

Repeated exposures to cobalt or chromate on the hands of patients with hand eczema and contact allergy to that metal

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The present study aimed at evaluating the effects of daily repeated exposures to low cobalt or chromate concentrations on the hands of patients with hand eczema and cobalt or chromate allergy. For 2 weeks, the patients immersed a finger for 10 min daily into the appropriate metal salt solution in water. During the 1st week, this was a 10 or 50 mg/l cobalt concentration or a 10 mg/l chromate concentration, and, during the 2nd week, a 100 or 200 mg/l cobalt concentration or a 100 mg/l chromate concentration. This regimen elicited a flare of hand eczema only in the chromate-exposed chromate-sensitive patients. During the exposure period, accumulation of cobalt or chromate in the nail was demonstrated. Standardization of chemical methods of quantification of skin exposure to allergens, combined with experimental exposure studies in patients with specific contact allergy, will increase the possibility of providing evidence-based medicine in the area of allergic contact dermatitis in the future.

Key words: chromate; cobalt; allergic contact dermatitis; hand eczema; exposure studies; nail; quantitative. © Munksgaard, 2000.

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The diagnosis of allergic contact dermatitis is based on the outcome of patch testing and the information on exposure to a specific allergen in the patient's environment. The latter process, called the "evaluation of relevance", is typically based upon qualitative, not quantitative, data.

Information on quantitative exposure data, combined with the outcome of experimental exposure studies in specifically sensitized individuals, will increase the accuracy of the diagnosis of allergic contact dermatitis. In a recent placebo-controlled study, the significance of nickel chloride exposure to the fingers of patients with nickel allergy and slightly active hand eczema was investigated (1). Measurements of nickel concentrations in nails secured an exposure concentration comparable to moderate occupational nickel exposure (2).

The present study represents a pilot study including chromate- or cobalt-sensitive patients, where the same finger immersion model was used, combined with quantitative exposure assessment by measuring chromate or cobalt in the fingernails.

Materials and Methods

The pilot study was performed as an open exposure study of 3 cobalt- and 3 chromate-sensitive outpatients attending the Department of Dermatology, Gentofte Hospital. All patients had had hand eczema for more than 3 months. The hand eczema was mild to moderate on the day of inclusion, without vesicles, fissures and scaling except in 1 of the chromate-sensitive patients who had a small number of vesicles. Before the study all patients were patch tested, using Finn Chambers on Scanpor tape (Norgesplaster; Oslo, Norway) with the European standard series (Hermal, Reinbeck, Germany). The tests were read according to the recommendations of the International Contact Dermatitis Research Group (ICDRG) (3). All patients had a positive reaction (+ to +++) to either cobalt or chromate. 1 of the chromate-sensitive patients also had a positive nickel patch test, while patch tests to the other metals in the standard series were negative in the

Table 1. Clinical responses to cobalt or chromate exposures in the model of allergic metal hand eczema: score of vesicles on the exposed finger on study day (D) 0 (before exposure) and on study days 7 and 14 (patient no. 402 on day 10); the score of vesicles was semi-quantitative and express the total number of vesicles in the exposed area (0=0, 1–10=1, 11–20=2, 21–30=3, 31–40=4, 41–50=5, >50=6)

			Patients with cobalt sensitivity					patch test reactivity (1% cobalt chloride)
			finger exposure concentration		score of vesicles			
No.	Sex	Age (years)	week 1	week 2	D0	D7	D14	
201	F	56	10	100	0	0	0	
202	F	46	10	100	0	0	0	
203	F	48	50	200	0	0	0	
Patients with chromate sensitivity								
			finger exposure concentration		score of vesicles			patch test reactivity (0.5% potassium dichromate)
No.	Sex	Age (years)	week 1	week 2	D0	D7	D14	
401	M	74	10	100	2	3	3	
402	F	65	10	100	0	2	3	
403	F	56	10	100	0	2	6	

other patients. From 2 days before inclusion and until the end of the 2-week exposure part of the study, use of topical corticosteroids and tar was not allowed. Neither did the patients receive other immunosuppressive treatments (including UVA, UVB or PUVA). Moisturizers were allowed throughout the study. Sex and age are presented in Table 1.

Exposure to metal

All patients exposed 1 finger 10 min daily at home. None of the patients were metalworkers. The exposures were 10 and 100 mg/l (mg/l=parts per million) cobalt during the 1st and 2nd week, respectively, in 2 cobalt-sensitive patients. Because the exposures did not elicit an eczematous reaction, the exposure concentrations were increased to 50 and 200 mg/l for the 3rd cobalt-sensitive patient. The 3 chromate-sensitive patients were exposed on 1 finger to 10 and 100 mg/l chromate during 1st and 2nd week, respectively. All solutions were made up at the Central Pharmacy, Copenhagen County, Copenhagen. All metal concentrations are given as the concentration of metallic cobalt or chromate. Cobalt and chromate solutions were made from cobalt-(II)chloride hexahydrate (purity >99.5%) and potassium dichromate (purity >99%) (Merck KGaA, Darmstadt, Germany) in aqua purificata. Ointment jars of glass (100 ml (PLM, Langeskov, Denmark)) were used for finger exposure. The jars were filled with 100 ml.

Evaluations

Evaluations of the exposed finger were performed on the day of inclusion (day 0), after the 1st week

(day 7), and after the 2nd week (day 14) of exposure. The number of vesicles (including intact and more advanced, broken vesicles) on the exposed finger were recorded on a semi-quantitative scale (0=0, 1–10=1, 11–20=2, 21–30=3, 31–40=4, 41–50=5, >50=6).

Determination of metals in fingernails

On days 0, 7 and 14 the nail on the exposed finger was cut with tungsten scissors. Digestion and chemical analysis of fingernails followed the previously described procedure for nickel (2). In brief, the weighed nail (5–12 mg) was washed with 1.5 ml acetone for 10 min, followed by washing with 1.5 ml aqueous 0.1% Triton X-100 solution in ultrasound bath for 15 min. Then the nail was washed with 5 portions of 1.5 ml water in ultrasound bath for 1 min, and dried at 70°C overnight. Subsequently 200 µl sulfuric acid, 10 µl nitric acid and 200 µl water was added the nail in a 10 ml test tube, and the mixture was placed in a hot (70°C) water bath for approximately 1 h. After cooling to room temperature, 550 µl aqueous ammonia was added to the solution and transferred to a 2.00 ml volumetric flask, adjusting the volume to 2.00 ml with water. Blank samples consisted of empty test tubes were treated as if they contained a nail sample. Samples were diluted 2× prior to analysis. The sample (20 µl) and 5 µl of neutralizing solution were injected into the graphite furnace. After drying and charring (1300°C), the sample was atomized at 2400°C and the atomic absorption measured at 357.9 nm (chromium) or 240.7 nm (cobalt). Peak area was used as the sample signal.

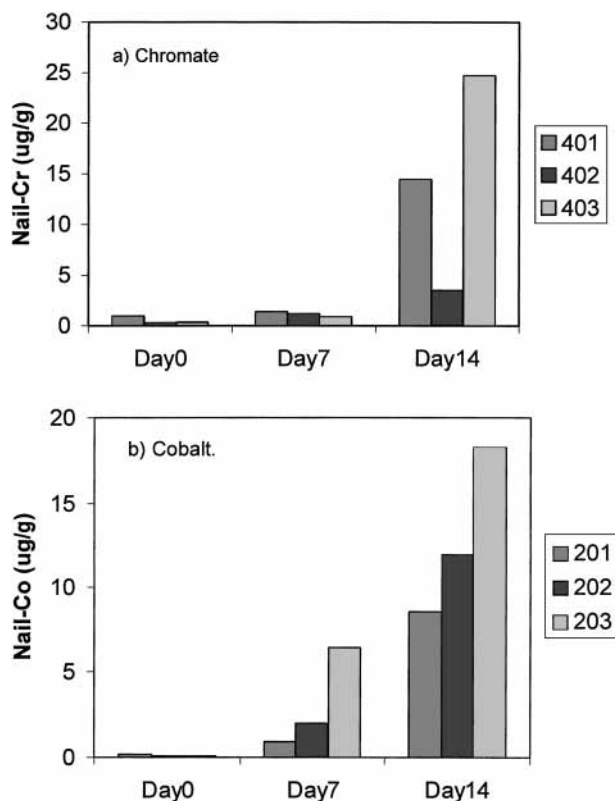


Fig. 1. Metal concentration in fingernails during the exposure study with chromate or cobalt (10 min per day for 7 days) at increasing concentration. Day 0: baseline level, day 7 after 6 days, exposure with low concentration, and day 14 after 7 days exposure with high concentration (patient no. 402 stopped exposure to 100 mg/l chromate after 3 days). See text for exposure concentrations.

Results

The numbers of vesicles on the exposed fingers in the patients appear in Table 1. None of the cobalt-exposed patients developed vesicles, whereas all 3 chromate-exposed patients had a vesicular reaction. Patient no. 402 stopped exposure to 100 mg/l chromate after 3 days because of an obvious vesicular reaction on the exposed finger.

Metal concentrations in nails are shown in Fig. 1. The baseline level for chromate was $0.53 \mu\text{g/g}$ (standard deviation (sd) = $0.36 \mu\text{g/g}$, $n=3$) and for cobalt $0.10 \mu\text{g/g}$ (sd = $0.047 \mu\text{g/g}$, $n=3$). The increase in nail cobalt was larger for patient no. 203 (high cobalt exposure levels). Nail chromate was lower in patient no. 402 at day 14 (only 3 exposures to 100 mg/l chromate).

Discussion

Exposure to low concentrations (10–100 mg/l) of water-soluble chromate elicited a flare of hand eczema in the chromate-sensitive patients. The con-

centrations employed for cobalt exposure did not elicit a flare of hand eczema in the cobalt-sensitive patients.

Throughout the world, chromate is still a significant occupational contact allergen (4–6). Chromate allergy in the building industry is now rare in areas where ferrous sulfate has been added to cement, in order to keep the concentration of hexavalent chromate below 2 mg/l in wet cement (7). Based upon worldwide quantitative exposure data on chromate in wet cement, it can be estimated that a concentration of 5–10 mg/l seems to generate significant skin problems (8).

According to a recent study by Fowler et al. (9), dermatitis was seen in chromate-sensitive individuals after a few days exposure to 25 mg/l hexavalent chromate, a forearm immersion model employing exposure on normal forearm skin.

As chromate and cobalt are more potent allergens, the present pilot study was expected to show more severe reactions than the placebo controlled finger immersion study in nickel-sensitive individuals on previously affected skin areas, where concentrations of 10 and 100 mg/l nickel were used (1).

All 3 chromate-sensitive patients reacted with severe vesicular eczema after the exposures. After 3 days exposure to the 100 mg/l chromate solution, 1 patient stopped further exposure due to a severe reaction. Nail chromate concentration increased during the study proportional to the number of days of exposure. The exposure levels used in this study clearly represent the upper limit. Future controlled studies need to be performed with concentrations between 5 and 25 mg/l, to establish the concentration threshold of significance for eliciting allergic chromate contact dermatitis. Such data, in combination with nail chromate concentration measurements, may enable the diagnosis of occupational chromate hand eczema to be based on objective criteria, and also to provide assessment of preventive measures.

None of the cobalt-sensitive patients reacted with eczema, although exposure was confirmed by nail cobalt measurements. This finding may support cobalt rarely being relevant to hand eczema except in a few specific occupations (10).

Standardization of chemical methods for quantification of skin exposure to allergens, combined with experimental exposure studies in specifically contact-sensitized individuals, will increase the possibility of providing evidence-based medicine in the area of allergic contact dermatitis in the future.

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