

LOCAL INHIBITORY EFFECT OF SUBCUTANEOUSLY INJECTED TRIAMCINOLONE ON THE IMMEDIATE AND DELAYED TYPES OF SKIN REACTIONS

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CHANGES in the immediate and delayed types of allergic skin reactions after administration of corticosteroids have been studied by many authors with inconclusive results. However, consistent local inhibition of skin reactivity to tuberculin has been shown after intradermal injections of corticosteroid suspension.^{1, 2}

Injections of suspensions of relatively insoluble corticosteroids,³⁻⁷ especially of triamcinolone, given into the upper layer of the subcutaneous tissue suppress the clinical manifestations in psoriasis and other dermatoses. The effect of the steroid is a local one and limited to the injected site.

The object of the present study was to observe the effects of such subcutaneous injections of triamcinolone on the immediate and delayed types of allergic skin reactions.

MATERIAL AND METHODS

One hundred sixty-six individuals were included in this study. The number of males and females was about equal. Their ages ranged from 31 to 71 years. They were divided into 3 groups. Group I consisted of 81 subjects; group II consisted of 80 subjects; group III contained 5 subjects. The subjects in groups I and II gave a negative history of tuberculosis and allergy. The patients in group III gave unequivocal histories of ragweed pollinosis. None of the subjects had received previous injections in the area of skin to be tested. This precaution is necessary, since it has been shown⁸ that after repeated subcutaneous injections with allergic extracts the skin test sites become less reactive.

For subjects in all 3 groups, 1.5 ml. of a 1/4 per cent triamcinolone diacetate suspension* was injected into the upper layer of the subcutaneous tissue of the left forearm. The second step, for group I, was an intradermal injection of 0.1 ml. of Mantoux (1:1000 old tuberculin) into the left forearm, where the triamcinolone suspension had previously been injected. The second injection was given at intervals of up to 7 days after the first injection, so that changes due

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*Aristocort Diacetate Intraleisional (Lederle).

to varying intervals between the triamcinolone and Mantoux injections could be observed. As a control, the right forearm received only the intradermal Mantoux injection. Subjects who had negative Mantoux tests on both arms were not included.

The second step for group II was an intracutaneous injection of 0.1 ml. solution containing 0.01 mg. of histamine acid phosphate. Twenty subjects in this group had additional control with saline to rule out the possibility of non-specific reaction. Group III received ragweed pollen extract.

Each subject was used for one test only. Subjects injected with Mantoux were evaluated after 48 hours. The reaction to histamine and ragweed extract was evaluated during the first hour after the injection. Results were graded 0 to 4+, depending on the size of the whealing and were designated as follows: $\pm$, questionable; 1+, wheal up to 5 mm.; 2+ wheal from 6 to 10 mm.; 3+, wheal from 11 to 15 mm.; 4+, wheal over 15 mm. Furthermore, to eliminate unavoidable differences in technique of injections, this arbitrary scale was modified in such a way that when the test and control were to be classified in two different scales, there had to be a visible and palpable difference in whealing and at least 2 mm. difference in size. Otherwise they were classified in the same scale.

RESULTS AND DISCUSSION

Table I shows results obtained in the 81 individuals in group I, who received the Mantoux injection after the triamcinolone injection at various intervals of up to 7 days. Only one, a 71-year-old woman, did not show any suppression. Fifty-one individuals representing 63 per cent of the tested subjects manifested complete inhibition.

Table II shows the results of the 80 individuals in group II, tested with histamine after triamcinolone injection at various intervals of up to 4 days. The inhibition was less consistent than with Mantoux. Forty-three subjects showed varying degrees of inhibition and 27 of these showed a suppression equal to or greater than a drop of 2+. Thirty-seven failed to show any suppression. In 10, suppression was complete. This represents 12.5 per cent of the test subjects. Twenty subjects who had the additional saline control had no significance on the over-all result.

Table III shows the results obtained from the 5 ragweed-sensitive patients in group III who were tested with ragweed pollen extract up to 3 days after triamcinolone injection. All the patients showed marked or complete inhibition.

In this study variations in age, sex, or the time of testing after triamcinolone injection had no significant influence on the inhibition. There were only 3 exceptions: (1) In group I, when the Mantoux testing was done immediately after triamcinolone injection, the suppression was relatively less marked than in the rest of the subjects in this group. (2) In group II, there was no suppression in the 3 subjects who were tested with histamine immediately after triamcinolone injection. (3) In group II, there was marked inhibition when the 10 subjects were tested with histamine 2 days after triamcinolone injection.

In this study, none of the subjects showed larger whealing at the site of the triamcinolone injection than at the control site.

TABLE I. RESULTS OF 81 SUBJECTS IN GROUP I TESTED WITH MANTOUX AT VARIOUS INTERVALS AFTER SUBCUTANEOUS INJECTION OF TRIAMCINOLONE

NUMBER OF PATIENTS	TIME OF MANTOUX SKIN TEST AFTER TRIAMCINOLONE INJECTION	TRIAMCINOLONE PLUS MANTOUX	MANTOUX ALONE
9	Immediate	0	++++
4		0	+++
2		0	++
10		+	++++
2		++	++++
5		+++	++++
1		++++	++++
1	12 hours	0	++++
3		0	+++
5		0	++
2	24 hours	0	+++
4		0	++
3	2 days	+	++++
7	3 days	0	++
11		0	+
3		+	++++
4	4 days	+	+++
2		+	++
1	7 days	0	+++
2		0	++

REVIEW OF LITERATURE

Many authors have studied changes in the immediate and delayed types of allergic skin reactions after administration of corticosteroids. In one study⁹ prednisolone was given orally in doses up to 40 mg. daily for 2 months to 20 subjects; 12 showed no appreciable variations of the tuberculin test, 3 showed a decreased positivity, 3 showed negative conversion, and 2 showed positive conversion in the course of steroid administration. Similar inconclusive results were obtained with injections of ACTH when tested with tuberculin¹⁰ and also when tested with pollen extract in hay fever patients.¹¹

Skin testing with ragweed¹⁰ and histamine^{10, 12} after ACTH showed no significant changes.

Slight to moderate degrees of inhibition of the histamine and pollen skin reactions¹³ could be detected only histologically with high doses of prednisolone after 4 weeks of treatment by mouth or ointment applied topically for several months.

Consistent local inhibition of skin reaction to tuberculin was demonstrated after intracutaneous injections of hydrocortisone acetate.¹² In a similar test¹ with the experimental histamine reaction, no changes could be seen over the control area. Intradermal injection of hydrocortisone acetate¹⁴ prior to mosquito bites had a definite local effect in a patient who was allergic to it. Similarly, of the 13 patients injected intracutaneously with hydrocortisone acetate,¹⁵ 11 patients showed a definite inhibiting effect on the diagnostic patch test reaction applied over the area.

The present study was added to these experimental reports. The results indicate that a suspension of triamcinolone diacetate injected into the upper layer of the subcutaneous tissue had a consistent local inhibitory effect on the skin response of the delayed type of allergic reactions. In the immediate type of allergic reaction, the inhibitory effect was less consistent. Furthermore, it appears that the inhibition was more consistent with this technique than with the other methods of administration of corticosteroids previously studied.

TABLE II. RESULTS OF 80 SUBJECTS IN GROUP II TESTED WITH HISTAMINE AT VARIOUS INTERVALS AFTER SUBCUTANEOUS INJECTION OF TRIAMCINOLONE

NUMBER OF PATIENTS	TIME OF HISTAMINE INJECTION AFTER TRIAMCINOLONE INJECTION	TRIAMCINOLONE PLUS HISTAMINE	HISTAMINE ALONE	SALINE ALONE
3	Immediate	+++	+++	
2	1 hour	0	++++	
1		++	++++	
3		+++	++++	
2	12 hours	+++	++++	
4		++++	++++	
3	24 hours	++	++++	
1		++	++++	0
2		++	+++	
3		++	++	
1		++	++	0
1		+++	+++	±
4		++++	++++	
1		++++	++++	+
1	2 days	0	+++	0
1		0	++	0
1		0	++	0
2		0	++	
1		+	+++	
1		+	+++	0
1		+	+++	±
1		+++	++++	0
1		+++	+++	0
2	3 days	0	+++	
1		0	++	0
2		+	++++	
1		+	+++	0
1		+	+	0
1		+	+	0
1		++	+++	±
1		++	++++	±
1		++	++++	
3		++	+++	
2		+++	++++	
5		+++	+++	
1		+++	+++	+
6		++++	++++	
1	4 days	+	++++	
1		+	+++	0
2		++	++++	
2		+++	++++	
1		+++	+++	±
4		++++	++++	

TABLE III. RESULTS OF 5 PATIENTS IN GROUP III TESTED WITH RAGWEED AT VARIOUS INTERVALS AFTER SUBCUTANEOUS INJECTION OF TRIAMCINOLONE

NUMBER OF PATIENTS	TIME OF RAGWEED TESTING AFTER TRIAMCINOLONE INJECTION	RESULT	CONTROL
1	15 minutes	0	+++
1	12 hours	0	+++
1		+	++++
1	3 days	+	++++
1		+	+++

SUMMARY

One hundred sixty-six individuals were injected with a suspension of triamcinolone diacetate into the upper layer of the subcutaneous tissue to observe the effects on the immediate and delayed types of allergic skin reactions in the injected area.

Eighty-one individuals were tested intracutaneously with Mantoux at various intervals of up to 7 days, after they were treated locally with subcutaneous injection of triamcinolone. Inhibition was present in 80 subjects.

Of the 80 individuals tested intracutaneously with histamine up to 4 days after triamcinolone injection, 43 showed varying degrees of inhibition.

Five allergic patients were tested with ragweed pollen extract up to 3 days after triamcinolone injection, and all showed inhibition.

Age, sex, or the time interval between the triamcinolone injection and the intracutaneous testing had no significant influence on the inhibition.

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