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EVALUATION OF DRUG INFLUENCE ON THE ITCH DURATION IN THE SKIN OF PATIENTS WITH ATOPIC DERMATITIS, VARIOUS ECZEMAS AND PSORIASIS

II. Experiments in unaffected skin. Comparison with itch threshold technique and clinical evaluation

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In previous double blind experiments it was shown that an antihistaminic preparation could diminish the itch duration as well as the itch threshold values in the involved skin among half of the patients with atopic dermatitis (prurigo Besnier), various eczematous lesions or psoriasis. It was therefore of interest to compare these findings to those in the uninvolved skin in these patients and furthermore to appraise there results in relation to clinical observations ("clinical evaluation").

I. Influence of antihistamine on the itch duration in the unaffected skin of patients with atopic dermatitis, eczema of various forms and psoriasis

1. *Estimation of itch duration (without drug administration)*

Material and methods. The itch-duration values of 30 patients were estimated by the technique described (8) on the "healthy", macroscopically unaffected skin of the overarms. Estimations were made for all the patients at intervals of one, two and three days, and in 28 instances also after an interval of one week.

Results. Table 1 gives a summary of the findings of these investigations and shows that similar itch-duration values were observed in 23 of the 30 patients (77 %) where estimations were made daily for three days and in 21 out of 28 (75 %) patients when tested after one week. This finding is the same as that noted in affected skin under similar conditions.

2. *Influence of administration of an antihistamine preparation*

A further investigation was made to ascertain if the administration of a new antihistaminic 1[2(p-chlorbenzhydryloxy) ethyl]-4[2(2-hydroxethyoxy)ethyl] piperazine hydrochloride, UBC 1486, in tablets of 10 mg was capable of modifying the itch-duration in unaffected skin (8).

Material and methods. In 20 patients suffering from atopic dermatitis, eczema of various forms and psoriasis with actual itching the itch duration of the unaffected skin of the overarms was recorded before starting the experiments. Over half of the patients were given UCB tables (=A) during a period of three days. The itch duration was estimated on the fourth day. For a further three days placebo tablets (=B) were administered, and the itch duration was again estimated on the eighth

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Table 1. *Itch duration in unaffected skin*

Case	Skin disease	Itch duration estimations in intervals of	
		1-2-3 days	1 week
1	Atopic dermatitis	c	c
2	„ „	c	d
3	„ „	d	d
4	„ „	d	c
5	„ „	c	c
6	„ „	c	c
7	„ „	c	d
8	Eczema	c	
9	„	c	c
10	„	c	d
11	„	c	c
12	„	c	c
13	„	c	c
14	„	c	d
15	„	c	c
16	„	d	c
17	„	d	c
18	„	c	c
19	„	c	c
20	„	d	c
21	Psoriasis	c	d
22	„	c	c
23	„	c	c
24	„	c	c
25	„	c	
26	„	c	c
27	„	d	d
28	„	c	c
29	„	c	c
30	„	d	c
30/28		23: c 7: d	21: c 7: d

c: congruent (unchanged) values
d: discordant values

day. The remaining patients were first given B tablets and, subsequently, A tablets.

Results. Table 2 shows the results of the investigations in the left columns. It is evident that in eleven out of the 20 patients investigated, itch duration was diminished. In 8 patients it was unchanged, and in one increased. If the antihistaminic effect is compared with the initial control values, 13 patients showed diminished, 6 unchanged and one increased levels.

II. Influence of antihistamine on the itch threshold in the unaffected skin of patients with atopic dermatitis, eczema of various forms and psoriasis

1. *Estimation of itch threshold in unaffected skin, without drug administration*

Material and methods. In 20 patients the itch threshold was estimated daily by the technique described (8), over a period of three days, and also after an interval of one week.

Results. Table 3 shows the test results: When the estimations were made daily over a period of three days, fourteen patients had similar values; with regard to the estimations after one week, the corresponding figure was fifteen out of 20 patients, i.e. the values were unchanged in about three-quarters of the patients.

2. *Influence of administration of an antihistamine preparation*

Material and methods. In the 20 patients, suffering from atopic dermatitis, eczema of various forms, and psoriasis (referred to under I: 2) the itch threshold was estimated at the same time as itch-duration values (for details see I: 2 and 8).

Results. Table 2 (right columns) shows the findings. It is evident that the itch threshold was improved in eight, and unchanged in twelve out of 20 cases. A comparison of the placebo with the controls showed that the levels were unchanged in 9 patients, improved in 5 and lowered in 6, whereas the corresponding figures for the antihistaminic compared with the initial control test, were unchanged in 10, improved in 9, and with lowered values in one instance.

Comments. The experimental itch techniques: estimation of duration or of threshold in involved and unaffected skin under the influence of an antihistaminic were compared in three days' investigation with double blind technic. The itch duration in involved or unaffected skin as well as the threshold values in involved skin showed approximately equal changes (improve-

Table 2. *Itch duration and threshold in unaffected skin during UCB 1486 and placebo*

Case	Skin disease	Itch duration estimations			Itch treshold estimations		
		UCB-P	UCB-C	P-C	UCB-P	UCB-C	P-C
1	Atopic dermatitis	o	—	—	o	—	—
2	Eczema	—	—	o	—	—	o
3	„	—	—	—	o	+	+
4	„	o	—	—	—	o	+
5	„	—	—	+	—	o	+
6	„	—	—	o	—	—	o
7	„	—	—	—	o	o	o
8	„	—	o	o	o	o	o
9	„	o	o	o	—	o	+
10	„	—	—	o	o	o	o
11	„	—	—	o	o	o	+
12	Psoriasis	o	o	o	o	—	+
13	„	o	o	o	—	—	—
14	„	+	+	o	—	—	—
15	„	—	—	o	—	—	o
16	„	o	o	o	o	o	o
17	„	—	—	—	o	o	—
18	„	o	o	o	o	o	o
19	„	o	—	+	o	—	o
20	„	—	—	—	o	—	—
20		11: —	13: —	6: —	8: —	9: —	5: —
		8: o	6: o	12: o	12: o	10: o	9: o
		1: +	1: +	2: +		1: +	6: +

UCB: UCB 1486 P: placebo C: starting control value
—: diminished itch duration/improved (elevated) itch threshold
o: unchanged
+: increased itch duration/deteriorated (lowered) itch threshold

ment), whereas the threshold on normal skin was less influenced by the drug. This is in accordance with the findings of Cormia and Dougherty (3) who showed that the latter values were not constant. Based on control experiments the results were similar with the three techniques, i.e. constant in about 3/4 of the cases. On the other side the itch duration and itch threshold values showed no stricter parallelism in the same individual. If one considers that repeated trypsin injections are somewhat uncomfortable for the patients and that the amount of the injected trypsin may influence the itch estimations, the itch duration techniques seem more appropriate and even much easier to perform than threshold technique.

III. Clinical evaluation of itch during antihistamine administration

Material and methods. The 35 patients, who had been given UCB 1486 and a placebo during the present or former (8) investigations, were asked to state how much itching they had experienced during the given test period (see above), and their statements were recorded.

Results. In table 4 the information obtained is summarized. This shows that the drug was more effective in nearly 60 per cent of the cases when compared with the placebo. However there was no difference of statistical significance between group a) and the other groups (b+c+d). There was further no strict parallelism between

Table 3. *Itch threshold in uninvolved skin*

Case	Skin disease	Itch threshold estimations in intervals of	
		1-2-3 days	1 week
1	Atopic dermatitis	c	c
2	„ „	c	c
3	„ „	c	c
4	„ „	c	c
5	Eczema	c	c
6	„	d	c
7	„	c	c
8	„	d	d
9	„	c	c
10	„	d	d
11	„	c	c
12	„	c	c
13	„	c	c
14	Psoriasis	d	d
15	„	c	c
16	„	c	c
17	„	d	d
18	„	c	c
19	„	d	d
20	„	c	c
20		14: c 6: d	15: c 5: d

c: d: see Table 1

Table 4. *Clinical evaluation of itch during UCB 1486 and placebo in 35 cases*

a)	UCB 1486 better than placebo	20 cases (57 %)
b)	UCB 1486 and placebo both effective	3 „
c)	Placebo better than UCB 1486	6 „
d)	Both ineffective	6 „
		35 „

"objective" (itch duration of threshold) and "subjective" (clinical response) values.

Comments. The literature on the itch-relieving effect of different drugs is vast and has not been surveyed in the present context. This applies also to drug influence on special itching diseases, such as chronic liver diseases or malign lymphomas. Double-blind method investigations into the influence of drugs (mostly antihistaminics) on itching have also been extensively reported. For our purpose it suffices to mention experiments with trimeprazine[1] (1, 2, 6, 9), prothypendyl[2] (5), dimethylpyrinden[3] (7), methdilazine[4] (4) and, more recently, most of the increasing number of antihistamine drugs which have been investigated with this technique.

In the clinical evaluation of a drug in pruritus, the critical remarks of Cormia and Dougherty (3) should be remembered. They emphasize the importance of selection of patients, the need for control of associated factors, the necessity of administrating drug as well as placebo and for critical interpretation of reproducible results. They also emphasize the suggestive role of the first administered medicament, either this is the drug or the placebo.

Summarizing the experiences of the duration, threshold and clinical evaluation itch experiments, it seems that the itch duration estimation in involved or uninvolved skin are to prefer primarily due to their relative constancy and relatively easy performance. Even if large series of experiments are difficult to perform because of difficulties in selection and observation of appropriate patients, a small series of well-selected cases may give useful information on the antipruritic effect of a drug. In addition, a large series of patients should be clinically evaluated adapting the criteria of Cormia and Dougherty (3).

SUMMARY

The itch duration as well as the itch threshold were investigated in the unaffected skin of patients with atopic dermatitis, various eczemas and psoriasis. These values were found to be constant in about three quarters of the patients and could be influenced by the administration of a new antihistamine (UCB 1486) in about half of the cases. It is stressed that itch duration estimations in involved or unaffected skin

[1] Theralen®. [2] Nozinan®. [3] Fenistil®. [4] Azacon®.

are preferable to threshold examinations but should be completed by a critical clinical evaluation of itch.

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