) and 23 women (58 %). The patients had 1 to 18 (mean 7.5; SD 4.3) and the controls 1 to 16 amalgam fillings (mean 7.8; SD 3.8). Although one female patient with various amalgam-associated complaints had her fillings removed six weeks ago, she still worried about a possible mercury poisoning and was therefore included.

The group of patients and the control group did not differ significantly with respect to age, sex or number and surface of amalgam fillings (Table 1). The quality of the fillings (polished/unpolished) and alterations of the oral mucosa did not show significant differences between the

Table 1. Dental status and toxicological parameters of patients and controls.

	Patients X (SD)	Controls X (SD)	Mean difference (95 % CI)	t (df)	p
Number of fillings	n = 40 7.5 (4.3)	n = 40 7.8 (3.8)	− .21 (− 2.04 − 1.62)	− .22 (77)	.820
Surface of fillings (mm^2)	n = 40 292.85 (190.86)	n = 40 250.85 (157.59)	42.00 (− 36.32 − 120.34)	1.06 (77)	.289
Serum Hg (μg/l)	n = 37 .65 (.42)	n = 40 .51 (.35)	.14 (.03 − .31)	1.55 (75)	.123
Mobilized Hg in saliva (μ/l)	n = 38 39.54 (49.24)	n = 39 83.36 (98.97)	− 43.81 (− 79.45 − − 8.18)	− 2.44 (75)	.017
Hg in 24-h-urine (μg/l)	n = 39 .95 (.90)	n = 40 .95 (.80)	− .00 (− .39 − .37)	− .03 (77)	.973

groups. One patient had a lichen ruber nearby to a large amalgam filling.

Dental examination

The number, material, and quality of the restorations were clinically examined in all participants. The oral mucosa was examined for periodontal diseases, lichenoid lesions or amalgam tattoos. Silicone casts (Permagum Putty Soft, Espe, Germany) were made of the upper and lower jaws and the total surface area of the fillings was determined.

Allergy examination

All participants were examined dermatologically and the personal and the family history of atopic diseases was recorded. A patch test with amalgam and amalgam-alloy metals (5% of amalgam in vaseline and 20% of a mixture of silver, copper, tin and zinc in vaseline, Hermal Reinbek, Germany) was performed and read after 48 and 72 h according to the recommendations of the International Contact Dermatitis Research Group (Wahlberg, 1992). Blood samples were taken for the determination of total IgE (Pharmacia CAP, Erlangen, Germany). Atopic disposition was assumed, if atopic dermatitis, allergic asthma and/or allergic rhinitis were diagnosed or the parents and siblings were known to have atopic diseases and if the serum IgE value was higher than 100 kU/l.

Biomonitoring

Mercury concentration was analyzed in serum, saliva and in 24-h-urine. The mercury concentration in serum reflects the part of mercury burden due to food intake. According to Schweinsberg et al. (1998) a saliva test is not appropriate, but we decided to conduct it as well, because in 1997 many patients were confused by the "Tübinger Amalgam Studie" (up to now not published in a scientific journal), which promoted saliva test kits for the estimation of mercury burden from dental amalgam in a publicity campaign. The analysis of mercury in 24-h-urine is appropriate to determine the amount of inorganic mercury due to amalgam fillings (WHO, 1991).

The participants were asked about their mercury exposure, the consumption of fish, use of medicine and homeopathic remedies containing mercury and earlier treatments with chelating agents for accelerated Hg excretion. Since methyl-mercury in sea food influences the mercury in serum they had to avoid fish or sea food for at least three days before the blood test. The serum of one patient was excluded because of fish consumption two days before testing.

From the arm vein, 7.5 ml blood was taken into test tubes of low heavy metal content (Sarstedt, Nümbrecht, Germany). Immediately after centrifugation the serum samples were frozen and stored at − 40 °C. The 24-h-urine was weighed and thoroughly mixed immediately after collection. An aliquot of 80 ml was frozen and kept at − 40 °C until analysis. Subjects were told to collect 5 ml of resting saliva in a test tube and then they had to chew a piece of paraffin for ten minutes. The stimulated saliva produced during this time was collected in a second test tube. 65 % nitric acid was added to the saliva samples at a ratio of 1 : 1 (by vol), then the samples were frozen and stored at − 40 °C. The difference of Hg in stimulated and Hg in baseline saliva shows the amount of mobilized mercury. The mercury analysis was carried out by AAS technique applying cold vapor (Perkin-Elmer instrument 3030 B) with a detection limit of 0.2 μg Hg/l.

Psychometric assessment

A psychologist performed the psychometric assessments separately for each participant. The participants filled in questionnaires regarding psychic strain, experienced distress, somatization, and depressive symptoms. We used the check list for symptoms SCL-90-R (Derogatis, 1977), as a means for the determination of self-reported psychic strain, the Beck-Depression Inventory BDI (Beck and Steer, 1987) for measuring depressive symptoms, and the Screening for Somatoform Disorders SOMS (Rief et al., 1997), a structured recording of complaints that cannot be explained by any diagnosable physical disease, which allows the application of the ICD-10-diagnosis of somatization disorder. All questionnaires are standardized, checked for validity and of good reliability (Cronbachs α between .80 and .89).

The study lasted one year, from January 1997 until January 1998. The tests were carried out during three days in one week. On the first appointment the dental and oral examination was performed and saliva samples were collected. The atopic predisposition was recorded, and after the dermatological examination the patch test was applied. The participants were instructed how to collect the 24-h-urine and were asked to avoid fish during the next three days. On the second appointment, the 48 h reaction of the patch test was recorded, a blood sample was taken

for Hg-analysis, the urine was processed and the psychometric tests were carried out. On the third appointment, the 72 h reaction of the patch test was recorded.

Statistical analysis

Data were statistically analyzed by the T-test for independent samples and the Chi^2-test using SPSS for Windows 8.0. Differences at the 5 % level were accepted as statistically significant. Bonferroni α-adjustments were made for the SCL-90 results because of several t-tests for the SCL-90-subscales.

Results

Patients with amalgam-associated complaints showed an average serum concentration of 0.65 µg/l mercury (95% CI 0.51 – 0.79) as compared to controls with the same number of amalgam fillings with 0.51 µg/l mercury (95% CI 0.40 – 0.62). Although the average mercury concentration in the serum of the patients was slightly higher, no significant differences were found between the two groups (Table 1). Patients had significantly lower concentrations of mobilized Hg in the saliva than the control group. The mean mercury concentration in the 24-h-urine was similar in patients (0.95 µg/l, 95 % CI 0.67 – 1.22) and controls (0.95 µg/l, 95 % CI 0.69 – 1.20). None of the participants showed mercury values higher than the reference values of the German population with 5 µg Hg/l in urine and 2 µg Hg/l in blood.

Atopy was diagnosed in eleven patients (28%), but only in five control group individuals (13%). Five of the eleven patients suffered from allergic rhinitis. One of these five patients had also allergic asthma and six had atopic eczema. In addition contact allergies toward textile dyes (n = 3) and Type I hypersensitivity to food (n = 2) were elaborated in the five patients. In the five atopic control individuals hay fever, asthma, and other allergies e.g. against house dust, animal hair, and apples had been diagnosed. The patch test with amalgam was positive only in one patient without atopy. She had a lichen ruber close to an extended amalgam filling that was confirmed by biopsy.

The patient group reported significantly ($p = 0.004$) higher psychic strain (0.61, SD 0.57, in the global index GSI of the SCL-90-R) than the control group (0.34, SD 0.37, see Table 2). Likewise the patients had significantly ($p = 0.02$) higher depression scores in the BDI (10.02, SD 8.01) than the controls (7.07, SD 5.38). A somatization disorder according to ICD-10 was significantly more frequent ($Chi^2 = 8.35$, $p = 0.003$) in the patients than in controls. Ten patients (25%) and only one control (2.5%) fulfilled the ICD criteria. Three of them and none of the controls showed BDI depression scores that were concomitantly elevated in a clinically relevant manner. Neither allergies nor affective or somatoform disorders were detected in 18 of the patients (45 %).

Discussion

Amalgam is a very controversial topic and only studies with matched control groups can seriously contribute to the elucidation of the question in which parameters patients who relate their health problems to amalgam differ from persons without such attributed complaints. The knowledge of these differences would also facilitate the referral to an adequate therapy.

Whether patients feel impaired by their amalgam fillings obviously does not depend on the exposure to mercury. In our study patients and controls did not differ significantly in the Hg serum concentration, although patients showed slightly higher values. The mercury concentration in serum mirrors predominantly short-term exposure with methyl-Hg present

Table 2. Psychometric scores of patients and controls.

	Patients X (SD)	Controls X (SD)	Mean difference (95 % CI)	t (df)	p
SCL-90-R	n = 36	n = 38			
Somatization	.89 (.74)	.42 (.47)	.46 (.17 – .74)	3.21 (72)	.001
Obsessive-compulsive	.85 (.86)	.51 (.48)	.34 (.02 – .66)	2.12 (72)	.018
Interpersonal sensitivity	.57 (.65)	.37 (.38)	.20 (– .04 – .44)	1.62 (72)	.055
Depression	.66 (.65)	.35 (.33)	.30 (.06 – .54)	2.56 (72)	.006
Anxiety	.59 (.62)	.31 (.29)	.28 (.05 – .50)	2.52 (72)	.007
Anger-hostility	.53 (.51)	.31 (.27)	.21 (.02 – .40)	2.27 (72)	.013
Phobic anxiety	.27 (.50)	.13 (.23)	.13 (– .04 – .31)	1.53 (72)	.069
Paranoid ideation	.53 (.61)	.39 (.40)	.13 (– .10 – .37)	1.10 (72)	.136
Psychoticism	.33 (.42)	.18 (.24)	.15 (– .08 – .31)	1.88 (72)	.031
Positive symptom distress index (PSDI)	1.51 (.43)	1.24 (.35)	.26 (.08 – .45)	2.93 (72)	.002

in fish and sea food. Two controls had remarkably high levels of mobilized mercury (283 and 504 μg/l). Hg concentration in saliva is influenced by several variables, can increase short-term and it is known that it varies over a broad range in individual cases (Staehle, 1998) Patients and controls did not differ significantly in their concentration of mobilized Hg in saliva after exclusion of these data from analysis.

Likewise the mean Hg concentration in urine, by which chronic burdens originating from the release of Hg from amalgam fillings can be assessed, were the same in patients and controls. The participants relating their complaints to amalgam did neither show a higher Hg concentration than the controls nor were they exposed to a greater degree than the German population. The Hg concentrations we found are one tenth lower than the values reported in epidemiological studies on toxic Hg effects (WHO, 1991). Even studies with a great number of participants did not show a relationship between the intensity of the subjective complaints and internal mercury exposure (Ahlqwist et al., 1988, Ahlqwist et al., 1999; Melchart et al., 1998).

Almost one fourth of the patients examined by us were atopic with symptoms like rhinitis allergica, atopic eczema, or allergic asthma, that would explain many of the patients' complaints. These patients, suffering from various well documented allergies, were encouraged by the heated public debate and hoped to find the cause for their atopic disease in amalgam. However, Scandinavian studies with a larger study population did not find any indication that amalgam increases the prevalence of atopic diseases (Herrström and Högstedt, 1994). The so called "amalgam allergy" has often been quoted by the media as a frequent side-effect of amalgam but the term amalgam allergy has been falsely used by these authors to describe various subjective health disturbances. Only one of our forty patients had a contact sensitization to amalgam classified as a type IV reaction and met the criteria of an allergy, a definition first introduced by Coombs and Gell. Even in case of a positive patch test the removal of the amalgam fillings is only recommended if a contact allergy is clinically relevant, i. e. only if there is a chronological or topographic correlation between the clinical picture of contact stomatitis, gingivitis, or lichen ruber and the application of an amalgam filling (Fuchs, 1994), as was the case in one individual in our patients' group. After removing this patient's amalgam fillings the lichenoid lesions healed up completely, whereas the reported vegetative and psychic complaints continued even after one year.

Patients showed increased psychic strain and striking experienced distress. They mostly stated moderately pronounced depressive symptoms, and in the psychometric tests they resembled patients with psychosomatic disorders. Twenty percent of the patients had considerable depressive symptoms. A major depression was diagnosed in five of these patients and three other patients showed a depression together with a somatization disorder. More than one fourth of the patients fulfilled the diagnostic criteria of a somatization disorder according to ICD-10, a result that agrees with other studies in amalgam patients (Bågedahl-Strindlund et al., 1997). These patients are strongly convinced that they are physically ill and refuse to consider that psychosocial factors might be responsible for their symptoms. Other studies found an even higher percentage of other psychiatric disorders like anxiety disorders and depression (Bratel et al., 1997). The questionnaires that we used were self-reported data and there is a tendency for underestimation of the influence of psychological factors if they are answered conforming to social desirability. It can be assumed that some patients filled in those forms where a psychological context was recognizable in a deliberately "inconspicuous" way because they were afraid that their complaints might be considered psychiatric. This tendency did not occur as much in the SOMS which deals predominantly with physical symptoms. Current studies do not support the theory that amalgam fillings may cause psychic or neurological disorders, as often mentioned by the opponents of amalgam (Björkman et al., 1996; Saxe et al., 1995, 1999).

Our findings suggest that psychotherapy or psychiatric treatment is the adequate therapeutic approach for many patients with amalgam-related complaints. No evidence was found for the necessity of detoxification by elimination therapies, as often recommended. Likewise we don't support the expensive replacement of the amalgam fillings with other dental materials that may be even more problematic from an allergologic point of view. The results of our study strengthen the need of an "environmentally psychosomatic" view in the expanding environmental health care system that mainly focuses on the intense testing of noxious substances. The insufficient consideration of psychosocial factors or, conversely, the undifferentiated classification of complaints as "psychogenic" prolongs the time to refer the suffering patients to an adequate therapy.

In summary, our study gives a heterogeneous picture of the patients with amalgam-related complaints. No symptoms of mercury intoxication or significantly elevated mercury concentrations were found in the patients. One fourth of the patients

suffered from various atopic diseases and in more than one third one or several psychic disorders were diagnosed. Further studies are needed in the group of patients who showed neither an atopic predisposition nor an influence of psychosocial factors.

Acknowledgements. The study was supported by a grant from the Deutsche Forschungsgemeinschaft DFG, TR 424/1-1.

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