

THE SIGNIFICANCE OF CHROMATE INGESTION IN PATIENTS ALLERGIC TO CHROMATE

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Abstract. A double-blind study was carried out to demonstrate the significance of chromate ingestion in the persistence of chronic chromate dermatitis. Each of 31 chromate-allergic patients was given one tablet containing 7.1 mg potassium dichromate, plus a placebo tablet.

The dermatitis of 11 of the 31 patients flared after the ingestion of chromate, but not after placebo. 3 patients had equivocal reactions to both tablets; the dermatitis worsened in 2 patients following ingestion of the placebo but not after the chromate tablet.

No statistically significant difference could be found between reactivity to chromate and eczema of dyshidrotic morphology. Nor was it possible to correlate the degree of patch test reactivity to the reaction following chromate ingestion.

It is concluded that a low-chromate diet is of value in the management of patients with chronic chromate dermatitis.

Key words: Chromate; Ingestion; Contact dermatitis; Pompholyx

Chromate is the most common cause of allergic contact dermatitis among men. In one study 6.6% of a group of patch-tested patients with eczema had a positive reaction to chromate (7). This particular dermatitis is chronic, with periodic exacerbations. The chronic nature of the dermatitis has been accounted for by the difficulty involved in locating the external source of the allergen (5). Among patients with cutaneous diseases, chromate dermatitis is one of the most frequent causes of permanent disability (13).

Among nickel-allergic patients with eczema on the hand, ingestion of nickel may be of greater significance in the persistence of the dermatitis than external contact (2). The dermatitis among patients allergic to chromate may also worsen if the allergen is ingested (6, 9, 12). Fregert (6) described vesiculation of the hands following ingestion of 50 µg potassium dichromate. 20 patients

with positive chromate patch tests suffered eczematous eruptions after ingestion of homeopathic drugs containing 1-10 mg potassium dichromate (9).

The following controlled trial was carried out to demonstrate the significance of oral ingestion of chromate in prolonging chromate dermatitis.

MATERIALS

All those patients who reacted positively to chromate when patch tested in the dermatology department of the Finsen Institute in 1974 and 1975 participated in this study. A positive patch test was defined as infiltration and papules (++) reaction) or infiltration and vesicles (+++ reaction) after 72 hours. A questionnaire was sent to the patients, and they were asked to inform us whether they still had dermatitis, which areas were involved, and what treatment they were receiving. Patients with dermatitis who were not receiving systemic steroid were asked to participate in our investigation. Of the 71 patients who had a ++ or a +++ chromate patch test, 62 returned the questionnaire. The patients were made aware that in the proposed study the dermatitis might well flare following the ingestion of chromate. 31 patients completed the study. Table I describes those patients who did not participate in or did not complete the study.

The sites of the eczema are detailed in Table II. The term dyshidrotic (pompholyx) morphology describes bilateral vesicular dermatitis on the palms, sides or volar surfaces of the fingers and/or soles of the feet.

13 of the 31 patients had no other positive patch test, 7 had one additional positive reaction, and 11 had 2 or more additional positive patch tests. Of these additional reactions, 12 were to other metals (6 to nickel, 4 to cobalt, and 2 to mercury).

METHOD

In this double-blind trial, tablets containing 7.1 mg potassium dichromate (2.5 mg chromium) and lactose placebo tablets were used. Hexavalent chromium was used, as trivalent chromium is not absorbed from the gastro-in-

Table I. Summary of 40 patients who either did not participate in or did not complete the investigation

9	did not return the questionnaire
12	had no dermatitis
13	had dermatitis but did not wish to participate
3	were receiving systemic steroid treatment
1	did not complete the study due to technical difficulties
2	received only chromate, not placebo

testinal tract (4). Both kinds of tablets were coated with Sunset Yellow, FCF, (C. I. 15985) and they were identical in appearance. The patients were randomized into two groups, and this determined whether the patients were first given the tablet containing chromate, or the placebo.

Black and white close-up photographs of the areas with dermatitis were taken immediately prior to initiation of the test. A nurse was present when the tablets were given. A clinical evaluation and comparative photographs were made 2 days after ingestion. The second tablet was given 1–2 weeks later.

Evaluation of the photographs was made with no knowledge of which tablet had been given. The photographs were magnified to 1.5 times life size and developed in exactly the same manner. The number of vesicles in one and the same area was recorded before and after ingestion of the tablets. Aggravation of the dermatitis was defined as either increased itching and a greater number of vesicles in more than one area of dermatitis, or itching and vesiculation in areas not previously affected. A questionable reaction was: either increased itching with no sign of aggravation, or an increase in the number of vesicles in only one of several affected areas with or without increased itching.

Following evaluation, the code was broken, and the reactions were compared with the contents of the tablets.

RESULTS

Table III describes the reactions of the 31 patients who received both chromate and placebo tablets as well as the 2 patients who received chromate only.

Table II. Site and morphology of dermatitis in the 31 patients who completed the study

Site	Number of patients	Dyshidrotic morphology
Hands	8	6
Feet	1	0
Hands and feet	11	9
Hands and/or feet and other sites	5	4
Other sites	6	0
	31	19

Table III. Results of ingestion of chromate and placebo in 31 patients and 2 additional patients given only chromate

+ designates aggravation, (+) a questionable reaction, – designates no reaction

Number of patients	Number of these with dermatitis of dyshidrotic morphology	Result of chromate ingestion	Result of placebo ingestion
11	9	+	–
14	5	–	–
3	2	(+)	(+)
1	1	+	+
2	2	–	+
2	2	+	Not done

When aggravation occurred there was usually an increase in itching on the affected areas 5–24 hours after ingestion of the tablets. Several patients also suffered eruption in areas which had been affected several years previously or on old chromate patch test sites. Vesicles often appeared on the palms or soles 1–3 days after ingestion.

Three patients complained of dyspepsia following ingestion of tablets which were later shown to have contained chromate. The symptoms were vomiting or abdominal pain, and transient diarrhea. After breaking the code, the placebo was again given to one of the two patients whose dermatitis was aggravated by the placebo. The aggravation occurred a second time. The patient who reacted to both chromate and placebo was given Sunset Yellow, with no resulting aggravation.

9 of 14 of those patients with dermatitis of dyshidrotic morphology reacted to ingestion of chromate, whereas only 2 of 11 patients who did not have dermatitis of dyshidrotic morphology reacted to chromate. This difference is not statistically significant ($0.05 < p < 0.10$ by Chi-square test with Yates' correction). No correlation could be demonstrated between patch test reactivity and the reaction following chromate ingestion.

DISCUSSION

The dermatitis of 11 of 31 patients worsened after oral ingestion of 7.1 mg potassium dichromate. 3 patients with an equivocal reaction might have shown a definite flare after the administration of a

larger dose. Both patients who reacted to the placebo and had no reaction to chromate were given the placebo first. It is therefore possible that the flare was caused by the psychological stress of an unusual situation. The eczema of both these patients was of dyshidrotic morphology, and this type of dermatitis is known to be exacerbated under conditions of stress (11).

Like Calnan, we observed eruptions on secondary sites such as cubital folds, sides of the neck or inner aspects of the thighs in a few patients (1).

The aggravation observed following ingestion of the placebo emphasizes the necessity of the use of placebo tablets in this type of study.

It is difficult to make a clinical evaluation of the variations in severity of dermatitis. Photographs of the same areas made before and after ingestion of the tablets enabled us to make this comparison without difficulty.

22 patients either did not answer the questionnaire or did not want to participate in the study. From the answers of the latter it was clear that many of these patients had very little eczema. The results of the study would probably be no different if this group had also been tested.

The daily intake of chromium varies greatly in different parts of the world. Schroeder (10) found that the mean intake in the United States is 60 μ g per day. A study performed in southern Sweden showed the daily mean chromium intake to be 0.74 mg (range 0.05–14.49 mg) (3). Chromium levels in many foods are determined by the soil in which they are grown. The soil in southern Sweden is comparable to that in Denmark, and we chose our test dose on the basis of the latter investigation. 2.5 mg chromium is more than the mean chromium intake but is within the range mentioned.

Christensen & Möller demonstrated that the dermatitis of 9 of 12 nickel-allergic patients with hand eczema of dyshidrotic morphology flared following oral ingestion of nickel (2). We could not demonstrate any significant difference between the reactivity of patients with eczema of dyshidrotic morphology and those without, although a reaction to chromate was more common among those patients with eczema of dyshidrotic morphology.

Reichenberger found 50 patients with eczema of dyshidrotic morphology among 101 with chromate dermatitis (8). No external contact with the allergen could be demonstrated for 41 of these patients, and the dermatitis was termed constitutional. It is pos-

sible that some of these constitutional eczemas were maintained by an oral intake of chromium.

The worsening of chronic chromate dermatitis following the ingestion of chromate in 35% of the patients who participated in the current study opens up new treatment perspectives. A low chromate diet should be instituted for patients suffering from chronic chromate dermatitis, particularly if the eczema is of dyshidrotic morphology.

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