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Nickel exposure and its effects

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Abstract

The aim of the study was to determine the nickel concentrations of soil and plant specimens taken from a rural area exposed to cement factory emissions and also to determine the blood concentrations and sensitivity conditions observed in humans residing in this rural area.

The study was carried out in Çukurhisar, a town in Eskişehir-Turkey, between May 2000 and March 2001. Beside the 108 soil (36 for control) and plant specimens, which were taken from 8 directions from the cement factory, blood samples of the individuals residing in this area were taken from 258 subjects (258 for control) following a physical examination, and patch tests were also applied.

The nickel concentrations of the soil and plant specimens taken from different places in different directions of the factory were higher than in the control areas.

The physical examination of subjects did not reveal results different from those of the control group except for the diagnosis of contact dermatitis. The analyses of venous blood samples showed that nickel concentrations were found to be within the reference values given for both groups, but higher in the subjects ($p < 0.001$). According to the results of patch tests, sensitivity to nickel was found to be more frequent for the subject group than the control group ($p < 0.05$).

According to these results, clinical tools revealed no toxic effects for the subjects, except contact dermatitis. However, sensitivity to patch tests showed that this subject group has been affected compared to the control group and that this effect increased with age.

Introduction

Environmental pollution is a serious problem receiving careful attention in our country as well as in the world. As a result of industrial development, lots of chemical substances have generated pollution in air, water and soil. Nickel is a ubiquitous trace metal and occurs in soil, water, air, and in the biosphere, which is emitted into the environment from both natural and man-made sources (Barrie, 1981; WHO, 1991).

Of concern is the increasing concentration of nickel deposited in agricultural soils by airborne nickel particles. The primary sources of nickel emissions into the ambient air are the combustion of coal and oil for heat or power generation, nickel mining, steel manufacture, and miscellaneous sources, such as cement manufacturing. In polluted air, the predominant nickel compounds appear to be nickel sulfate, oxides and sulfides, and to a lesser extent, metallic nickel (WHO, 1991). Nickel can be absorbed in human beings and animals via inhalation or ingestions or percutaneously. Respiratory absorption with secondary gastrointestinal absorption of nickel (insoluble and soluble) is the major route of entry during occupational or for the

people residing near a source. Nickel apparently has a limited acute toxicity in humans, including airway irritation, but the important adverse effects relate to allergic eczema and respiratory cancers (Grandjean, 1992).

Exposure to soluble nickel compounds and nickel carbonyl, which is metabolized to form nickel ions and carbon monoxide, may be evaluated by analysis of nickel concentrations in plasma and urine (WHO, 1991). Nickel is transported in the blood, principally bound to albumin. The biological half-life in the body and the release from particles retained in the lungs will depend on the solubility of the nickel compounds concerned. Nickel in the blood seems to be cleared relatively rapidly by the kidneys and animal experiments suggest a half-life of a few days. (Grandjean, 1992, IARC, 1984).

One of the factories, which cause particle pollution, is a cement factory. Although they are generally established far from city centers, local areas are affected negatively. Cement dusts spread along a large area through wind, rain, etc. are accumulated on plants, animals and soil and can affect human health badly (Ayvaz, 1992).

The aim of the study was to determine the nickel concentrations of soil and plant specimens taken from a rural area exposed to cement factory emissions and also to determine the blood concentrations and sensitivity conditions observed in humans residing in this rural area.

Material and methods

The study, sponsored by Research Fund of Osmangazi University, was carried out between May 2000 and March 2001 in Eskişehir-Turkey. Çukurhisar, the town where the study was conducted, is located in an area that is 500 m from the Eskişehir Cement Factory. The cement factory had been operating in the area since 1954. The records of medical center indicate that there are 1798 male (49.9%) and 1806 female (50.1%) subjects, forming a total population of 3604, in this town.

The soil of this area is rough, with good drainage, and was structured through accumulation. Soil specimens were taken from surface soils in nine groups that were 500 meters away from the factory in the directions of west, southwest, south, southeast (the residence place), east, northeast, north and northwest and 1000 m away from the factory in the southeast direction. Each group consisted of 12 specimens. Control specimens were taken in the same directions but 2000 m away from the subject specimens and each of the nine groups consisted of four specimens.

The subject and control plant specimens were taken from rural plants (Cynodon dactylan) with their roots from the same points as the soil specimens were taken. Only cynadon dactylon was selected for analysis. It was the only widespread plant. We wanted to take the plant samples from the same points as the soil samples were taken. They were washed with bidistile water before analyses in order to exclude superficial contamination by dust.

The samples were taken 1 month after the last rain. Then they were dried at 110 °C for 1 h. The dried samples were ground, sifted, and weighed to 3.0 ± 0.001 gr. After treatment with $HClO_4$, HNO_3, and HCl, samples were filtered twice and the filtered solution diluted to 50 ml.

The human subject group included people who had lived in the town since their birth and who were over 15 years of age. According to the medical center records, there were 2581 residents who were over 15, 1264 male (49%) and 1317 female (51%). These residents were classified into six groups on age basis with intervals of 10 years. Ten percent of each age group formed the sample group. We also divided the village into 10 zones. Ten percent of each age group was randomly chosen from each zone. Six of the subjects refused to give blood samples and new ones were selected from the neighborhood. Individuals employed at the cement factory were not included in the study; instead, their neighbors were chosen. The randomly chosen individuals were examined systematically, their venous blood samples were taken, and patch tests were applied after their permission was given.

The human control group, on the other hand, consisted of people who lived in the city center of Eskişehir. They were chosen between September–December 2000 from the outpatients of the department of dermatology who had not had a prior contact dermatitis diagnosis and history of agricultural job and cement dust exposition. The number of controls was the same as that of the subject group and the members of both groups were similar in age and sex.

The subject and control groups each consisted of 258 people. The ages of both groups ranged between 15 and 82 years with a mean of 38.07 ± 1.04 years. Of the subject group, 125 (48.4%) were male and 133

Table 1. The age and sex distribution of the subject group*

Age Groups	Male		Female		Total	
	n	%	n	%	N	%
15–24	32	25.6	35	26.3	67	26.0
25–34	29	23.2	34	25.6	63	24.4
35–44	23	18.4	26	19.5	49	19.0
45–54	14	11.2	13	9.8	27	10.5
55–64	17	13.6	13	9.8	30	11.6
65+	10	8.0	12	9.0	22	8.5
Total	125	100.0	133	100.0	258	100.0

*Similar to the age and sex distribution of the population.

(51.6%) were female. The age and sex distribution of the subject group are given in Table 1.

The venous blood samples of the subjects and controls were taken into heparinized tubes, transferred to laboratory in iceboxes and stored at $-20\,^{\circ}C$ until analyses. The samples were prepared for analyses as described by Que Hee and Boyle (1988) and then analyzed in a Hitachi (180–70) Polarized Zeaman Atomic Absorption Spectrophotometer to determine nickel ions. Nickel atomic absorption standard solution (980 μg Ni/ml in 1% HNO_3, Sigma) was used for the calibration of the atomic absorption spectrophotometer for every 25th reading.

Nickel sulfate patch test materials, an allergen produced by French Firm Stallargens with vaseline used as solvent, as applied and covered with a hypoallergenic plaster. Two days after the application, plasters were uncovered and patches were checked (first reading); the next day, a second reading was done. After second reading, the patches showing erythema and edema, which are defined as weak reaction (one positive) by the International Contact Dermatit Research Group (ICDRG), were considered positive (Rycroft, 1998, Adams, 1993). For some subjects and controls patch tests were repeated because of dropouts. Six of the subjects refused to give blood samples and new six subjects were selected by the same random method. None of the controls refused to give blood samples.

The differences between the environments, nutrition, etc., of the subject and control groups were not taken into account. The structure (heating power) of the houses of the subjects was similar to the ones in the city center, so we ignored this kind of source of contamination.

Cement samples were taken from cement produced in Eskişehir Cement Factory in three different periods and analyzed as described by Gündüz T. (1993) to determine the concentrations of elements.

Mean correlations were given as 'mean ± SE'. 'SPSS version 10.0 for Windows' was used to evaluate the data and Chi Square tests, t tests and correlation analyses were used to determine significance.

Results and discussion

During cement manufacturing, nickel is emitted, either as a component of the clays, limestones, and shales, used as raw materials, or as an oxide formed in the high temperature process kilns (WHO, 1991).

The analyses of the three different cement samples showed that they contained 19.20 ± 0.11 mg/kg nickel. In a study conducted by Wahlberg *et al.* (1977) Swedish cement was found to contain 5–59 mg nickel/kg.

Although the average nickel concentration of the earth's crust was reported as 80 mg/kg by Grandjean (Grandjean, 1992), it is also reported that farm soils contain nickel between 3 to 1000 mg/kg (WHO,1991). Average nickel concentrations of the subject soil and subject plant specimens taken from different places in different directions from the cement factory are given in Figure 1.

The mean nickel concentration of the soil samples taken from the residential area place ($n = 12$) (88.416 ± 1.31 mg/kg) was higher than the mean nickel concentration of the samples taken from 1000 meters away residential area (59.114 ± 1.14 mg/kg) and it was higher than the mean nickel concentration of the control residential area, 2500 meters to factory, ($n = 4$) (46.837 ± 3.43 mg/kg) (respectively; $t = 16.820$, $p < 0.001$ and $t = 14.007$, $p < 0.001$). The mean nickel concentration of the samples taken from inside and around the residential area (east, southeast and south of the factory) ($n = 36$) was 81.238 ± 2.45 mg/kg and was higher than the mean nickel concentration of the control areas ($n = 12$) which was 43.375 ± 1.93 mg/kg ($t = 8.566$, $p < 0.001$).

High levels of nickel in soils result from nickel-emitting industrial sources (Gignac & Beckett, 1986). While the average nickel concentration of the subject soils was lower than the values given by Grandjean (1992), it was higher than that of the control areas. Shallari *et al.* (1998) reported a maximum 3579 mg/kg nickel concentration for soils in a study to demonstrate environmental pollution of nickel. In this study the

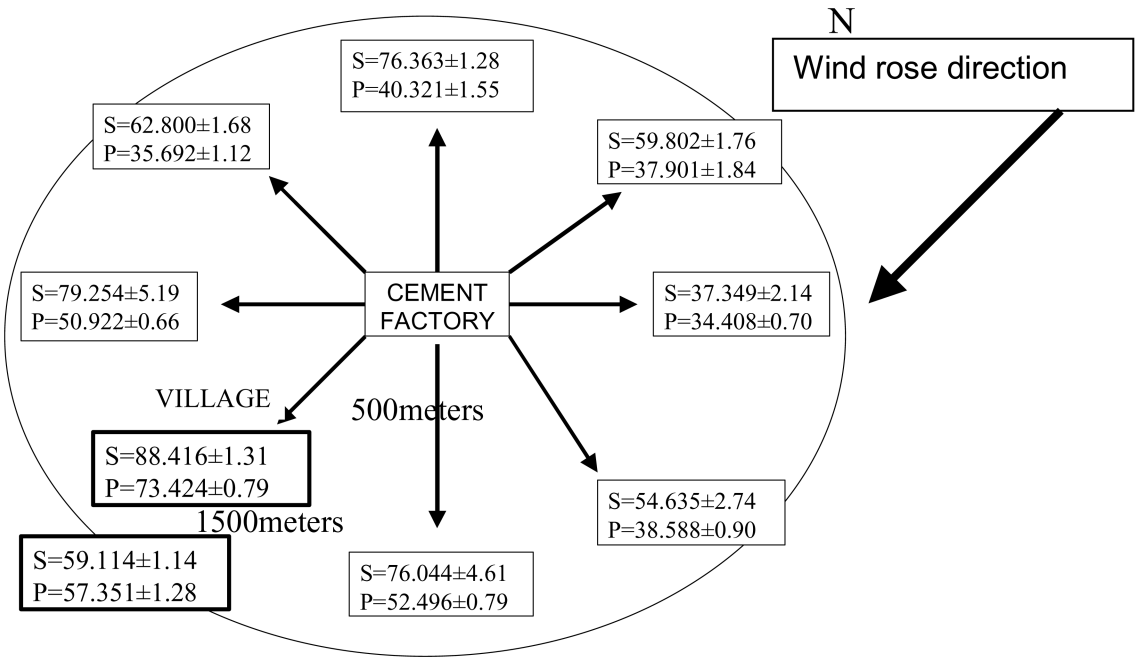

Figure 1. The average nickel concentrations of the subject soil and subject plant specimens taken from different places in different directions of the cement factory (mg/kg). S = the average nickel concentration of the soil samples (mg/kg). P = the average nickel concentration of the plant samples (mg/kg).

nickel concentration of the subject soils was between 21.21–107.44 mg/kg.

Terrestrial plants take up nickel from soil primarily via the roots (WHO, 1991). The amount of nickel uptake from soil depends on various geochemical and physical parameters including the type of soil, the soil pH and humidity, the organic matter content of the soil, and the concentration extractable nickel. The major source of nickel accumulation in terrestrial plants is the increased occurrence of nickel in soils (Gignac & Beckett, 1986).

Although nickel levels above 50 mg/kg in plants are usually toxic, the effects of long term, low-level exposure to nickel are only manifested in growth decrements with no visible signs. Nickel toxicity in plants is characterized by chlorosis and necrosis of the leaves, stunting of the roots, deformation of various plant organs and wilting (Prokipcak & Ormrod, 1986).

The mean nickel concentration of the plant samples taken from the residential area place ($n = 12$) (73.424 ± 0.79 mg/kg) was higher than the mean nickel concentration of the samples taken from 1000 m away (57.351 ± 1.28 mg/kg) and was higher than the mean nickel concentration of the control residential area ($n = 4$) (29.447 ± 2.01 mg/kg) (respectively; $t = 10.540$, $p < 0.001$ and $t = 24.773$, $p < 0.001$). The mean nickel concentration of the samples taken from inside and around the residential (east, southeast and south of the factory) ($n = 36$) was 58.447 ± 1.78 mg/kg and was higher than the mean nickel concentration of the control specimens ($n = 12$) which was 29.563 ± 1.38 mg/kg ($t = 9.153$, $p < 0.001$). Both the mean nickel concentration of soil and plant samples decreased as the distance increased from the factory, but there was no correlation between the elevation of nickel concentration of plants and soils.

Shallari *et al.* (1998) reported a maximum 808 mg/kg nickel concentration in the plants in their study. In this study the nickel concentration of the subject plants was between 27.12 and 77.48 mg/kg.

The mean nickel concentration of the inner circle (the factory as the center with a 500 meters of semi-diameter) was higher than that of the outer circle (the factory as the center, with a 2500 m semi-diameter) with regard to soil ($t = 7.432$, $p < 0.001$) and plants ($t = 7.408$, $p < 0.001$).

Nickel exposure may cause to dsypne, headache, dizziness, and contact dermatitis (Grandjean, 1992). Both study groups had minor health complaints but the frequency of contact dermatitis was higher in the subject group. Forty-eight subjects (%18,6) and nine

Table 2. The distribution of whole blood nickel levels according to age groups

Age Groups	Whole blood nickel values μg/l Subject Group	Control Group	t =
15–24	5.18 ± 0.23	4.20 ± 0.13	3.658 $p < 0.001$
25–34	7.08 ± 0.26	4.34 ± 0.19	8.666 $p < 0.001$
35–44	8.69 ± 0.33	5.96 ± 0.33	5.838 $p < 0.001$
45–54	9.13 ± 0.39	6.05 ± 0.59	4.388 $p < 0.001$
55–64	10.50 ± 0.55	7.43 ± 0.57	3.860 $p < 0.001$
65+	10.72 ± 0.80	8.34 ± 0.76	2.155 $p < 0.05$
Total	7.82 ± 0.19	5.49 ± 0.16	9.264 $p < 0.001$

controls (%3,5) were found to have contact dermatitis ($x^2 = 29.99$, $p < 0.001$). Because of the question that this was a nickel effect, we determined blood concentrations and performed sensitivity tests on subjects in comparison with controls. Any clinical finding could be found that specifically be attributed to nickel toxicity.

Nickel determinations in blood and urine, are widely used and accepted methods for monitoring nickel exposure (Grandjean, 1988). Although more data available for urine, no clear-cut choice can be made between the use of blood or urine. In our study we preferred to use blood. Data of normal nickel values in urine, blood, plasma and serum published in the last decades, vary widely (WHO, 1991). The blood reference value for nickel is between 1.0–28.0 μg/l (Painter *et al.* 1999). For the subject group, this value was between 3.2 and 18.0 μg/l, the average being 7.82 ± 0.19 μg/l. For the control group, blood nickel levels were between 2.1 and 17.7 μg/l, the average being 5.49 ± 0.16 μg/l. The distribution of whole-blood nickel levels according to age groups is given in Table 2.

Although the average blood nickel levels were between the reference values given for both groups, these values were significantly higher for the subject group compared to the control group ($t = 9.264$, $p < 0.001$). This difference was observable in all age groups. In the researches conducted in the last 30 years, it was reported that normal values for the individuals who are healthy and not exposed to cement dust were changeable (WHO 1991). For such people, Linden *et al.* (1985) found blood nickel level as 0.05–1.05 μg/l with an average of 0.34 ± 0.28 μg/l. However, these values can be said to increase because of environmental pollution. Indeed Mattila (2001)reports

Table 3. The distribution of the patch test results

Patch test	Subject Group		Control Group		Total	
	n	%	n	%	N	%
Positive	61	23.6	22	8.5	83	16.1
Negative	197	76.4	236	91.5	433	83.9
Total	258	100.0	258	100.0	516	100.0

$\chi^2 = 21.83$, $p < 0.05$.

that nickel sensitivity for female university students in 1986 (13%) increased up to 39% in 1995. This percentage increases also depending on exposure level (WHO 1991).

In our study the average blood nickel level increased as exposure period (age) increased for the subjects and for the controls ($r = 0.589$, $p < 0.001$ and $r = 0.525$, $p < 0.001$, respectively), although significant differences were found between the subject and control groups in means of all age groups (Table 1).

When we performed nickel patch test to see the skin sensitization of the subjects and controls, higher frequency of sensitivity was observed for the subject group compared to the control group ($\chi^2 = 21.83$, $p < 0.05$). The distribution of the patch test results, applied to determine nickel sensitivity for both groups, is shown in Table 3.

In several countries, it has been reported that 10% of the female population and 1% of the male population are sensitive to nickel. In our study no difference was found between male and female in the subject group in means of average blood nickel concentration ($t = 0.574$; $p > 0.05$) and in means of the frequency of positive nickel sulfate patch test ($\chi^2 = 0.514$; $p < 0.05$).

Dermal exposure in the general environment is important for the induction and maintenance of contact hypersensitivity caused by daily skin contact with nickel-plated objects or nickel-containing alloys (e.g., jewellery, coins, clips). In our study we ignored the influence of ornaments, because the members of both groups had similar characteristics in terms of age and sex. Piercing is a major source of induction of nickel sensitization. In general most of the Turkish women use earrings, and there was no difference between the subjects and controls in means of piercing.

Kanerva *et al.* (2000) reported that they identified 6.9% nickel sensitivity in 2543 subjects, Schubert *et al.* (1987) 7.3% for 2400 subjects, Lee and Lam

(1996) 16.4% for 490 subjects, Castigloni *et al.* (1992) 18% for 834 subjects and Greig *et al.* (2000) 20% for 219 subjects. These results show that the findings in literature are quit varied according to environment and life conditions.

Cobalt is also present in cement and should be considered as a confounder. In this study, the second substance, which caused sensitivity, was cobalt chloride. Fifty-four (20.9%) of the subjects and twenty-two (8.5%) of the controls were found to be sensitive to cobalt. For the subject group, higher frequency of sensitivity was observed compared to control group ($x^2 = 15.80$, $p < 0.001$). Chromium is also a frequent cause of dermatitis associated with exposure to cement. In our study, the third substance, which causes sensitivity, was potassium di chromate. Thirty-one (12.0%) of the subjects and twelve (4.7%) of the controls were found to be sensitive to chrome. Higher frequency of sensitivity was observed for the subject group compared to the control group ($x^2 = 9.15$, $p < 0.05$).

The average blood nickel level for 61 nickel patch test positive subjects was 8.86 ± 0.33 μg/l and it was higher than the average blood nickel level for 22 nickel patch test-positive controls, which was 7.37 ± 0.55 μg/l ($t = 2.358$, $p < 0.05$). Significant differences were found between the patch test positive (8.860 ± 0.33 μg/l) and negative (7.494 ± 0.23 μg/l) subjects ($t = 3.084$, $p < 0.05$) and the patch test positive (7.368 ± 0.55 μg/l) and negative (5.318 ± 0.17 μg/l) controls ($t = 3.610$, $p < 0.001$) in means of average blood nickel concentration.

Of these 61 in the subject group, 24 subjects (39.3%) and of 22 subjects in the control group, five subjects (22.7%) were found to have contact dermatitis symptoms. The frequency of contact dermatitis for nickel patch test-positive subjects was higher for subject group ($\chi^2 = 13.19$, $p < 0.001$).

Conclusion

In conclusion, there was an environmental pollution in means of nickel and although a clinical finding to explain toxic effects except contact dermatitis was not found for the subject group living near a cement factory, patch test results revealed nickel sensitivity whether this effect was due to cement particles or coal combustion or nickel content of food stuffs which may be grown in the area. It was also concluded that this effect increased by age.

Future industrial sites must be set up away from the residential area and the existing ones must take precautions and use new techniques to protect the environment from pollution. This study underlines the need for other studies on environment and human health.

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