

Treatment of Alopecia areata with Dinitrochlorobenzene

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Temmerman L, de Weert J, de Keyser L, Kint A. Treatment of alopecia areata with dinitrochlorobenzene. *Acta Derm Venereol (Stockh)* 1984; 64: 441-443.

Thirty patients with severe alopecia areata (A. A.) were treated with weekly applications of dinitrochlorobenzene (DNCB) in acetone solution. In only four patients regrowth of hair was complete and dense; sixteen patients experienced temporary results and in ten the treatment was a failure. *Key words: Topical therapy; Contact allergy.* (Received March 7, 1984.)

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The treatment of long-standing alopecia areata is often disappointing. Numerous modalities have been proposed: corticosteroids (topical, intralesional, systemic), PUVA, irritating compounds such as phenol, or anthralin; none was totally convincing.

In a discussion remark on the Memphis Society of 1974, Rosenberg & Drake (10) reported regrowth of hair in two patients with alopecia areata treated with topical DNCB. Since then excellent results were described by several authors (2, 4, 8) whereas less encouraging data were reported by others (5, 7).

In this paper we present our long term experiences of this DNCB treatment in 30 patients with severe A. A.

PATIENTS AND METHODS

The study included 30 patients with a persistent refractory alopecia areata. The group comprised 12 men and 18 women aged 13 to 57 years. There were 4 patients with alopecia universalis, 13 with alopecia totalis and 13 with extensive hair loss ($\geq 50\%$ bald area). In all the cases we asked for associated disorders (atopy, alopecia areata in close relatives). When there was a personal and/or familial history of atopy, complementary intracutaneous tests with the most common atopic allergens were done.

Routine laboratory data were obtained from all patients. Autoantibodies to the thyroid, gastric parietal cells, smooth muscles were determined as well as antinuclear-, anti-DNA-, antimitochondrial antibodies, immunoglobulins and complement. All patients were informed of the treatment and consent was obtained. Patients were then sensitized and challenged with an acetone solution of 1 chloro-2,4-dinitrobenzene, applied on the arm, according to the method of Catalonia (3). Forty-eight hours after challenge the patches were removed and the weakest strength that produced mild dermatitis was then chosen to initiate therapy. By means of a small syringe DNCB, dissolved in acetone, was applied to the head. Subsequently the appointments were made at weekly intervals over the entire hairless area of the scalp, the aim being to maintain a mild dermatitis. For these purposes varying samples between 0.0125% and 2% were used. Because of the mutagenic effect of the contaminant mononitrochlorobenzene in bacteria (6) only solutions without this contaminant were allowed for the treatment. Cimetidine treatment was employed when a tolerance to DNCB occurred.

RESULTS

The results were excellent in 4 of the 30 cases (group I, Table I), the hair regrowth being diffuse and dense. After painting DNCB on the scalp, the skin reactions were intense and appeared very early. Small concentrations of DNCB (mean 0.25%) were enough to produce a severe dermatitis. The mean time of appearance for regrowth was seven weeks. The occipital area turned out to be the most difficult area for regrowth. Duration of treatment varied between 8 months and 2 years. The applications of DNCB has now been stopped for 10 months. In two patients small relapses occurred.

The treatment results were poor in 16 of the 30 patients (group II, Table I), who showed only incomplete regrowth. In 10 patients with this partial response some hairs fell out although the weekly treatment was continued. The treatment duration for this group varied from 5 to 30 months. The mean time of appearance for regrowth was 10 weeks. The contact dermatitis obtained was of a variable intensity. It was severe in 3 patients but moderate to low in the others. One patient acquired tolerance to DNCB. After administration of cimetidine, sensitization reappeared and was followed by hair regrowth. This regrowth was only transient.

No result were obtained in 10 patients (group III, Table I). Treatment duration varied from 3 to 19 months. Five patients showed no regrowth at all, 5 had a few downy hairs although without evolution to normal hairs. The skin reaction to the topical treatment was intense in only 3 patients. The other seven showed only a moderate to low reaction in spite of increasing DNCB concentrations.

Side effects

All patients complained of an immediate burning sensation after use of the acetone solution and a mild irritation of the skinhead for 2 to 3 days. Three patients disclosed a few patches of eczema at a distance and one patient had an urticaria-like reaction (itching, oedema of the eyes, dyspnoe). Cervical lymphadenopathy was common. These complaints were only temporary. No patient dropped out of the study by reason of one of these reactions.

DISCUSSION

Extensive alopecia areata is difficult to treat. Spontaneous remissions may occur. Corticosteroids, PUVA, various irritants have been recommended often without success.

During the last few years, because of a possible auto-immune etiology of A. A., immunotherapy with DNCB has been advocated. Since the first report of Rosenberg (10) numerous hopeful publications appeared (2, 4, 8).

For the interpretation of these brilliant results, one has to take full account of the selection criteria, as in these studies even moderate alopecia areata was allowed. The criteria for a therapeutic success are not clearly defined: regrowth of hair seemed to be a satisfying criterion without noting the quality and density of the regrown hairs.

Some authors (5, 7) recorded less impressive results. In this report, we obtained minor therapeutic effects of DNCB, while only 4 of the 30 cases showed complete regrowth of hair (13,3%). Among these patients 2 had a relapse.

Table I. *Characteristics of the three groups of patients treated with DNCB*

	Group I: 4 patients	Group II: 16 patients	Group III: 10 patients
Clinical type	3 patients: A.A. 1 patient: A.T.	6 patients: A.A. 7 patients: A.T. 3 patients: A.U.	5 patients: A.A. 4 patients: A.T. 1 patient: A.U.
Disease history in years	3 months-13 years	Mean 6.6 years	Mean 7.8 years
Atopy	1 patient	3 patients	5 patients
Auto-antibodies	1 patient	5 patients	1 patient
Family history of Alopecia areata	0 patient	5 patients	5 patients

A.A.=means alopecia areata ($\geq 40\%$ bald area), A.T.=alopecia totalis, A.U.=alopecia universalis.

As already mentioned (5), the treatment result seems to depend on the reaction to DNCB. In our study, most outstanding hairgrowth was obtained in 4 patients, who showed and maintained a severe reaction to low-concentrated ($\leq 0.25\%$) DNCB even with distant eczematization.

An other important factor to the success of DNCB is the duration of the disease. The best results were obtained with hair loss of short duration ($\leq 1\frac{1}{2}$ years).

Atopy and alopecia areata in close relatives seem to be bad prognostic features. Only 1 of the 9 atopic patients showed hair growth and none of the patients with alopecia areata in their family history obtained an acceptable result.

We found auto-antibodies in 23% of our patients (7 of 30 cases). In this study of 30 patients it was not possible to determine the influence of these antibodies to the success of the therapy.

During treatment, acquired tolerance to DNCB has been reported (1). This tolerance can be reversed by the administration of a H_2 receptor antagonist Cimetidine (1). In our study, only one patient showed an acquired tolerance to DNCB. It was successfully reversed by cimetidine. However, the resulting hair regrowth was only temporary.

In conclusion, we can say that DNCB is certainly effective in stimulating the regrowth of hair. However, we do not recommend DNCB as a routine therapeutic approach in severe alopecia areata even when the patient has favorable prognostic features. One has to remember that this local therapy is difficult for the patient to bear without definite long term results being guaranteed.

Happle encourages the use of other potent contact allergens: squaric acid (8) and diphenylprone (9). Perhaps these and other sensitizers, in investigation, might open new perspectives in the treatment of severe alopecia areata.

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