

Nickel sensitization in orthodontically treated and non-treated female adolescents

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Summary

Background. The importance of the nickel exposure from fixed orthodontic appliances is under continuous discussion.

Objectives. Our aim was to investigate nickel allergy and the risk of nickel sensitization among female adolescents during orthodontic treatment with fixed appliances as compared with non-treated female adolescents.

Subjects and methods. Female patients starting or with ongoing orthodontic treatment ($n = 30$) and young females without a history of orthodontic treatment ($n = 140$) were studied. Patch testing with 5% nickel sulfate was carried out twice on each participant with an approximately 1-year interval. The subjects completed a questionnaire before the first testing.

Results. None of the 7 orthodontic patients with a positive patch test reaction to nickel had any clinically visible intraoral allergic symptoms during their treatment. No significant difference was seen in the occurrence of positive nickel reactions in regard to orthodontic treatment, or between the first and second tests. In the treatment group, 2 patients changed from nickel-positive to nickel-negative during the observation period, and one patient showed an opposite change. The quantity and course of changes in the repeated nickel patch test reactions did not differ significantly between the subjects with and without orthodontic treatment experience.

Conclusions. Nickel sensitization from orthodontic appliances is improbable, but nickel sensitization may develop also during orthodontic treatment.

Key words: nickel sensitization; orthodontic treatment; patch testing.

During the last decades, the prevalence of nickel contact allergy among young adults has been high. Some decrease in the prevalence of nickel allergy among young females was reported after the implementation of the Nickel Directive in Europe (1–3). However, even in Scandinavian countries, >10% of young females still

seem to become sensitized. Among Danish 31–49-year-old female patients (1), as well as among female North American patients, the occurrence of nickel sensitization has increased (4).

The importance of nickel exposure from fixed orthodontic appliances is under continuous discussion (5, 6), as fixed orthodontic appliances contain nickel from 8% up to >50% (7, 8). *In vitro* and *in vivo* studies have shown release of nickel ions from metallic orthodontic appliances during treatment (8–12). The amounts released *in vitro* have been distinct but low, at approximately 22–40 µg/day from commonly used full fixed appliances including both the upper and lower jaw. Significantly

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increased nickel contents have also been detected in the dental plaque of orthodontic patients (25 µg/g) as compared with control subjects (15 µg/g) (9, 10). However, several case reports have described allergic reactions caused by nickel in orthodontic patients (5, 13–16). On the other hand, oral exposure from nickel-containing orthodontic appliances has been suggested to decrease the risk of sensitization (17, 18) and, in spite of occasional case reports, allergic symptoms during orthodontic treatment are rare (19, 20).

Our aim was to investigate the importance of nickel allergy and the risk of nickel sensitization among female adolescents during orthodontic treatment with fixed appliances as compared with non-treated female adolescents.

Subjects and Methods

The study was carried out during the years 2006–2008 in Turku, Finland. Ethical approval was given by the ethical board of the Intermunicipal Hospital District of Southwest Finland.

Study design and subjects

The study group consisted of female patients starting or with ongoing orthodontic treatment ($n = 30$) and young females without a history of orthodontic treatment ($n = 140$). The study included two nickel patch tests per participant at approximately 1-year intervals and a questionnaire, which the subjects completed before the first test. The questions included personal data, information on previous skin symptoms while in contact with metallic objects, and the number of piercings in ears and/or elsewhere in the body. Written informed consent from each participant and/or her legal representative was required before inclusion in the study.

Non-treatment group

Six secondary schools in the city of Turku were visited, and all female students with no history of previous orthodontic treatment with fixed appliances were invited to participate in the study. Information on the study was given in the classrooms both verbally and by delivering written information, which, along with a consent form, was given to the students to take home to their parents. A total of 140 students agreed to participate. Their age ranged from 12 to 17 years, and the mean age was 13.7 years [standard deviation (SD) ± 1.3 years].

For the retesting, the subjects were invited by a letter and/or a telephone call. Eleven subjects did not attend for the second test, and they were excluded from the study, giving a total of 129 participants in the non-treated group.

Treatment group

The orthodontists and orthodontic postgraduate students working in the dental school and the municipal health centre in Turku were recruited to pass the information to their female adolescent/young adult patients starting or undergoing orthodontic treatment with fixed appliances, and to invite them to participate in the study. The total number of patients agreeing to participate was 30. Their age ranged from 10 to 39 years, and the mean age was 14.7 years (SD ± 6.3 years). In 16 participants, the first patch test was performed before treatment, and in 14 the orthodontic treatment was already ongoing at the time of the first test. The retesting was carried out during the regular orthodontic visits.

Fixed orthodontic appliances

Orthodontic appliances used in the study patients consisted of bands, brackets, arch wires in one jaw or in both jaws, and occasionally intraoral/face bows (Fig. 1). All bands, brackets and intraoral/face bows were made of stainless steel with 8–12% nickel. Several arch wires were routinely used during the treatment of each orthodontic patient, starting with elastic arch wires with a high nickel content (50% or even more), and finishing with stiff arch wires with a low nickel content. The number of brackets and the details of the fixed appliance varied somewhat between the patients, depending on the treatment plan.

Nickel patch tests

Patch tests with nickel sulfate (5% in petrolatum; Chemotechnique Diagnostics, Vellinge, Sweden) were

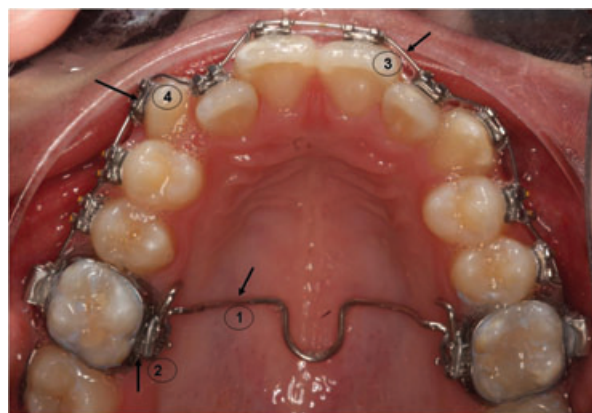


Fig. 1. A typical fixed appliance in the upper jaw with the palatal bow (1), stainless steel bands (2), a flexible nickel–titanium arch wire (3), and stainless steel brackets (4).

applied with Finn Chambers® (Epitest, Tuusula, Finland) on Scanpor® tape (Norgesplaster A/S, Vennesla, Norway) to the lateral aspect of the upper arm. The location of the patch allowed each subject to remove the patch by herself, which was done on day 2 (D2). The reaction was interpreted 1–3 days after the removal (D3, D4, or D5), according to the International Contact Dermatitis Research Group criteria. A positive reaction required erythema and oedema and/or papules. All doubtful reactions were separately recorded.

The application of the patches and the interpretation of the test reactions at schools were performed by a dermatologist (KL) and the orthodontist chief investigator (HK) together. In the later stage of the study, the patch tests were carried out by KJ and HK, or HK alone; they were trained in patch testing by the dermatologist (KL). In the treatment group, the tests were applied during the regular visits to the orthodontist. All five orthodontists involved in patch testing were trained by the dermatologist (KL) at the allergy unit of Turku University Hospital.

All positive and doubtful patch test reactions were read by either HK or KL. In addition, all doubtful reactions were photographed, and their interpretations were confirmed by the dermatologist (KL) with blinded reading of the reactions in the photographs. Regarding clearly negative test results, the reading was performed either by HK or by the treating orthodontist.

Statistical analysis

Data from the questionnaires and patch tests were installed and analysed in spss® for Windows® (version 17.0). In prevalence calculations, nickel allergy was considered to be present if either of the two nickel patch test results were positive. Pearson's chi-square test was used to test the differences between groups. ANOVA was used to compare means between groups. Multivariate logistic regression was used to estimate the predictive value for nickel allergy of age, orthodontic treatment, number of piercings, and previous skin symptoms while in contact with metal items. In the logistic regression model, the independent variables were dichotomized (0 and 1), except for

age, which was entered as a continuous variable. The number of piercings was dichotomized: 0 = 0–2 piercings; 1 = 3 or more piercings. A general linear model (GLM) for repeated measurements was used to analyse the effects of the follow-up time and orthodontic treatment and their interaction on the change in nickel reactivity between groups with and without orthodontic treatment.

Results

The mean intervals between the first and second patch tests were 11.6 months ($SD \pm 1.40$ months) in the non-treatment group and 12.4 months ($SD \pm 4.39$ months) in the treatment group. Positive patch test reactions were seen in 16–23% of the subjects (Table 1). No significant difference was seen in the occurrence of nickel reactions in regard to orthodontic treatment, or between the first and second tests (Table 1).

None of the 7 orthodontic patients who had positive patch test results had any clinically visible intraoral allergic symptoms during their treatment, regardless of previous skin symptoms while in contact with metals, as reported by 5 of them.

Predictive data for a positive nickel test reaction

Eighty-six per cent of the adolescents had piercings in ears or elsewhere in the body at the time of the first as well as the second nickel test. Those with three or more piercings had positive patch test reactions significantly more often than those with one to two piercings or no piercings at all: 57%, 17%, and 4%, respectively ($p < 0.001$). The logistic regression analysis showed that the odds of having a positive nickel patch test reaction in at least one of the two patch tests was five-fold [odds ratio (OR) 4.7, 95% confidence interval (CI) 1.7–13.0, $p = 0.003$] for the subjects with three or more piercings as compared with those with only zero to two piercings, and ninefold (OR 9.4, 95% CI 3.7–23.9, $p < 0.001$) for the subjects who had experienced previous skin symptoms while in contact with metals. Neither age of the subject nor orthodontic treatment significantly affected the odds of having a positive nickel patch test reaction.

Table 1. Changes in the patch test reactions at 1-year intervals among the subjects with and without orthodontic treatment experience

	Nickel patch test reaction			
	No orthodontic treatment ($n = 129$)		Orthodontic treatment ($n = 30$)	
	Positive reaction, no. (%)	Negative reaction, no. (%)	Positive reaction, no. (%)	Negative reaction, no. (%)
Patch test 1	21 (16)	108 (84)	7 (23)	23 (77)
Patch test 2	27 (21)	102 (79)	6 (20)	24 (80)

Doubtful reactions are included in the negative reactions. Chi-square between non-treatment and treatment groups not significant ($p > 0.05$).

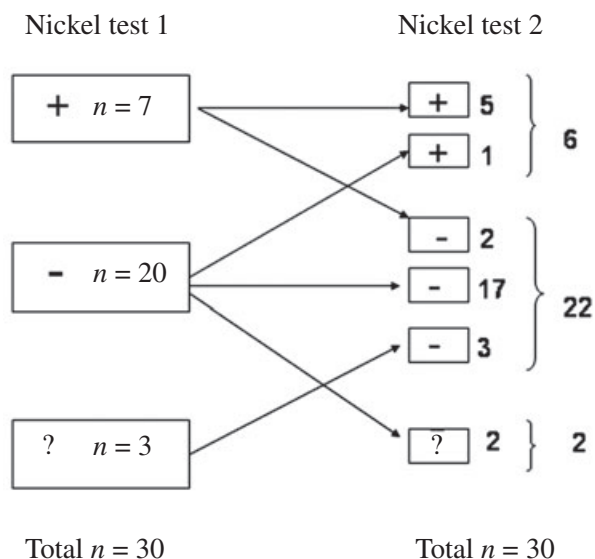


Fig. 2. Changes in nickel patch test results of the individual participants with fixed orthodontic appliances, from test 1 to test 2. The interval between the tests was approximately 1 year.

Changes in the patch test reactivity of repeated tests

In the treatment group, the first test yielded 7/30 positive patch test reactions, two of which changed to negative in the second test (Fig. 2). An opposite change, from a negative to a positive reaction, was seen in one patient. Doubtful reactions changed to negative in 3 patients, and an opposite change was seen in 2 patients (Fig. 2).

In the non-treatment group, a change from a positive to a negative reaction was seen in 1/21 patients; the rest of the positive reactions remained positive (Fig. 3). Negative reactions changed to positive in 6/93 subjects. Only one of the doubtful reactions changed to positive, whereas the majority of the doubtful reactions changed to negative after the follow-up period in the second testing (Fig. 3).

The quantity and course of changes in the repeated nickel patch test reactions did not significantly differ between the subjects with and without orthodontic treatment experience ($p = 0.13$).

Individual orthodontic patients with changes in patch test reactivity

Case 1. A 13-year-old girl with a history of childhood rheumatoid arthritis had permanent medication with methotrexate 5 mg weekly and hydroxychloroquine 300 mg daily. The first test was carried out before the orthodontic appliances were inserted, and the test result

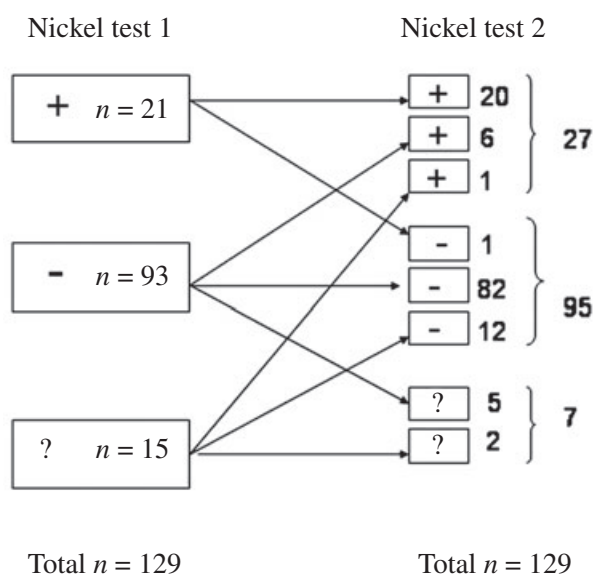


Fig. 3. Changes in nickel patch test results of the individual participants with no experience of orthodontic treatment, from test 1 to test 2. The interval between the tests was approximately 1 year.

was negative, although the patient had a history of dermatitis caused by jewellery. The medication remained similar, and the second test 1 year later gave a positive patch test reaction.

Case 2. A 39-year-old woman without any history of skin symptoms while in contact with metals had a history of atopic dermatitis, atopic mucosal symptoms, and food allergies. The first patch test was carried out 2 months after the insertion of the orthodontic appliances, and a positive reaction was seen. The second patch test yielded a negative result.

Case 3. A 13-year-old girl with a history of allergic rhinitis was tested before the insertion of the orthodontic appliances, and a positive (+) reaction was seen. She had neither a history of metal contact dermatitis nor any piercings. One year later, the patch test result was negative.

Discussion

Our results do not suggest any increased risk of sensitization to nickel among orthodontic patients treated with nickel-containing orthodontic appliances. The nickel sensitization rate was roughly similar in the treatment group (22%) and in the control group (20%). Although nickel sensitization seemed to increase among the young control

group females during the 1-year follow-up period (from 16% to 20%), while no corresponding increase was registered in the treatment group, the changes in nickel reactivity were not significantly different between the groups. However, for this type of data, where the majority of test results remained the same, the statistical power of the GLM analysis is small, and eventual trends that might be clinically interesting will not reach statistical significance. The group of patients with orthodontic appliances was rather small in this study, and inferences regarding the risk of nickel sensitization between the groups should be made with caution.

A number of patients in the treatment group (14/30) were patch tested after the insertion of the fixed appliances, and this restricts interpretation of the results regarding the induction of nickel sensitization. In this group, 4/14 had a positive patch test reaction to nickel. Those 4 patients had also reported a history of skin symptoms while in contact with metals, but no symptoms developed after the insertion of the oral appliances in these 4 or in the other nickel-sensitive patients. A generalized skin reaction was reported by one patient, who had no history of metal intolerance, after the nickel-containing orthodontic appliance was inserted. No association of the skin reaction with the orthodontic appliance could be shown, as the patch test soon after the skin eruption gave a doubtful reaction, and the second patch test during the treatment gave a clearly negative result, suggesting increased skin irritability during the first test.

A positive nickel test reaction in the first test was seen in 2 patients, who had no history of metal contact dermatitis, and the second test gave negative results (cases 2 and 3). These patients had atopic histories, and it appears probable that the first patch test reaction was elicited by skin irritation. Non-specific patch test reactivity may be seen in atopic subjects with increased skin irritability (21), and irritant patch test reactions caused by metal salts are common (22).

Oral nickel exposure has even been suggested to provide tolerance against nickel sensitization (17). Our results support the view that, at least, orthodontic treatment with fixed appliances does not increase the risk of nickel sensitization in patients. One patient in the treatment group (case 1), however, had a negative nickel test result in the first test, but after 1 year of orthodontic treatment the test result was positive. As the patient had a history of dermatitis caused by cheap jewellery, the first test result was probably a false negative. Treatment of the rheumatoid arthritis could have suppressed the patch test reactivity, although no alteration in the medication was recorded.

Piercings were seen in the majority of the treatment group (81%) as well as of the non-treatment group (86%). Piercings were significantly associated with nickel sensitization, and this association has been frequently reported (23–25). The same is true for the history of metal contact-associated skin symptoms, although a recent study suggested that the validity of self-reported nickel allergy may be lower than previously believed (26). In the course of the follow-up year, 7 control subjects developed nickel sensitization. Possible sources of sensitization were not queried, but cheap jewellery is typically worn by girls of the age of the subjects in our study group. It appears evident that the Nickel Directive does not cover all types of item in contact with the skin, that we still have sources of nickel sensitization, and that sensitizing nickel exposure still occurs despite EU regulations (27, 28). On the other hand, nickel-releasing jewellery can also be purchased from countries outside the EU area (29).

The number of doubtful reactions was high among the participants, in the first test in particular. Those reactions were probably mainly irritant reactions, as 15/18 doubtful reactions changed to negative and only one of them changed to positive in the second test. The limit between a positive 1+ and a doubtful reaction may vary, whereas negative reactions are mainly obvious. The variation in patch test reactivity may be attributable to multiple intra-individual or technical reasons (30–32). Inadequate contact after the application, an inadequate amount of the test substance, friction or inter-individual variation in the reading of patch tests may contribute to variation (33–35). The arm is not the preferred location for patch testing, and increased friction may have led to doubtful reactions in this study. The positive reactions were interpreted by the dermatologist investigator, but some variation in technical details was possible, and the removal of the patch was carried out by each participant herself. The subjects were advised to observe the ring of the Finn Chamber® in the skin, and none of them reported problems. Intra-individual variation in patch test reactivity may occur, and fluctuations in systemic T-cell reactivity have been reported in association with the variation in nickel test reactivity in the same individual (36). Those 7 subjects who developed positive patch test reactions in the second test, however, seemed to have developed nickel sensitization during the follow-up year.

Conclusions

Nickel sensitization from orthodontic appliances is improbable, but nickel sensitization may also develop during orthodontic treatment.

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