

ORAL CORTISONE THERAPY IN RAGWEED HAY FEVER

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ORAL cortisone* and intramuscular cortisone or ACTH produce striking benefit in the symptomatic relief of bronchial asthma and associated allergic diseases.¹⁻⁹ Relief occurs within 24 to 96 hours after therapy is started and is confined to the period during, and immediately following, administration of either ACTH or cortisone. With most patients the symptoms return within several hours to two weeks after these hormones are discontinued. There is no relationship between the total dosage or duration of therapy, or both, and the length of remissions. With large doses, prolonged or repeated courses of therapy, metabolic and hormonal side effects are apt to occur more frequently.

The remarkable effects and symptomatic relief obtained cannot be ignored even though these effects may be only temporary. The symptoms of hay fever are limited, depending mostly on the duration of the pollination season. It was felt that cortisone is an ideal agent in any type of self-limited disease that would respond to its use. Also, if one were to administer the smallest possible dose to obtain therapeutic results, and exclude patients with hypertension, diabetes mellitus, hemorrhagic tendencies, peptic ulcer, congestive heart failure, coronary heart disease, pregnancy, and psychopathic personalities, the occurrence of possible side effects would be minimized.

Previous attempts have been made to treat ragweed pollinosis by the use of injectable cortisone. Carryer and associates¹⁰ reported the use of cortisone in three cases of bronchial asthma and hay fever resulting from ragweed sensitivity. The patients were given intramuscular injections of 100 mg. daily during the ragweed hay fever season. Each patient experienced prompt relief from the symptoms of hay fever and asthma. The symptoms of asthma were more quickly relieved than those of hay fever. Relief was confined to the period during, and immediately following, cortisone administration. Friedlander and Friedlander¹¹ have used oral cortisone in eight patients with severe ragweed hay fever. Administration was started at a period of high pollen concentration. Coincidentally this was soon followed by a rapid fall in the pollen count and the counts remained low during the balance of the season. Remarkable symptomatic relief was experienced in six of the eight patients. It was felt that the initial symptoms were relieved by cortisone and that the continued remissions were due to the low pollen concentration present for the balance of the season.

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Feinberg, Dannenberg, and Malkiel¹² treated three ragweed sensitive patients with ACTH and no relief was obtained as a result of the ACTH therapy. In their discussion they stated that, thus far, unpublished reports of the effect in hay fever have been controversial, and the impression gained is that the hormones, cortisone, and ACTH may not be very useful for that purpose. Gelfand¹³ treated two patients with severe ragweed hay fever, uncontrollable by combined hyposensitization and antihistaminic therapy, with 50 mg. of cortisone on the days when the pollen count was very high, with marked clinical improvement and no adverse metabolic disturbances.

SCOPE OF STUDY

A study was undertaken to determine whether the symptoms of ragweed hay fever could be influenced by the oral use of cortisone. A total of 25 patients were included in this study. There were 4 men and 21 women, ranging in age from 21 to 60 years. The duration of hay fever varied from 2 to 18 years, and previous preseasonal and coseasonal ragweed hyposensitization ranged from 2 to 15 years' treatment. In previous years the patients experienced various degrees of relief. However, invariably the great majority of these patients had symptoms varying from slight to a marked degree during the height of the ragweed season. Although hyposensitization alone or combined with antihistamine therapy had afforded significant symptomatic relief and prevented seasonal asthma in most of the patients, the symptoms were still marked enough for them to seek further relief.

The patients were again divided roughly into three classes as to sensitiveness. This was ascertained by the strength of ragweed solution that produced a marked reaction in intracutaneous tests. The injections were given pre-seasonally and the largest optimal dose was attained with each patient. The top dose of ragweed extract, or a smaller one, depending upon the patient's sensitiveness, was given once weekly during the season in addition to the cortisone tablets. No other medication was administered.

It was ascertained by following the pollen counts of the previous years that the height of the season in our locality occurred approximately from August 25 to September 8. On this basis, cortisone was administered for a period of fifteen days, from August 25 to September 8 inclusive. The average pollen concentration during the period of this study was slightly higher than the average of the previous 5 years. These patients were all having hay fever symptoms at the time cortisone was started.

An attempt was made to minimize the occurrence of possible side effects. Patients with hypertension, coronary arterial disease, congestive heart failure, hemorrhagic tendencies, peptic ulcer, diabetes mellitus, pregnancy, and psychopathic personalities were not included in this study. All patients were given low sodium diets and 15 drops of a saturated solution of potassium iodide three times daily. It was felt that with these precautions and careful observation as to the side effects, it was reasonably safe to administer cortisone in the doses used for a period of 15 days.

TABLE I. RESULTS OF ORAL CORTISONE THERAPY IN RAGWEED HAY FEVER

PATIENT	SEX	PREVIOUS TREATMENT*	RESULTS†	SIDE REACTIONS	COMMENTS
1. S.G.	M	2 yrs.	4 plus	None	Excellent result. Had only slight symptoms 5 days after termination of therapy.
2. C.S.	M	4 yrs.	4 plus	None	No improvement until after the third day of cortisone therapy, then experienced excellent relief. Symptoms returned 48 hours after cessation of therapy.
3. A.C.	F	2 yrs.	4 plus	None	Complete relief of asthma which had been present for 2 yrs. Hay fever also completely relieved. Symptoms returned 48 hrs. after cessation of therapy.
4. M.R.	F	13 yrs.	4 plus	Headache and constipation	Excellent relief noted 1 hr. after start of cortisone therapy; 48 hrs. after cessation of therapy, had very severe symptoms that were relieved again within 1 hr. after resumption of cortisone.
5. E.R.	M	9 yrs.	4 plus	None	Excellent complete relief of hay fever symptoms and incidentally relief of arthritic symptoms that were present intermittently all year. Symptoms returned 48 hours after cessation of therapy.
6. A.G.	F	1 yr.	4 plus	None	Excellent relief. Still had no symptoms 3 days after cessation of treatment.
7. E.M.	F	7 yrs.	4 plus	None	Excellent result. Completely asymptomatic. Still no symptoms 5 days after termination of therapy.
8. C.P.	F	15 yrs.	3 plus	Palpitations	Obtained excellent relief of daily asthma, and good relief of hay fever symptoms. Symptoms recurred 48 hrs. after cessation of therapy.
9. T.S.	F	4 yrs.	3 plus	Insomnia	Marked relief. Only a rare occasional symptom. Still had no return of symptoms 5 days after cessation of therapy.
10. M.A.	F	2 yrs.	4 plus	Trace of sugar in urine.	Excellent results. Still feeling well 5 days after termination of treatment.
11. J.T.	F	5 yrs.	4 plus	None	Excellent result. Was still asymptomatic 5 days after cessation of treatment.
12. J.G.	M	7 yrs.	0 on 100 mg. 4 plus on 200 mg.	Collapsed during work as longshoreman. Perspired excessively. Relieved with salt tablets.	No relief of symptoms during first week on 100 mg. per day. Excellent relief on 200 mg. daily, for 3 days and then reduction to 100 mg. and relief continued. Symptoms returned within 48 hrs. after cessation of therapy.
13. M.W.	F	15 yrs.	4 plus	Trace of sugar in urine.	Excellent result. Asymptomatic 3 days after termination of therapy.
14. M.M.	F	1 yr.	0	None	Patient very uncooperative. Did not follow instructions. Did not take the cortisone regularly. Claims she felt better last year.

TABLE I—CONT'D

PATIENT	SEX	PREVIOUS TREATMENT*	RESULTS†	SIDE REACTIONS	COMMENTS
15. M.D.	F	3 yrs.	4 plus	None	Excellent result. Completely asymptomatic. Symptoms returned 48 hrs. after cessation of therapy.
16. D.R.	F	1 yr.	2 plus	None	No relief until the 4th day of treatment. Then experienced moderate improvement. Felt better the previous year. Symptoms returned within 24 hours after cessation of treatment.
17. H.Y.	F	1 yr.	4 plus	None	Obtained complete relief of both her asthma and hay fever after the 2nd tablet. Excellent result. The symptoms recurred within 48 hours after cessation of therapy.
18. J.M.	F	1 yr.	3 plus	None	Asymptomatic for first 10 days of treatment. Then had some moderate symptoms with a purulent nasal discharge which patient thought was due to an upper respiratory infection.
19. R.R.	F	3 yrs.	3 plus	1 day of abdominal pain, belching, nausea, diarrhea at onset.	Marked relief after first day. Occasional slight symptom. Return of symptoms 48 hours after cessation of treatment.
20. A.D.	F	6 yrs.	4 plus	Headache and precordial pain	Excellent result. Could sleep through the night for the first time during any hay fever season.
21. M.S.	F	13 yrs.	4 plus	Palpitations	Excellent relief. This was first time her asthma was relieved during hay fever season. No other symptom. Still no return of symptoms 3 days after cessation of therapy.
22. L.D.	F	4 yrs.	3 plus	None	Marked relief. Had an occasional symptom. Felt much better than last year. Symptoms returned 3 days after termination of therapy.
23. M.B.	F	4 yrs.	3 plus	Insomnia	Marked relief. Experienced best year in 15 years of hay fever. Had only an occasional symptom. Had gradual return of symptoms 2 days after termination of therapy.
24. G.R.	F	12 yrs.	4 plus	Headache, weakness, nervousness on 2nd day of therapy only.	Excellent relief of hay fever symptoms starting on 2nd day of therapy. Had previously had a closed tear duct which caused great discomfort during hay fever season because of continuous flow of tears from eyes. This was greatly relieved. Only had a slight moisture from eye. Symptoms returned 48 hours after termination of therapy.
25. R.K.	F	3 yrs.	0	Discontinued therapy.	After 6th tablet developed dizziness, nausea, and vomiting and was unable to continue medication. No relief of symptoms.

All patients received cortisone for 15 days unless otherwise noted. Daily dose, 100 mg.

*Ragweed hyposensitization.

†4 plus — excellent relief of symptoms.

3 plus — marked relief of symptoms.

2 plus — moderate relief of symptoms.

0 — no relief.

DOSAGE SCHEDULE

The dosage schedule consisted of 25 mg. of cortisone 4 times a day, a total daily dose of 100 mg. Twenty-four patients were able to tolerate this dose very well. One patient complained of dizziness, nausea, and vomiting and discontinued cortisone after the sixth dose.

RESULTS OF TREATMENT

Oral cortisone in doses of 25 mg. 4 times a day remarkably relieved the usual symptoms of ragweed hay fever in 21 of 25 patients selected for this study. Fifteen patients obtained excellent relief, and 6 patients, marked relief. One patient experienced moderate relief, and 3 patients, no relief (Table I). Case 12 was classified as a failure since on the dosage used in this study (100 mg. daily) he had no relief of symptoms. However, he experienced excellent relief when the dose was increased to 200 mg. daily, without side effects. In those patients who obtained relief it was far superior to that produced by any other previous treatment. Relief occurred in from one to 72 hours after the beginning of therapy. In general, the maximum relief of symptoms was obtained by the third day of treatment. The patients continued asymptomatic as long as oral cortisone was administered. Discontinuation of cortisone resulted in a recurrence of symptoms. In 15 patients there was a return of symptoms in 48 hours.

In one patient, treatment was discontinued because of dizziness, nausea, and vomiting after the sixth tablet. A transient, slight glycosuria occurred in two cases. Other side effects consisted of headache in 3 cases, palpitations in 2, insomnia in 2, precordial pain in 1, constipation in 1, abdominal cramps, nausea and diarrhea in 1 case, and weakness and nervousness in 1 case. These side effects were mild and of brief duration. They did not interfere with the continuation of cortisone. The majority of patients stated that they were able to be more active and many were engaged in increased physical activity while taking cortisone. It was noted that most patients experienced an initial weight loss of 2 to 3 pounds. This may have been due to the low salt diet. There were no significant changes in blood pressure in any of the cases.

DISCUSSION

Cortisone therapy is not a substitute for hyposensitization. Only by the production of blocking antibodies can one ultimately obtain complete and lasting benefit. It is also by this method that the patients are less prone to develop asthma.

However, the good results obtained with cortisone in this series of cases far surpassed any previously obtained by hyposensitization and/or antihistamine therapy. Cortisone should be reserved, however, for those cases in which the indications are strong, i.e., in those patients who have marked symptoms during the height of the season, after the usual therapeutic measures, such as hyposensitization and antihistamines have failed. No serious side effects occurred in this series. In order to minimize the occurrence of side effects one should

be careful not to administer cortisone to hay fever patients who have a coexisting hypertension, coronary arterial disease, congestive heart failure, hemorrhagic tendencies, peptic ulcer, diabetes mellitus, pregnancy, or psychopathic personalities. It was found that short term therapy could be carried out safely without extensive laboratory tests if there were proper cooperation between patient and physician and careful observation as to the possible occurrence of side effects. The patient's weight, fluid intake and output, blood pressure, and the results of the urine examination for sugar should be charted daily. To further minimize the possible occurrence of side effects the patients were given a low sodium diet and potassium iodide. The relatively small dose of 100 mg. of cortisone daily and the short duration of therapy (15 days) were other factors that also possibly minimized the occurrence of severe side effects. The dosage schedule was arbitrarily adjusted to 25 mg. of cortisone four times daily, a total of 100 mg. per day. It is possible that a smaller dose of cortisone, either alone or in combination with an antihistamine, may produce the same symptomatic relief and further decrease the incidence or severity of possible side effects.

SUMMARY

1. Twenty-five selected hay fever patients were treated with oral cortisone tablets in addition to preseasonal and coseasonal ragweed hyposensitization. There were 21 women and 4 men, ranging in age from 21 to 60 years. The duration of their hay fever was from 2 to 18 years, and the duration of previous ragweed hyposensitization ranged from 1 to 15 years.

2. Twenty-one of the 25 patients obtained marked or complete relief. Fifteen obtained excellent or complete relief; 6, marked relief; 1, moderate relief, and 3 patients had no relief of symptoms.

3. Side effects were observed in 10 patients, and in 9 they were mild and of brief duration and did not interfere with the continuation of cortisone. One patient discontinued its use because of dizziness, nausea, and vomiting. No severe side effects were encountered in this series.

4. Oral cortisone therapy combined with hyposensitization in ragweed hay fever produced much greater relief than that obtained previously with any other treatment. The results justify its use in selected cases after the usual therapeutic measures have failed.

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