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THE INFLUENCE OF CORTICO-STEROIDS ON THE ALLERGIC SKIN WHEEL REACTION

By

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When allergic patients apply to an allergy clinic, many of them are already receiving treatment with corticosteroids. Does this steroid treatment change the immediate skin wheal reaction? Should steroid treatment prove to diminish considerably, possibly abolish, the immediate skin wheal reaction, this may mean missing the correct diagnosis, and consequently the patient may be deprived of specific antiallergic treatment. Corticosteroid treatment does have some inhibitory effect on the delayed-type allergy reaction (1, 2), but with the usual therapeutic dose-level it has no certain influence on the immediate skin wheal reaction. In 1965, however, *Hauge & Vale* (3) published a trial carried out with 10 allergic patients and concluded that the immediate skin wheal reaction was reduced by about 40 per cent proportional to the area before treatment, after short term oral treatment with triamcinolone.

It was decided to re-examine this problem by testing a series of grass pollen hay fever patients with the specific antigen before and after 6 days' treatment with corticosteroids. The cutaneous reactivity towards grass pollen was measured before and after treatment with either triamcinolone or prednisone, as one might assume the possibility of different steroid preparations having different effects. Furthermore, the applicability of the method was examined in untreated controls.

MATERIAL AND METHODS

In 25 and 35 hay fever patients, suffering from clinically typical hay fever with pronounced allergy towards grass pollen, the immediate skin wheal reaction towards grass pollen in a concentration of 1:10,000 and towards histamine in the same concentration was determined before and after administration of 50 milligrammes prednisone or 40 milligrammes triamcinolone taken as shown in Table 1. On the 7th day, intradermal tests were again carried out with grass pollen 1:10,000 and histamine 1:10,000. The aqueous grass pollen allergen was produced by the Allergological Laboratory, Copenhagen, the histamine preparation in the Copenhagen University Hospital's Dispensary. The tests were carried out in the same way as all other intradermal tests at the University Hospital's Allergy Clinic, in the median third of the skin on the volar surface of the forearm. Sufficient fluid is injected intracutaneously to produce a wheal with a diameter of 5 mm; for this purpose 0.02-0.03 ml is used. Care was taken not to place the post-therapeutic intradermal test on the same site as the first one, in order to avoid the phenomenon demonstrated by *Lowell* (4) that the immediate skin wheal reaction may be reduced as a consequence of a previous injection of allergen at the same site. Ten minutes after the allergen was injected the wheal size was delineated on a transparent plastic sheet. The areas of the grass pollen- and histamine wheals were measured with a Haff planimeter 317 before and after corticosteroid therapy. As the trial was carried out in the months January-May, *i.e.* preseasonally, it was possible for the patients to follow the request not to take other drugs in the experimental period than the steroid tablets (apart from contraceptive tablets taken by two women). All the patients were between 16 and 45 years. The sex distribution can be seen from Table 2. Another group of 24 persons (18 allergic, 6 nonallergic), randomly selected for the investigation of the possible variation of the size of the histamine wheal at 7 days' interval, was tested with histamine 1:10,000 without having any kind of therapeutic treatment within this period. The purpose of this control material is to illustrate the method's range of variation. As with all biological methods, a certain variance was to be expected, and in case this variance turned out to be greater in the test group than in the control group, allowance for these findings was to be made.

TABLE 1

Dosage Scheme of 5 mg Prednisone or 4 mg Triamcinolone Tablets.

1st day	1 tablet morning, noon, and evening
2nd day	1 tablet morning, noon, and evening
3rd day	1 tablet morning, noon, and evening
4th day	1 tablet morning, and 1 tablet evening
5th day	1 tablet morning
6th day	½ tablet morning
7th day	No tablets. Retest.

TABLE 2

*Size of Allergic Wheal before and after 6 Days' Treatment with Triamcinolone or Prednisone.
Size of Histamine Wheal in Control Material on 1st and 7th Day (no Treatment).*

Triamcinolone treatment					Prednisone treatment					Control group		
Patient number	Grass pollen wheal		Histamine wheal		Patient number	Grass pollen wheal		Histamine wheal		Patient number	Histamine wheal 1st and 7th day	
	before	after	before	after		before	after	before	after			
1	1,0	1,9	1,5	1,5	1	1,8	1,6	1,0	1,0	1	1,2	1,2
2	2,0	2,9	2,9	1,3	2	0,9	0,8	1,0	1,1	2	1,8	1,4
3	1,4	1,5	1,4	1,3	3	0,8	1,7	1,1	1,3	3	1,0	1,0
4	1,5	0,8	1,5	3,0	4	1,2	1,0	1,7	1,7	4	1,5	1,5
5	1,5	1,6	1,2	2,0	5	1,0	1,5	1,1	1,3	5	1,3	1,2
6	1,4	1,6	1,4	1,4	6	0,8	0,9	1,0	1,0	6	1,2	1,1
7	0,7	0,3	1,5	1,0	7	0,4	0,3	1,3	1,0	7	1,5	0,9
8	1,3	1,0	1,2	1,2	8	0,3	0,3	0,9	0,9	8	1,2	1,4
9	1,0	0,9	1,2	1,2	9	1,0	1,2	1,1	1,1	9	1,3	1,0
10	0,9	1,3	1,3	1,5	10	0,8	0,6	1,3	1,4	10	1,4	1,4
11	0,7	0,5	1,5	1,1	11	1,1	3,0	1,2	1,4	11	0,9	1,0
12	1,2	2,0	1,2	1,3	12	0,6	0,5	1,3	1,0	12	1,3	1,4
13	1,5	1,8	1,4	1,7	13	1,2	1,7	1,8	1,0	13	1,8	1,8
14	0,8	1,2	2,0	1,8	14	0,5	0,4	1,0	1,3	14	1,5	1,5
15	0,7	1,1	1,6	1,0	15	0,8	0,8	1,7	1,5	15	1,3	1,2
16	1,6	2,0	1,3	1,2	16	0,5	0,3	1,3	1,3	16	1,2	1,7
17	1,4	2,6	1,0	1,0	17	0,4	0,4	1,7	1,1	17	1,2	1,2
18	1,4	1,9	1,1	1,3	18	0,8	0,9	1,2	1,2	18	1,3	1,3
19	1,0	1,2	1,9	1,4	19	0,4	0,6	1,0	1,6	19	1,1	1,0
20	1,3	1,3	1,0	2,0	20	1,9	1,4	1,4	1,8	20	1,3	1,2
21	1,2	1,0	1,4	1,1	21	1,6	1,4	1,2	1,2	21	1,2	1,2
22	1,0	2,5	1,4	1,7	22	1,6	1,8	1,6	1,7	22	1,3	1,3
23	1,8	1,9	1,8	2,6	23	0,8	0,8	1,3	1,5	23	1,4	1,2
24	1,4	1,9	1,4	1,1	24	0,8	0,9	1,3	1,4	24	1,0	1,0
25	0,9	0,8	1,3	1,1	25	1,4	1,2	1,3	1,7			
26	1,5	1,5	1,4	1,4	Triamcinolone group: 14 females, 21 males.							
27	1,5	1,7	1,6	1,7	Prednisone group: 9 females, 16 males.							
28	0,9	1,1	1,9	1,7	Control group: 11 females, 13 males.							
29	1,2	1,3	1,4	1,4	All figures are square centimeters.							
30	1,3	2,5	1,9	2,0								
31	1,2	1,4	1,5	1,0								
32	0,8	0,7	1,4	2,0								
33	1,2	1,6	1,3	1,3								
34	1,4	1,1	1,5	1,4								
35	0,7	0,7	0,8	1,4								

Triamcinolone group: 14 females, 21 males.

Prednisone group: 9 females, 16 males.

Control group: 11 females, 13 males.

All figures are square centimeters.

TABLE 3

Mean Values before and after Treatment. T-Test for the Deviation of the Difference.

		Number of patients	Mean value of the areas of wheals	Difference	s	t
<i>Triamcinolone</i>						
Grass pollen	Before	35	1.21			
	After	35	1.46	-0.25	0.48	-3.10
Histamine	Before	35	1.46			
	After	35	1.49	-0.03	0.53	-0.35
<i>Prednisone</i>						
Grass pollen	Before	25	0.94			
	After	25	1.04	-0.10	0.47	-1.10
Histamine	Before	25	1.27			
	After	25	1.30	-0.03	0.30	-0.47
<i>Control</i>						
Histamine	1	24	1.30			
	2	24	1.25	0.05	0.20	1.09

Statistician's comments: The table shows that one of the mean differences is significant. It is that of grass pollen with triamcinolone therapy, where the *t*-value is beyond the 1 per cent limit; apart from this there is no significant difference in the material.

RESULTS

The variation in size of the histamine wheals read after 10 minutes in the control group is shown in Table 2, as well as mean values of wheal size before and after treatment with corticosteroids. The statistic analysis of the figures did not show any statistically significant decrease in the size of the grass pollen- or the histamine wheals after corticosteroid therapy, and this applies to both prednisone and triamcinolone (Table 3). The only statistically proved difference which was found, was an *increase* of the wheal size towards grass pollen after one week's treatment with triamcinolone. The statistic analysis of the control material shows the applicability of the method of measurement.

DISCUSSION

The intracutaneous wheal, being the result of a biological process, is bound to be subject to certain variations from patient to patient, and from investigator to investigator. The first variation should be eliminated by a relatively great number of patients. The second variation factor should be neutralized by the control material. The finding by *Hauge & Vale* of a decreased wheal reaction after steroid treatment cannot be explained by the size of the corticosteroid dosage, as the doses given in our study were somewhat higher than those employed by the Norwegian workers. It is also difficult to explain why *Hauge & Vale* found a decrease in the allergic immediate skin wheal reaction after steroid therapy, but not in the corresponding histamine reaction after a steroid therapy. We have to assume that histamine release is an important factor in the appearance of the allergic wheal. Therefore, it is difficult to understand how corticosteroid could inhibit the allergic wheal, which mostly appears as a consequence of a histamine release, but not the histamine wheal itself.

The main purpose of this study was to investigate whether the cutaneous reactivity towards a specific allergen is reduced after 6 days' treatment with corticosteroids in normal therapeutic doses. We could show no reduction in wheal size in the present study. However, the investigation also showed that by treatment with triamcinolone an *increase* of the wheal size may appear at the end of 6 days' therapy.

CONCLUSION

In the present material comprising 60 patients allergic to grass pollen, who were tested with grass pollen and histamine before and after six days' treatment with corticosteroid, no statistically significant decrease of the immediate skin wheal reaction was found after administration of a therapeutic corticosteroid dosage (50 mg prednisone/40 mg triamcinolone). A control group consisting of 24 patients who did not receive any treatment at all, but who was tested twice with histamine

1:10,000, 0.5 ml intracutaneously at a week's interval, serves to confirm the applicability of the method.

SUMMARY

The immediate skin wheal reaction was investigated in grass pollen allergic patients by measuring the size of the immediate skin wheal reaction towards grass pollen before and after treatment for 6 days with a therapeutic dose of 50 mg prednisone or 40 mg triamcinolone respectively. Furthermore, the size of a histamine wheal with an initial diameter of 5 mm and measured after 10 minutes, was determined at 7 days' interval in 24 randomly selected individuals (18 allergic, 6 non-allergic). These patients were not given corticosteroid therapy.

In the group of 60 allergic patients who had received therapeutic doses of corticosteroids, no decrease in the grass pollen or histamine skin wheal reaction was demonstrated.

In the control group the size of the histamine wheals showed variations similar to those of the prednisone-treated patients.

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