Acta Derm Venereol (Stockh) 1990; 70: 417–420

Nickel in Nails, Hair and Plasma from Nickel-hypersensitive Women

B. GAMMELGAARD[1] and N. K. VEIEN[2]

[1]*Royal Danish School of Pharmacy, Department of General Chemistry, Copenhagen, and Dermatology Clinic, Ålborg, Denmark*

The concentrations of nickel in finger-nails, toe-nails, hair and plasma from 71 nickel-hypersensitive women and 20 non-hypersensitive women were determined. Nickel concentrations in finger-nails were significantly higher than in toe-nails in both the nickel-hypersensitive group and the control group. Nickel-sensitive women had significantly higher levels of nickel in toe-nails, hair and plasma than had control subjects, whereas there was no significant difference in nickel concentration in finger-nails between the two groups. No correlation could be demonstrated between nickel levels in any combination of nails, hair and plasma in the nickel-hypersensitive or in the control group.

(Accepted February 26, 1990.)

Acta Derm Venereol (Stockh) 1990; 70: 417–420.

B. Gammelgaard, Royal Danish School of Pharmacy, Department of General Chemistry, 2 Universitetsparken, DK-2100 Copenhagen, Denmark.

A number of investigations have been carried out to determine the uptake and excretion of nickel in individuals who are occupationally exposed to this metal. Determination of the levels of nickel in blood or/and urine over a period of time has been the usual method of studying nickel exposure (1–4).

The concentrations of nickel in the body fluids of healthy individuals are reasonably well established (5–8). Only a few studies have been made, however, of nickel levels in nickel-hypersensitive individuals (9, 10). The amounts of nickel in blood and urine vary significantly from day to day and increase rapidly a few hours after oral challenge with nickel (11, 12). The determination of the nickel status of an individual therefore requires several 24-h collections of urine pools or the collection of several blood samples.

The determination of nickel in nails or hair should be pursued as an alternative to blood and urine analysis. The nickel levels in nails and hair are less likely to be subject to diurnal variations than blood levels. The normal nickel concentrations in nails and hair are several orders of magnitude higher than the levels in blood and urine (13–15) thus reducing contamination during analysis to a minor problem. The sampling procedure is simpler, and there are no storage problems during the period between sampling and analysis.

The purposes of the present investigation were 1) to determine the levels of nickel concentrations in finger-nails, toe-nails, hair and plasma in nickel-hypersensitive women: 2) to ascertain whether there is any difference between nickel concentrations in nickel-hypersensitive and normal women, and 3) to determine if there is any correlation between the nickel levels in nails, hair and plasma.

MATERIALS AND METHODS

Seventy-one women (age distribution 34.7 ± 12.7 years, range 18–68 years) with positive patch tests to 5% nickel sulfate in petrolatum and 20 women of comparable age (age distribution 34.1 ± 10.3 years, range 22–53 years) with no history of nickel hypersensitivity participated in the study. None of the patients or control subjects were employed in the nickel plating industry or were otherwise heavily exposed to nickel. Samples of finger-nails, toe-nails, hair and plasma were obtained from as many of the 91 persons as possible. Due to nail-biting or recently cut nails, samples from all sites were not obtainable from all persons. Samples of finger-nails, toe-nails and hair were cut with a pair of scissors made of stainless steel. In control experiments, it was shown that the scissors did not release nickel.

Approximately 50 hairs were cut close to the scalp and trimmed to a length of 2 cm from the end closest to the scalp. Nails were cut from as many fingers or toes as possible. The samples were stored in acid-cleaned plastic containers until the analyses were carried out.

Prior to determining their weight, the nail and hair samples were washed as follows. Samples were first treated with a 0.1% solution of the surfactant Triton X-100 in an ultrasonic bath for 15 min. Then the samples were washed five times with ultrapure water followed by 5 one-minute treatments with ultrapure water in an ultrasonic bath. The rinsing solution contained less than 0.1 μg Ni/l. Finally the samples were dried at 70°C overnight in an oven. The washed samples were digested with a mixture of concentrated nitric and sulfuric acid and the nickel content was determined by adsorption differential pulse voltammetry, as

Table I. *The nickel content (ng/g) of nails, hair and plasma from nickel hypersensitive women and controls. N* = number of patients

	N	Mean	S.D.	Median	Range
Nickel-hypersensitive persons					
Fingernails	65	1080	1606	407	24–10309
Toe-nails	43	147	186	87	20–968
Hair	64	429	371	340	21–1739
Plasma	71	0.52	1.19	0.12	0.1–8.57
Control persons					
Finger-nails	18	1331	2139	450	31–8744
Toe-nails	13	63	43	69	20–144
Hair	16	244	245	149	23–946
Plasma	20	0.14	0.15	0.10	0.10–0.79

described elsewhere (16). The limit of detection of this method is less than 0.01 ng/g. Taking the uncertainty on determination of blank values of the wet ashing into account, the limit of determination amounts to 20 ng/g. Any result below this limit was assigned the value 20 ng/g.

Blood samples were collected with Venflon (TM) cannulas in heparinized, acid-cleaned polyethylene tubes. Plasma samples were stored at −20°C. Prior to analysis, plasma samples were diluted 1+1 with an aqueous solution 10^{-3} M in nitric acid and 0.1% in Triton X-100 and quantified by Zeeman-corrected atomic absorption spectrometry as previously described (17). The limit of detection was 0.10 µg/l, and any result below this limit was assigned the value 0.10 µg/l.

Statistics

The Mann-Whitney test was applied for comparison of the medians of two samples and the Spearman rank correlation coefficient was used to test the correlation of two variables (18). Differences were considered to be significant for $p < 0.05$.

RESULTS

The nickel content of nails, hair and plasma from the nickel-hypersensitive women and the control group are shown in Table I. The values do not follow a normal distribution and the results are therefore better characterized by their medians than by the mean ± standard deviation (S.D.). The mean values are given to make it possible to compare the results with previously published levels.

Significantly higher levels of nickel were found in the toe-nails ($p < 0.04$), hair ($p < 0.03$) and plasma ($p < 0.001$) from the group of nickel-hypersensitive females, compared with the controls, while there was no statistically significant difference between the nickel content of finger-nails from the two groups.

The nickel content of finger-nails from both the nickel-hypersensitive group and the control group was significantly higher than that of toe-nails from the two groups ($p < 5 \times 10^{-11}$ for the nickel-hypersensitive group and $p < 2 \times 10^{-5}$ for the control group). Twenty-nine of the nickel-hypersensitive patients suffered from hand eczema. The nickel content of their finger-nails seemed to be greater than the level in the remainder of the the nickel-hypersensitive persons, whereas there was no evident difference

Table II. *Nickel content (ng/g) of finger-nails from the groups of nickel-hypersensitive patients for whom significantly different nickel levels were found N* = number of patients

	N	Mean	S.D.	Median	Range
Hand eczema	29	1279	1972	537	108–10309
No hand eczema	35	761	1228	246	24–5725
Severe treatment-refractory eczema	7	3260	3367	2570	400–10309
Remainder of the patients	57	735	1001	396	24–5725

between the content of nickel in toe-nails, hair or plasma from these two groups of patients.

Seven of the nickel-hypersensitive patients suffered from severe, treatment refractory eczema on the hands or other locations. These patients had higher nickel concentrations in the finger-nails than the remainder of the nickel-hypersensitive group, while there were no apparent differences in the content of nickel in toe-nails, hair or plasma of those with eczema, compared with those who had no eczema. The nickel concentrations for these groups of patients are shown in Table II.

High concentrations of nickel in finger-nail samples were not associated with specific occupations. There was no correlation between the nickel levels of finger-nails, toe-nails, hair and plasma within the group of nickel-hypersensitive patients, nor within the group of controls. Nor was any correlation found between the strength of patch-test reactivity and the levels of nickel in any of the types of specimens.

DISCUSSION

Significantly higher nickel levels were found in plasma, hair and toe-nails from nickel-hypersensitive women than from the control group. These findings may reflect generally higher endogenous nickel levels in nickel-sensitive women.

Plasma concentrations indicate the current, transitory, endogenous level. Toe-nails are normally well protected against external contamination, and their nickel levels may reflect an average endogenous level at the time of formation. It is less likely that hair reflects the endogenous nickel level as the metal content of hair (as well as certain other factors) is believed to be dependent on geographic location and treatment with various shampoos, dyes, etc. (19).

The higher nickel levels seen in nickel-sensitive persons compared with non-sensitized control persons have not been observed before. The higher levels may be due to increased absorption or impaired excretion of the metal in nickel-hypersensitive persons (12). Spruit & Bongaarts (20) could not demonstrate any difference in the amounts of nickel in the plasma or hair of nickel-sensitive and non-sensitive persons, and the present results should probably be followed up by a study of larger populations of patients.

There was no difference between the nickel content of finger-nails from nickel-hypersensitive and non-nickel-hypersensitive women. Finger-nail levels reflect the current external contamination plus the endogenous level at the time of the formation in the nail matrix. Nickel (and other compounds) probably accumulates as small dirt particles in minute pits in the surface of the finger nails. These particles are very difficult to wash out of the nails and it has been shown that the heavier the exposure, the larger the nickel content of the finger-nails (21). This external contamination overshadows the endogenous levels. The finding of significantly higher nickel levels in finger-nails compared with toe-nails in boths groups is in agreement with this. Similar results have been reported by others (15, 16).

The 29 patients in the present study with hand eczema and the 7 patients with severe, treatment refractory eczema showed high nickel levels in finger-nails compared with the other allergic patients. The two groups are interdependent, as some of the patients with severe, treatment refractory eczema also had hand eczema. No eczema-related differences were seen in the other types of samples. The association between hand eczema and elevated nail nickel levels may be due to increased nickel contact. The hand eczema cannot be explained by increased endogenous levels, as the levels in the other types of samples did not vary in accordance with the degree of eczema. By the same token the increased nickel content of the finger-nails of the patients with severe, treatment refractory eczema is not likely to have an endogenous cause.

The nickel levels found in the present study are in fairly good agreement with previously published values. The finger-nail medians of 407 and 450 ng/g are not significantly different from the median of 488 ng/g (n = 95) in a concurrent study in which the same washing procedure was used (21). For non-washed finger nail samples, mean values of 1360 ng/g (n = 3) (14), 1380 ng/g (n = 5) (15) and 2.14 μg/g (n = 14) (16) have been reported.

Mean nickel levels in toe-nails of from 260 ng/g to 0.78 μg/g have been reported (14–16).

Takagi et al. (22) made an international study of trace elements in hair and found mean values varying from 0.26 to 2.70 μg/g, depending on nationality. A reference material of a mixture of hair from about 1000 Japanese males contained 1.8 μg/g nickel (19).

Mean nickel concentrations in plasma of 0.46 ± 0.26 μg/l (n = 39) and 0.3 ± 0.3 μg/l (n = 30) have been reported (23, 24). All the values mentioned

above were obtained in studies on persons who did not have nickel allergy.

We did not expect to find any correlation among the amounts of nickel in nails, hair and plasma. As mentioned above, there is a considerable lapse of time between the incorporation of nickel into nails and hair and the time of analysis. As nickel levels of nails and hair are dependent on such factors as growth rates and dietary habits, different sections of hairs and nails show different concentrations of nickel. Furthermore, different nails and hair from different sections of the scalp contain different amounts of nickel (13, 19, 25, 26, 27).

In conclusion, the levels of nickel in the toe-nails, hair and plasma of a group of nickel-hypersensitive persons were seen to be higher than the levels of non-nickel-hypersensitive controls. There was no difference between the two groups with regard to the levels of nickel in finger-nails.

REFERENCES

1. Hassler E, Lind B, Nilsson B, Piscator M. Urinary and fecal elimination of nickel in relation to airborne nickel in a battery factory. Ann Clin Lab Sci 1983; 13: 217–224.
2. Bernacki EJ, Zygowicz E, Sunderman FW. Fluctuations of nickel concentrations in urine of electroplating workers. Ann Clin Lab Sci 1980; 10: 33–39.
3. Høgetveit ACh, Barton RTh, Kostøl CO. Plasma nickel as a primary index of exposure in nickel refining. Ann Occup Hyg 1978; 21: 113–120.
4. Rahkonen E, Junttila M-L, Kalliomäki P L, Olkinouora M, Koponen M, Kalliomäki K. Evaluation of biological monitoring among stainless steel workers. Int Arch Occup Environ Health 1983; 52: 243–255.
5. Stoeppler M. Analysis of nickel in biological materials and natural waters. In Nriagu J O, ed. Nickel in the environment. New York: John Wiley & Sons, Inc., 1980; 29: 661.
6. Sunderman F W. Analytical biochemistry of nickel. Pure Appl Chem 1980; 527–544.
7. Sunderman F W. A review of the metabolism and toxicology of nickel. Ann Clin Lab Sci 1977; 7: 377–398.
8. Sunderman F W, Aitio A, Morgan L G, Norseth T. Biological monitoring of nickel. Toxicol Ind Health 1986; 2: 17–78.
9. Katz S A, Bowen H J M, Comaish J S, Samitz M H. Tissue nickel levels and nickel dermatitis. Br J Dermatol 1975; 92: 187–190.
10. deJongh GJ, Spruit D, Bongaarts PJM. Duller P. Factors influencing nickel dermatitis. I. Contact Dermatitis 1978; 4: 142–148.
11. Christensen OB, Möller H, Andrasko L, Lagesson V. Nickel concentration of blood, urine and sweat after oral administration. Contact Dermatitis 1979; 5: 312–316.
12. Christensen OB, Lagesson V. Nickel concentration of blood and urine after oral administration. Ann Clin Lab Sci 1981; 11: 119–125.
13. Alder J F, Batoreau M C C. Determination of lead and nickel in epithelial tissue by electrothermal atomic absorption spectrometry. Anal Chim Acta 1983; 199–207.
14. Ostapzuk P, Valenta P, Stoeppler M, Nürnberg H W. Voltammetric determination of nickel and cobalt in body fluids and other biological materials. In: Brown S S, Savory J, eds. Chemical Toxicology and Clinical Chemistry of Metals. London: Academic Press, 1983: 61–64.
15. Ostapzuk P, Froning M, Stoeppler M, Nürnberg H W. Square wave voltammetry: A new approach for the sensitive determination of nickel and cobalt in human samples. In: Brown SS, Sunderman FW, eds. Prog Nickel Toxicol. Proc 3rd Int Conf Nickel Metab Toxicol, Paris, 1984: 129–132.
16. Gammelgaard B, Andersen J R. Determination of nickel in human nails by adsorption differential-pulse voltammetry. Analyst 1985; 10: 1197–1199.
17. Andersen J R, Gammelgaard B, Reimert S. Direct determination of nickel in human plasma by Zeeman-corrected atomic absorption spectrometry. Analyst 1986; 111: 721–722.
18. Statgraphics. Statistical graphics system. Statistical Graphics Corporation, STSC 1987.
19. Okamoto K, Morita M, Quan H, Uehiro T, Fuwa K. Preparation and certification of human hair powder referencce material. Clin Chem 1985; 31: 1592–1597.
20. Spruit D, Bongaarts P J M. Nickel content of plasma, urine and hair in contact dermatitis. Dermatologica 1977; 154: 291–300.
21. Peters K, Gammelgaard B, Menné T, Unpublished results.
22. Takagi Y, Matsuda S, Imai S, et al. Trace elements in human hair: An international comparison. Bull Environ Contam Toxicol 1986; 36: 793–800.
23. Sunderman F W, Chrisostomo M C, Reid M C, Hopfer S M, Nomoto S. Rapid analysis of nickel in serum and whole blood by electrothermal atomic absorption spectrophotometry. Ann Clin Lab Sci 1984; 14: 232–241.
24. Leach C N, Linden J V, Hopfer S M, Chrisostomo M C, Sunderman F W. Nickel concentrations in serum of patients with acute myocardial infarction or unstable angina pectoris. Clin Chem 1985; 31: 556–560.
25. Robertson J. Trace elements in human hair – a significant forensic future? TrAC Trends Anal Chem 1987; 6: 65–69.
26. Li H-K, Malmqvist K G, Carlsson L-E, Akselsson K R. A PIXE system for routine longitudinal scanning of single hair strands. Nucl Instr and Meth 1984; B3: 347–351.
27. Bos A J J, van der Stap C C A H, Valković V, Vis R D, Verheul H. Incorporation routes of elements into human hair; implications for hair analysis used for monitoring. Sci Total Environ 1985; 42: 157–169.