

STATISTICAL STUDY OF THE THERAPEUTIC RATIO OF DEXAMETHASONE (DECADRON), A NEW CORTICOSTEROID*

Comparative Study of Dexamethasone and Prednisone in Treatment of Ragweed Pollinosis

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ALMOST a decade has elapsed since Carrier and associates¹ reported the first clinical use of cortisone for the relief of symptoms induced by allergy. Since then synthesis of cortisone and modification of its basic molecular structure have resulted in many analogues with increased potency and diminished side reactions. The latest of these is dexamethasone, an analogue of prednisolone to which has been added a fluorine atom at carbon 9 and a methyl radical at carbon 16.

Bunim and his co-workers² reported favorably on the use of this new preparation in the treatment of patients with rheumatoid arthritis. Studies on thirty patients with various allergic disorders who were on constant steroid therapy also impressed us favorably.

It was our impression that this drug had five to six times the potency of prednisolone, with no apparent increase in side reactions. Previous experience^{3,4} had shown us that a double-blind study involving patients sensitive to ragweed was probably one of the better methods of testing the therapeutic ratio of a new potent steroid compound. The patients used in this study all live in the same general environment; thus, in almost all instances they were exposed to an equal amount of pollen on the same day. Since it has been amply proved that corticosteroids will relieve symptoms of ragweed pollinosis, controls were not used in this study.

PROCEDURE

One hundred twenty-three patients who had either responded poorly to hyposensitization or had no previous treatment were followed in this study. Of these, sixty-six were placed on dexamethasone and fifty-seven were given prednisone. Since there was no clinical difference between the therapeutic

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effects of prednisone and prednisolone,⁵ prednisone was used in this study. A previous study³ had shown that 20 mg. of prednisone per day was adequate to give at least 75 per cent relief to seventy-five out of seventy-nine patients. Since dexamethasone was presumed to be five to six times more potent, a dosage of 2.25 mg. of dexamethasone was compared with 15 mg. of prednisone per day.

PATIENTS with NO SYMPTOMS

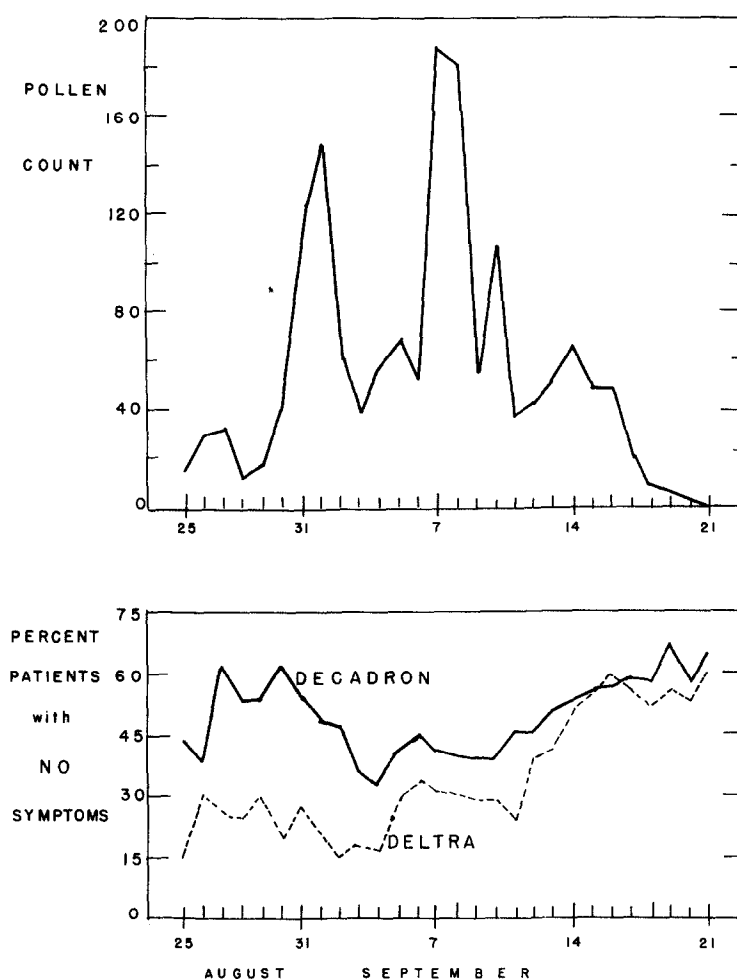


Fig. 1.

The study was conducted by the double-blind method. Neither the doctor, the nurse, nor the patient knew which drug was given. The steroids were distributed in vials containing twenty-one tablets of 0.75 mg. of dexamethasone or 5 mg. of prednisone. Each vial was numbered from 1 to 150. A master list showing the assignment of drugs to numbers was available to the statistician

TABLE I. SEVERITY OF SYMPTOMS
LOW POLLEN COUNT

WEEK	AVERAGE DAILY POL- LEN COUNT	TOTAL (100 %)	DEXAMETHASONE				TOTAL (100 %)	PREDNISONE			
			SEVERE	MODERATE	SLIGHT	NONE		SEVERE	MODERATE	SLIGHT	NONE
Aug. 18-24	19	79	6.3	22.8	30.4	40.5	62	9.7	21.0	48.3	21.0
Aug. 25-31	38	156	3.2	18.0	25.6	53.2	150	6.7	29.3	38.7	25.3
Sept. 1-7	20	191	8.4	16.8	15.7	59.1	196	9.2	8.7	26.0	56.1

For the periods noted, data refer to total number of trials and per cent of patients who reported indicated symptoms.

TABLE II. SEVERITY OF SYMPTOMS
HIGH POLLEN COUNT

WEEK	AVERAGE DAILY POL- LEN COUNT	TOTAL (100 %)	DEXAMETHASONE				TOTAL (100 %)	PREDNISONE			
			SEVERE	MODERATE	SLIGHT	NONE		SEVERE	MODERATE	SLIGHT	NONE
Sept. 1-7	86	285	9.1	25.6	24.9	40.4	246	12.2	23.2	39.8	24.8
Sept. 8-14	76	323	7.4	20.7	27.3	44.6	285	19.6	10.9	34.4	35.1

For the periods noted, data refer to total number of trials and per cent of patients who reported indicated symptoms.

only. Once started on a preparation, the patient continued on the same medication throughout the period of study. In all cases diagnosis of ragweed pollinosis was confirmed by history and by intracutaneous tests. Hyposensitization therapy was continued throughout the study in all patients who had been seen prior to June, 1958.

Each patient was given a card, described previously,⁴ to record his symptoms. In this way a daily tabulation of symptoms (severe, moderate, slight, or none) was recorded. A duplicate card was maintained by the statistician. On the reverse side of the duplicate card there was a check list of all previously noted common side reactions induced by steroid medications. Each patient was required to return weekly for one week's supply of medication and to exchange the old vial for a new one bearing the same number. The patient was seen by one of the physician authors, and any side reactions were noted. The quantity of unused tablets remaining in the returned vial was also noted, unknown to the patient. Each patient's report of symptoms, side reactions, and other data was transcribed to the master list. As each patient completed his course of treatment, his card was collected and an IBM card was punched. The data were then tabulated from these punch cards. Of the sixty-six patients on dexamethasone, 44 per cent were males with a mean age of 35 years, and they had spent an average of seventeen days on this steroid. Of the fifty-seven patients on prednisone, 44 per cent were males with a mean age of 33 years, and they had spent an average of nineteen days on the drug.

RESULTS

Pollen counts were charted from August 25 to September 21. As indicated by Fig. 1, patients on dexamethasone (Decadron) had more symptom-free days than those on prednisone. When the pollen count was at its height, however, the dexamethasone was far superior to prednisone (Table II). From the results

TABLE III. PATIENTS WITH NO SYMPTOMS

PREPARATION	NO SYMPTOMS	SYMPTOMS	TOTAL	PER CENT WITH NO SYMPTOMS
Dexamethasone (Decadron)	455	500	955	47.6
Prednisone (Deltra)	307	570	877	35.0
Totals	762	1,070	1,832	41.6

Probability of difference (47.6 per cent—35.0 per cent) is significant at 0.01 level.

of the five weekly periods (Table III), a significant difference in relief obtained was noted between the two preparations. Of the patients on dexamethasone, 48 per cent were symptom-free as compared to 35 per cent of those on prednisone, while only 7 per cent on dexamethasone had severe symptoms as compared to 12 per cent on prednisone (Fig. 2 and Table IV).

This increased efficacy in relief of symptoms was achieved without significant increase in side reactions (Table V). New side effects noted in patients

on dexamethasone not previously noted on prednisolone (Table VI) included an increase in libido in one woman and a complaint of muscular weakness in another.

PATIENTS with SEVERE SYMPTOMS

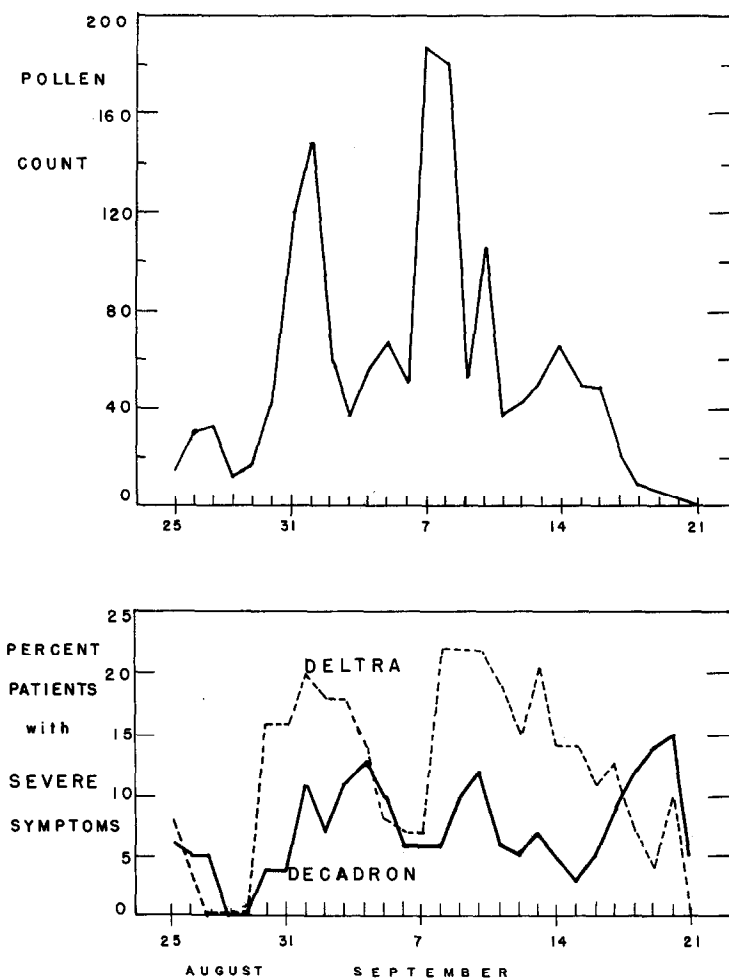


Fig. 2.

Records of patients' weekly weight changes were also maintained. These indicated that differences between the two preparations for most types of weight change were not significant. Only with reference to both a gain and a loss of weight in the same patients was the difference statistically significant. That is, only 1.5 per cent of patients on dexamethasone showed both a gain and a loss during the period, as compared with 10.5 per cent of the patients on prednisone.

TABLE IV. PATIENTS WITH SEVERE SYMPTOMS

PREPARATION	SEVERE SYMPTOMS	OTHER OR NO SYMPTOMS	TOTAL	PER CENT WITH SEVERE SYMPTOMS
Dexamethasone (Decadron)	71	884	955	7.4
Prednisone (Deltra)	114	763	877	13.0
Totals	185	1,647	1,832	10.1

Probability of difference (7.4 per cent—13.0 per cent) is significant at 0.01 level.

TABLE V. PATIENTS WITH SIDE REACTIONS

PREPARATION	NO SIDE REACTION	WITH SIDE REACTION	TOTAL	PER CENT WITH NO REACTION
Dexamethasone (Decadron)	25	41	66	37.9
Prednisone (Deltra)	28	29	57	49.1
Totals	53	70	123	43.3

Probability of difference (37.9 per cent—49.1 per cent) is not significant.

TABLE VI. SIDE REACTIONS

SIDE REACTION	DEXAMETHASONE	PREDNISONE	TOTAL
Patients with reactions	41 (100 %)	29 (100 %)	70 (100 %)
Genitourinary system	83.4	62.1	75.7
Urinary frequency	39.0	31.0	35.7
Nocturia	46.3	31.0	40.0
Gastrointestinal system	80.5	65.5	74.3
Heartburn	19.5	17.2	18.6
Flatulence	17.1	13.8	15.7
Abdominal cramps	12.2	10.3	11.4
Appetite change	12.2	10.3	11.4
Epigastric distress	9.8	6.9	8.6
Constipation	7.3	3.4	5.7
Hyperacidity	2.4	—	1.4
Nausea	—	3.4	1.4
Nervous system	78.0	62.1	71.4
Insomnia	34.1	10.3	24.3
Euphoria	22.0	6.9	15.7
Headache	9.8	24.1	15.7
Fatigue	9.8	20.7	14.3
Libido	2.4	—	1.4
Muscular	12.2	10.3	11.4
Cramps	9.8	10.3	10.0
Weakness	2.4	—	1.4
Skin	12.2	—	7.1
Acneform eruption	9.8	—	5.7
Itching	1.4	—	1.4
Cardiovascular	7.3	20.6	12.9
Palpitation	2.4	17.2	8.6
Flushing of face	4.9	3.4	4.3
Metabolic	—	3.4	1.4
Moonface	—	3.4	1.4

Note: Percentages add up to more than 100 per cent because of multiple reactions occurring in patients. Dexamethasone caused an average of 2.76 reactions per patient, while prednisone produced an average of 2.24 per patient.

COMMENT

Dexamethasone has been shown to be a potent new steroid with a favorable dosage ratio. With only one-seventh the dose (2.25 mg. versus 15.0 mg.), dexamethasone is more effective than prednisone in the treatment of ragweed pollinosis, particularly during periods of high pollen count, without a significant increase in side reactions. In all probability, if the same amount of relief as that obtained with prednisone is desired, much smaller doses of dexamethasone can be used with a correspondingly lower incidence of side reactions.

TABLE VII. WEIGHT CHANGE

TYPE OF CHANGE	NUMBER OF PATIENTS			PER CENT OF PATIENTS		
	DEXA-METHASONE	PREDNI-SONE	TOTAL	DEXA-METHASONE	PREDNI-SONE	TOTAL
None	30	22	52	45.5	38.6	42.3
Gain	28	23	51	42.4	40.4	41.4
Loss	7	6	13	10.6	10.5	10.6
Gain and loss	1	6	7	1.5	10.5	5.7
Totals	66	57	123	100.0	100.0	100.0

It is interesting to note that even on these relatively small doses, over a short span of time side reactions were reported by more than 50 per cent of the patients on both preparations. In no case was it necessary to stop medication because of these undesirable effects, but of course all these patients were supervised closely.

SUMMARY

1. Statistical analysis comparing daily doses of 2.25 mg. of dexamethasone with 15.0 mg. of prednisone in the treatment of ragweed pollinosis is reported.
2. Dexamethasone in a dose only one-seventh as large, is more effective than prednisone for relief of symptoms induced by ragweed pollen.
3. There was no significant difference in side reactions in patients on the two preparations.
4. There was significantly less weight change of both gain and loss in the same patients on dexamethasone than on prednisone.
5. There were no significant differences between the two preparations for all other types of weight changes (gain only, loss only, no change in weight).
6. Dexamethasone is a potent new corticosteroid which may be given in a smaller dose.

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