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Characterization of health complaints before and after removal of amalgam fillings — 3-year follow-up

GUNVOR BENTUNG LYGRE[1], THERESE THORNTON SJURSEN[2], JOHANNA SVAHN[1], VIGDIS HELLAND[1], BIRGITTE FOS LUNDEKVAM[1], KNUT DALEN[3,4] & LARS BJÖRKMAN[1,2]

[1]*Dental Biomaterials Adverse Reaction Unit, Uni Health, Uni Research, Bergen, Norway,* [2]*Department of Clinical Dentistry,* [3]*Department of Biological and Medical Psychology, University of Bergen, Norway, and* [4]*Institute of Health and Society, University of Oslo, Norway*

Abstract

Objective. Some patients attribute health complaints to amalgam fillings and report improvement of health after replacement of amalgam fillings. The aim of the present study was to characterize the changes of different health complaints after replacement of amalgam fillings and compare with an external reference group from the general population. ***Materials and methods.*** The study group included 20 patients with health complaints attributed to amalgam fillings who were participants in the treatment group of a clinical trial at the Norwegian Dental Biomaterials Adverse Reaction Unit. The patients were asked to indicate the intensity of local and general health complaints on numeric rating scales (0–10) before removal of amalgam fillings and at follow-up 3 years after removal. Data from the patient group were compared with data from an external reference group ($n = 441$). ***Results.*** Before treatment the mean intensity of complaints were on a higher level in the treatment group compared to the reference group. The most frequently reported complaints in the treatment group were gastrointestinal symptoms, fatigue, pain from muscles and joints, symptoms from ear/nose/throat and difficulty concentrating. From pre-treatment examination to the 3-year follow-up 20 of 23 health complaints decreased, being statistically significant for taste disturbances, pain from muscles and joints, gastrointestinal complaints, complaints from ear/nose/throat and fatigue. ***Conclusions.*** The inter-individual variation of intensities of health complaints was considerable and the reduction of health complaints varied for the different complaints. Several factors may be of importance for the observed reduction of complaint intensity.

Key Words: *amalgam fillings, health complaints, removal*

Introduction

A number of persons report to be concerned about potential health risks associated with amalgam fillings [1,2].

Patients with health complaints attributed to amalgam fillings comprise a heterogeneous group, with complaints ranging from local intra-oral complaints to multiple general health complaints associated with several organ systems [3–5]. However, it has been shown that, after removal of amalgam fillings, health complaints are not reduced to normal levels [6].

In a controlled before-and-after study with participants recruited from previously examined patients at the Dental Biomaterials Adverse Reaction Unit [7], a reduction of self-reported health complaints (measured by numeric rating scales for orofacial and general health complaints) was observed at follow-up at 3 years after replacement of all amalgam fillings. Changes in index scores for intra-oral and general health complaints were significantly reduced from inclusion into the study to the 3-year follow-up. Changes of the separate items within the index scores were not reported.

The aim of the present study was to further investigate and characterize the reduction of the different health complaints 3 years after replacement of amalgam fillings and compare with health complaints in an external reference group from the general population.

Correspondence: Gunvor Bentung Lygre, Dental Biomaterials Adverse Reaction Unit, Uni Health, Uni Research, Årstadveien 17, N-5009 Bergen, Norway. Tel: +47 55 58 60 27. Fax: +47 55 58 98 62. E-mail: gunvor.lygre@odont.uib.no

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Materials and methods

Participants

During the period 1993–1999, a total of 368 patients were referred to the Dental Biomaterials Adverse Reaction Unit for examination of suspected adverse reactions to dental materials. Among the main tasks of the unit is dental and medical examination of patients with health complaints attributed to dental materials [8,9].

The referred patients had a number of different health complaints and the majority was referred to the unit because of general health complaints attributed to amalgam fillings. Among these, some patients also had lesions in contact with specific dental materials (lichenoid contact lesions) and these patients were generally recommended replacement of the materials. Patients with only subjective health complaints were not recommended replacement.

During the period 2000–2001, 358 of the patients were asked to complete a follow-up questionnaire (Questionnaire 1) [7,9]. Completed questionnaires were returned by 207 patients (response rate 58%). Based on responses from Questionnaire 1 and after application of inclusion and exclusion criteria (Table I), the final treatment group consisted of 20 patients (14 women and 6 men) [7]. The treatment group had all amalgam fillings removed and replaced with other dental restorative materials.

Table I. Eligibility criteria. Inclusion criteria were applied based on information from initial examination and Questionnaire 1. Exclusion criteria were applied in relation to the pre-treatment examination in September 2002.

Inclusion criteria
Referred to the Norwegian Dental Biomaterials Adverse Reaction Unit for examination of health complaints attributed to amalgam fillings
Amalgam fillings still present
No diagnosed contact allergy to substances in resin-based dental materials
Health complaints from at least three different organ systems
Data on mercury in blood and urine from initial examination
Aged 25–55 at initial examination
Accepted to be contacted in a follow-up study
Exclusion criteria
Severe medical disorders (e.g. Multiple Sclerosis, ALS, severe rheumatoid arthritis)
Severe food allergies
Psychological difficulties or psychiatric disorders which could influence the dental treatment
Complicated therapy (severe periodontitis, high caries activity and/or need for complicated dental rehabilitation, e.g. bridges)
Inclusion criteria no longer fulfilled

Instruments

Information of education, recent dental treatment and current health complaints was obtained by a questionnaire sent by mail (Questionnaire 1). Health complaints were measured by numeric rating scales included in the questionnaire. The patients were asked to indicate the intensity of orofacial health complaints (intra-oral; six items, and extra-oral; five items) and general health complaints (12 items) on horizontal scales marked from 0–10, where 0 indicated no health complaints and 10 indicated worst possible complaints [7,9]. Internal consistency, estimated by Cronbach's alpha, for these three scales were 0.662, 0.723 and 0.803, respectively [7].

Mercury concentration in blood and urine was analysed by cold vapour atomic absorption spectrophotometry [10] and mercury concentration in serum by sector field inductively coupled plasma-mass spectrometry [11].

Treatment

The participants ($n = 20$) underwent a pre-treatment examination consisting of a medical examination with collection of blood and urine samples and a dental examination [7]. At this pre-treatment examination the participants were also asked to complete a questionnaire and to indicate the intensity of their health complaints on the same type of scales as included in Questionnaire 1.

Table II. Background data obtained at pre-treatment ($n = 19$).

Women, *n* (%)	13 (68)
Age (years) at pre-treatment, *M* (SD)	49 (6.8)
Age (years) at 3-year follow-up, *M* (SD)	53 (6.7)
Education[a] (years), *M* (SD)	11.2 (3.3)
On sick leave or disability pension, *n* (%)	8 (42.1)
Used medication last 12 months, *n* (%)	
Analgesics	14 (73.7)
Antidepressants	3 (15.8)
Vitamins/dietary supplements	13 (68.4)
Participants' assessments of risks associated with dental amalgam, *n* (%)	
Very high	16 (84.2)
Medium	3 (15.8)
Low	0
Very low	0
Number of amalgam surfaces at pre-treatment, *M* (SD)	24.3 (10.3)
Concentration of mercury at pre-treatment, *M* (SD)	
Blood (nmol/L)	14 (6)
Urine (nmol/L)	19 (13)

[a]Obtained at initial examination.

The participants had all dental amalgam fillings removed and replaced with other restorative materials. The replacement was performed by the patients' own dentists according to written guidelines from the Dental Biomaterials Adverse Reaction Unit. The guidelines included use of rubber dam, high-volume suction and water cooling and the dentists were advised to remove the fillings in chunks using a new, sharp metal bur [12]. The replacement of amalgam fillings was completed between April 2003 and June 2005 and the cost of the replacement was covered by the unit.

The participants were examined at the unit 3 years after completed removal of amalgam fillings. One patient stayed abroad for a long time and could not participate at 3-year follow-up, leaving 19 patients for further analysis (Table II). At 3-year follow-up, the patients were asked to complete a questionnaire and to indicate the intensity of orofacial and general health complaints on the same type of scales as used in Questionnaire 1 and in relation to the pre-treatment examination.

External reference group from the general population in Norway

The intensities of the participants' health complaints were compared with data from a questionnaire sent to an external reference group from the general population in Norway. The sampling was performed during spring 2004 by Statistics Norway in conjunction with a previous study [9] and this group was similar to the treatment group regarding age, gender and education. Responses were received from 441 of 800 individuals, yielding a response rate of 55%.

Statistical analyses

Paired sample *t*-test was used to analyse differences in symptom scores before replacement of amalgam and 3 years after replacement. Mann-Whitney U-test and independent-sample *t*-test were used to test differences between groups. Spearman's correlation was used to examine correlations between variables. Effect size for the differences between symptoms at pre-treatment and follow-up at 3 years was calculated as standardized response mean (SRM). Values of ≥0.20, ≥0.50 and ≥ 0.80 have been proposed to represent small, moderate and large responsiveness, respectively [13].

A *p*-value equal to or less than 0.05 was considered statistically significant. The statistical software SPSS 15 (SPSS Inc., Chicago, IL) was used.

The study was approved by the Regional Committee for Medical Research Ethics in Western Norway and registered at ClinicalTrials.gov (NCT00346944).

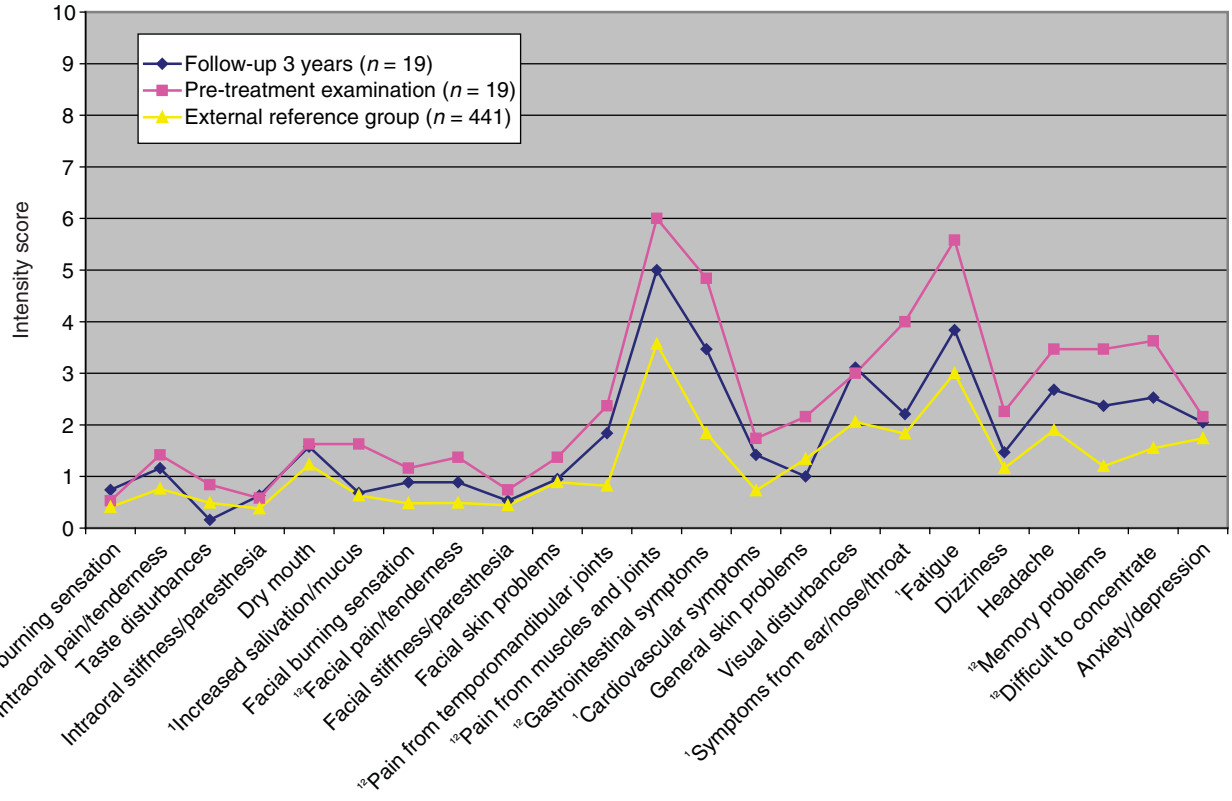

Figure 1. Mean intensity of health complaints in treatment group before and 3 years after removal of amalgam fillings and mean intensity of health complaints in the external reference group. [1] Statistically significant difference between treatment group at pre-treatment and external reference group. [1,2] Statistically significant difference between treatment group, both at pre-treatment and at 3 year follow-up, and external reference group.

Table III. Number of patients with different intensity of health complaint at pre-treatment, number of patients with changed complaint intensity at 3-year follow-up and number of patients with intensities of complaints above the mean levels in reference group at pre-treatment and 3-years follow-up (n = 19).

	Pre-treatment, no of patients						Three-year follow-up, no of patients			
	Intensity of complaints[a] grouped									
	0	1–3	4–6	7–9	10	Intensity of complaints above the reference group mean	Decreased intensity	No change	Increased intensity	Intensity of complaints above the reference group mean
Orofacial complaints										
Intra-oral complaints										
Burning sensation	13	6	0	0	0	6	3	13	3	5
Pain/tenderness	8	8	2	1	0	11	6	8	5	9
Taste disturbances	13	5	1	0	0	6	6	11	2	3
Stiffness/paresthesia	13	5	1	0	0	6	5	10	4	5
Dry mouth	11	4	3	1	0	6	3	10	6	5
Increased salivation	9	6	4	0	0	10	8	9	2	5
Extra-oral complaints										
Facial burning sensation	14	3	1	1	0	5	4	11	4	5
Facial pain/tenderness	14	2	0	3	0	5	4	10	5	8
Facial stiffness/paresthesia	15	2	2	0	0	4	4	11	4	6
Facial skin problems	10	8	0	1	0	9	7	9	3	6
Pain from temporomandibular joint	9	4	3	3	0	10	9	4	6	11
General complaints										
Pain from muscles and joints	1	2	11	2	3	16	10	5	4	15
Gastrointestinal complaints	1	4	10	3	1	18	13	1	5	14
Cardiovascular complaints	9	8	1	1	0	10	8	8	3	8
General skin problems	9	4	5	1	0	9	6	11	2	7
Visual disturbances	4	8	5	1	1	10	8	2	9	9
Complaints from ear/nose/throat	2	7	7	2	1	17	13	4	2	11
Fatigue	1	5	4	8	1	13	11	4	4	12
Dizziness	8	7	1	3	0	8	8	8	3	7
Headache	5	6	3	4	1	9	8	6	5	12
Memory problems	3	7	8	0	1	15	11	3	5	12
Difficult to concentrate	2	6	10	0	1	14	10	4	5	12
Anxiety/depression	8	5	5	1	0	8	7	5	7	7

[a]Numeric rating scales (0–10).

Results

Complete data from 3-year follow-up were received from 19 of the 20 patients in the treatment group, as one patient was not able to attend the 3-year follow-up.

Background data obtained at the pre-treatment examination (n = 19) is presented in Table II. There were no statistically significant differences in intensities of complaints between the time when participants were selected (Questionnaire 1) and the time of examination at the unit before removal of amalgam fillings (pre-treatment examination), except for anxiety/depression, which had decreased from 3.0 (SD = 3.2) to 2.2 (SD = 2.7) (paired t-test; p = 0.048, n = 19).

At pre-treatment examination the mean intensity of all complaints was on a higher level in the treatment group (n = 19) compared to the external reference group (n = 441) (Figure 1). In the treatment group

Table IV. Mean and standard deviations of separate orofacial and general items at pre-treatment examination and at 3-year follow-up and calculated effect size (n = 19).

	Pre-treatment		Follow-up at 3 years			
	M	SD	*M*	SD	*p*-value[a]	Effect size SRM[b]
Orofacial complaints						
Intra-oral complaints						
Intra-oral burning sensation	0.5	0.91	0.7	1.72	0.586	−0.127
Intra-oral pain/tenderness	1.4	1.90	1.2	1.83	0.654	0.105
Taste disturbances	0.8	1.39	0.2	0.38	0.050*	0.483
Intra-oral stiffness/paresthesia	0.6	1.12	0.6	1.64	0.905	−0.028
Dry mouth	1.6	2.41	1.6	2.43	0.916	0.025
Increased salivation	1.6	1.98	0.7	1.86	0.064	0.452
Extra-oral complaints						
Facial burning sensation	1.2	2.19	0.9	1.94	0.685	0.094
Facial pain/tenderness	1.4	2.75	1.2	1.83	0.457	0.174
Facial stiffness/paresthesia	0.7	1.70	0.5	1.17	0.429	0.186
Facial skin problems	1.4	2.22	1.0	1.87	0.306	0.242
Pain from temporomandibular joints	2.4	2.90	1.8	2.46	0.538	0.144
General complaints						
Pain from muscles and joints	6.0	2.60	5.0	2.38	0.040*	0.507
Gastrointestinal complaints	4.8	2.54	3.5	2.57	0.038*	0.512
Cardiovascular complaints	1.7	2.42	1.4	2.39	0.488	0.162
General skin problems	2.2	2.59	1.0	1.41	0.053	0.476
Visual disturbances	3.0	2.79	3.1	2.90	0.882	−0.035
Complaints from ear/nose/throat	4.0	2.54	2.2	2.15	0.002*	0.833
Fatigue	5.6	2.91	3.8	2.27	0.006*	0.717
Dizziness	2.3	3.00	1.5	1.81	0.135	0.359
Headache	3.5	3.70	2.7	2.50	0.284	0.253
Memory problems	3.5	2.41	2.4	2.43	0.101	0.397
Difficult to concentrate	3.6	2.48	2.5	2.34	0.078	0.465
Anxiety/depression	2.2	2.65	2.1	2.72	0.840	0.047

*Statistically significant.
[a]Paired sample *t*-test.
[b]Standardized response mean (Mean change score/Standard deviation of change score).
Values of ≥ 0.20, ≥ 0.50 and ≥ 0.80 have been proposed to represent small, moderate and large responsiveness, respectively.

(n = 19), the most frequently reported complaints were pain from muscles and joints, gastrointestinal symptoms, symptoms from ear/nose/throat, fatigue and difficulty concentrating (Table III). The mean intensities of these complaints were 6.0, 4.8, 4.0, 5.6 and 3.6, respectively (Table IV), compared to the external reference group (n = 441), with mean intensities of 3.6, 1.8, 1.8, 3.0 and 1.6. Pain/tenderness was the most frequently reported intraoral complaint at pre-treatment (Table III).

At pre-treatment, significant positive correlations (Spearman's correlations) were seen between several local and general complaints, including gastrointestinal complaints which were positively correlated to facial skin problems, visual disturbances, fatigue, dizziness, memory problems and difficulty concentrating. Fatigue was positively correlated to dizziness, memory problems, difficulty concentrating and anxiety/depression.

A general decrease of the mean intensity of health complaints was seen from pre-treatment to the follow-up after 3 years, except for a small, non-significant, increase in intra-oral burning and visual disturbances and no change in intra-oral stiffness/paresthesia and dry mouth (Figure 2 and Table IV). Decreased intensity of one or more general health complaints was

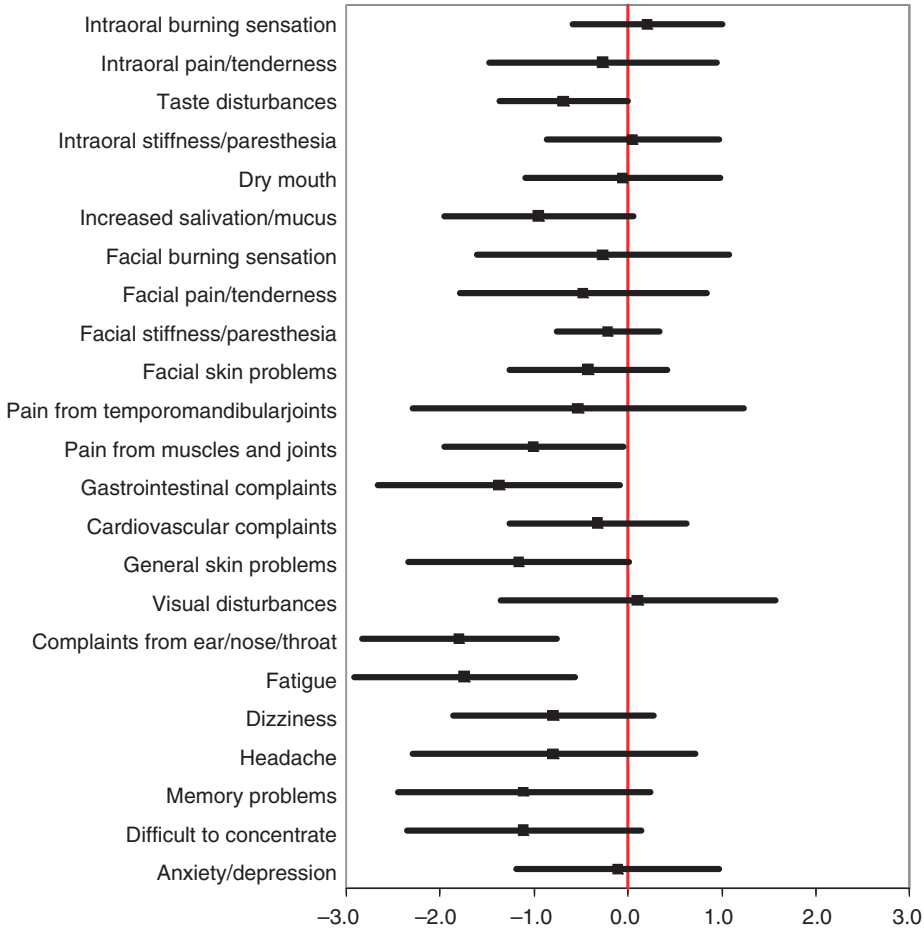

Figure 2. Mean difference (and 95% confidence interval) in intensity of local and general health complaints (value at 3-year follow-up minus pre-treatment value).

observed in all patients and decreased intensity of one or more local complaints was observed in 17 patients. However, the variation between patients was high. The mean difference in intensity of each single complaint from pre-treatment to follow-up after 3 years was statistically significant (paired sample *t*-test) for five items including taste disturbances ($p = 0.050$), pain from muscles and joints ($p = 0.040$), gastrointestinal symptoms ($p = 0.038$), symptoms from ear, nose and throat ($p = 0.002$) and fatigue ($p = 0.006$) (Table IV). The largest response was seen for complaints from ear/nose/throat and fatigue. Moderate responsiveness was seen for pain from muscles and joints and gastrointestinal complaints (Table IV) [13]. No statistically significant correlations were seen between change scores of these five items. Neither were there any significant correlations between the change scores of these items and reduction of mercury in blood serum.

At 3-year follow-up the mean intensities of six items (facial pain and tenderness, pain from temporomandibular joints, pain from muscles and joints, gastrointestinal symptoms, memory problems and difficult to concentrate) were still significantly higher in the treatment group compared to the external reference group from the general population (Figure 1). The prevalence of complaints rated 3 or higher is presented in Figure 3.

Most patients reported some reduction in intensity of general complaints. For orofacial complaints, most patients reported no change. Some patients reported increased intensity of complaints (Table III). The number of patients who reported intensity of complaints above mean level in the external reference group was reduced from pre-treatment to 3-year follow-up for 11 of 12 general complaints and all six intra-oral complaints (Table III).

Discussion

The aim of the present study was to characterize the reduction of health complaints after replacement of all amalgam fillings observed in a controlled before-and-after study [7] and to compare the results with health complaints in a reference group from the general population.

Three years after removal of amalgam fillings different health complaints in 19 patients were characterized. In the present study detailed information

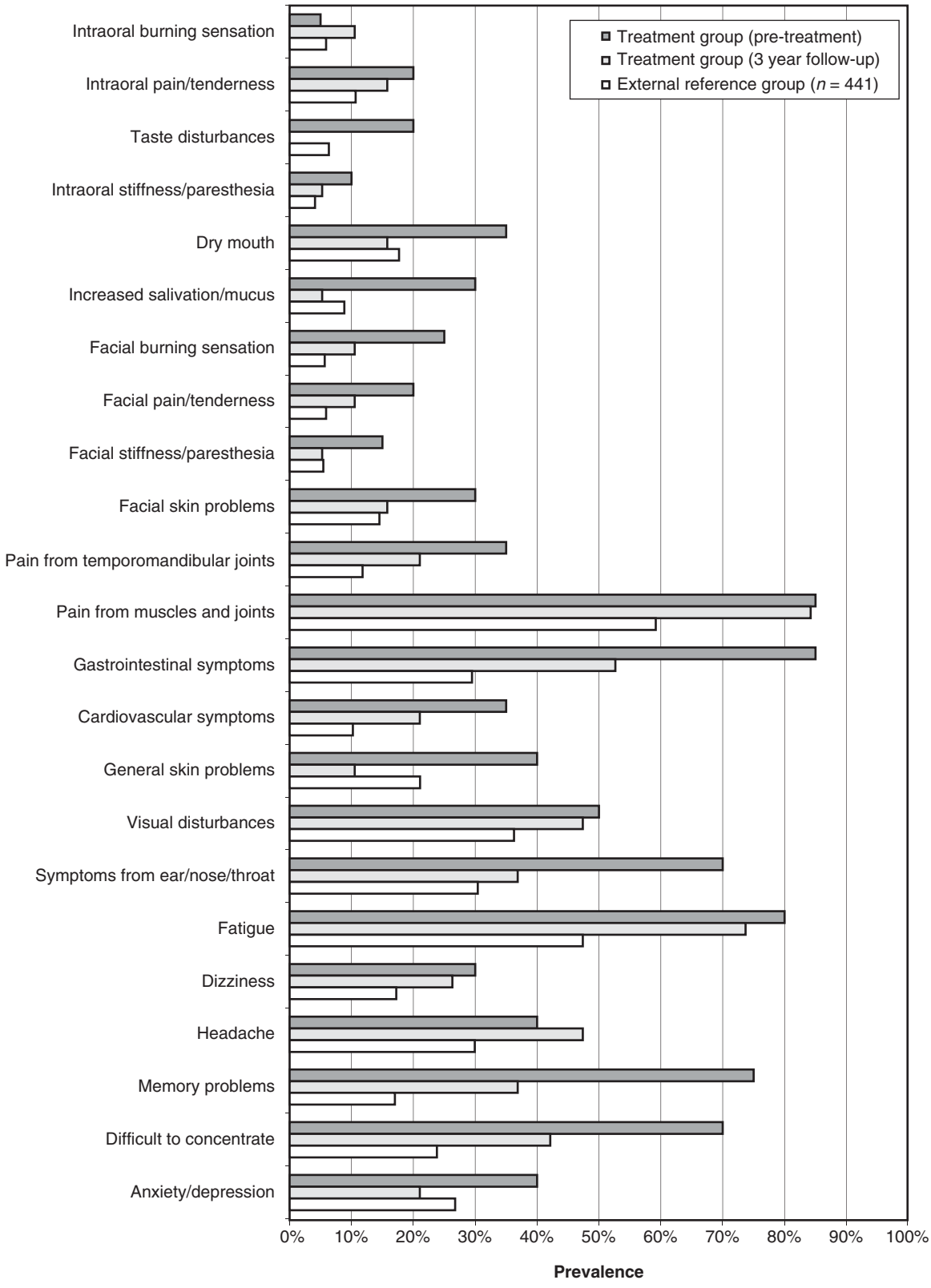

Figure 3. Health complaints with intensity rating value 3 or higher. Prevalence in treatment group at pre-treatment (n = 19) and at 3-year follow-up (n = 19) and in the external reference group (n = 441).

of both the nature of the different health complaints as well as the changes of these is described. The strength of the study is the prospective design and the long follow-up period.

The results show that health complaints in a group of individuals with health complaints attributed to amalgam fillings were reduced after removal of the fillings. Results from other studies also show

reduction of health complaints after removal of dental materials [6,14–16]. However, the extent to which the complaints were reduced varied for the different complaints and the inter-individual variation of intensities of health complaints was considerable.

The largest reductions in intensity of health complaints were seen for gastrointestinal symptoms, symptoms from ear, nose and throat and fatigue. At pre-treatment examination the patients reported high intensities of these complaints, indicating a high potential for improvement. Nevertheless, these symptom scores were still high at follow-up 3 years after the replacement of amalgam fillings.

The participants reported several health complaints and it is possible that some of these complaints are connected to each other. Eriksen et al. [17] describe three clusters of general complaints labelled 'Musculoskeletal complaints', 'Gastrointestinal complaints' and 'Pseudoneurological complaints'. Our study showed that several different complaints were positively correlated to gastrointestinal complaints and that fatigue, dizziness, memory problems and difficulty concentrating were positively correlated to each other. The cluster of pseudoneurological complaints, which includes fatigue, headache, memory problems and difficulty concentrating, is also reported by patients with 'unexplained medical symptoms' [18] and fibromyalgia [19]. One could assume that these complaints are connected to each other and will appear together.

The highest intensity of complaints was seen for musculoskeletal complaints both before and after removal of amalgam fillings. Despite that the decrease of pain from muscles and joints was statistically significant, the reduction was moderate (from score 6 to score 5) (Table IV). These complaints are also high in the general population, as shown in other studies [17,20]. It is possible that the relatively high intensities of pseudoneurological complaints (including fatigue, memory problems and difficult to concentrate) could be due to high intensity of musculoskeletal complaints. Even if the clusters are independent of each other, there could be a high degree of comorbidity [21,22].

The patients were selected from patients who had completed a follow-up questionnaire (Q1) with a response rate of 58% (n = 207). Similar response rates are also reported in other studies [6]. It has been suggested that individuals with most health complaints may not respond to health-related surveys [23]. This may have influenced both the treatment group and the reference group. However, in an earlier study by Lygre et al. [9], no statistically significant differences in intensities of health complaints between responders and non-responders were found. In addition, the response rate in the reference group (55%) [9] was similar to the response rate in the patient group for Questionnaire 1 (2000–2001).

The participants in the present study represent a selected group of patients who were referred to and examined at the Dental Biomaterials Adverse Reaction Unit several years earlier because of adverse reactions to amalgam restorations, assumed either by themselves or by medical or dental professionals [7]. At the initial examination at the unit (1993–1999) there were no indications to recommend replacement of amalgam fillings and the patients included in this study had acted according to this and had not removed their amalgam fillings. In a previous study we found that patients with higher intensities of complaints more often had dental materials removed, despite the lack of such recommendations from experts and the difference was highest regarding intra-oral complaints [24]. This could explain why the individuals included in the present study reported relatively low intensity of intra-oral complaints. Thus, the degree of possible reductions of local health complaints after removal of amalgam fillings was limited.

According to the exclusion criteria, individuals with severe medical disorders, severe food allergies and psychological difficulties or psychiatric disorders were excluded from the study. This could have influenced the results towards lower differences in health complaints between the treatment group and the general population.

The patients reported a similar profile of symptoms as the group of comparable individuals from the general population. The main difference was the intensity of the different complaints which was on a higher level in the patient group compared to the general population. The variation in intensities of health complaints between the individuals, both in the treatment group and in the general population, was large. The reported differences in symptom intensities between patients and the reference group were highest for general symptoms. For orofacial complaints the mean levels of different complaints were considerably lower in both groups and the differences were smaller. However, the patient group was heterogeneous and some patients reported high intensities of local complaints, whereas others had no local complaints at all.

After removal of amalgam fillings the health complaints were not reduced to the same levels observed in the general population. Similar results have been reported in other studies [6]. Nerdrum et al. [6] reported reduced physical and mental symptom load after removal of amalgam fillings. However, their findings did not support that removal of dental amalgam will reduce health complaints to normal levels.

Several different factors have to be assessed to interpret the results. After replacement of amalgam fillings the exposure to mercury is reduced [16,25,26]. However, in the present study, no significant correlations between the significantly reduced items and mercury levels were found. Further, no relationship between

number of amalgam fillings and number of self-reported health complaints has been observed in other studies [5,27]. However, Weidenhammer et al. [16] reported significant correlations between symptom score before amalgam removal and both inorganic mercury in plasma and mercury in urine.

Decrease of taste disturbances after removal of amalgam restorations has also been reported previously [28]. Since relatively high concentrations of mercury are found in oral tissues after exposure to amalgam restorations [29], mercury or other corrosion products released from amalgam restorations could be hypothesized to cause taste disturbances. Taste disturbances were statistically significantly reduced in our study, despite the fact that the mean intensity was low also before removal of amalgam fillings. However, no correlation between reduction of taste disturbances and reduced mercury in blood serum was observed.

Pain from muscles and joints, gastrointestinal complaints and fatigue had standardized response means greater than 0.5, while complaints from ear/nose/throat had a standardized response mean greater than 0.8, indicating moderate and large responsiveness, respectively. It may be hypothesized that these changes reflect side-effects from amalgam in sensitive individuals. Additional prospective studies are warranted to support or reject these findings.

Interestingly, a minor decrease of some pro-inflammatory markers in serum was observed in the same patient group after amalgam removal [30]. The potential role for immune mediated effects related to exposure to corrosion products released from amalgam restorations and possible interactions with co-existing morbidity needs to be further studied.

It has been hypothesized that health worries may predict the development of bodily complaints [31]. The patients' worry about negative health effects of existing amalgam fillings has been eliminated by removing the fillings, and this could have influenced the patients' experience of decreased intensity of health complaints.

At the examinations and follow-up at the unit the patients were taken care of by health personnel who were interested in and had the time to listen to patients' experiences. General care in association with the amalgam replacement and follow-up could also have influenced the results [32].

It has been suggested that the improvement may be due to normal fluctuations over time among patients with severe health complaints [6]. However, during the time interval from completing Questionnaire 1 to pre-treatment examination there were no statistically significant reductions in intensity of health complaints, except for anxiety/depression. At the pre-treatment examination the patients' anxiety/depression may have decreased because they could have felt that their complaints were taken seriously by health professionals and they looked forward to have their fillings replaced.

Conclusions

In a group of individuals with health complaints attributed to amalgam fillings the complaints were reduced after removal of the fillings. To which level the complaints were reduced varied for the different symptoms and the inter-individual variation of intensities of complaints was considerable. Several factors may be of importance for the observed reduction of complaint intensity.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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