

REPOSITORY EMULSION THERAPY FOR MOUNTAIN CEDAR POLLINOSIS: A DOUBLE-BLIND STUDY

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THE pollen of mountain cedar (*Juniper sabinoides*) is responsible for allergic respiratory symptoms in Central Texas and adjacent areas. This tree is not limited to mountain ranges, because it is used for Christmas trees and other ornamental purposes. Large amounts of pollen are produced from December through February and lesser amounts in November and March. It often causes marked pollinosis, and sneezing and pruritus are particularly troublesome.

A double-blind placebo study using repository emulsion therapy for mountain cedar pollinosis was undertaken during the 1962-1963 season.

SELECTION OF PATIENTS

Thirty-four patients with a definite history of mountain cedar pollinosis were selected for the study. Each had a positive intradermal skin test to a 1:500 dilution of the pollen extract. All of the patients had allergic rhinitis, and 11 had bronchial asthma in addition. Their ages ranged from 6 to 67 years, and 3 were non-Caucasian. Only 6 patients had not received prior therapy. Eight had received less than 12 injections of aqueous extract the previous season, and 6 others had been given emulsion therapy in 1961. None received mountain cedar pollen extract later than March, 1962.

MATERIALS AND METHODS

The specially prepared mountain cedar pollen extract* contained 10,000 protein nitrogen units per milliliter with thimerosal as the preservative. Arlat-16† was used, and the final emulsion contained 6 parts mineral oil, 1 part Arlacel A, and 5 parts aqueous extract. Normal saline was substituted for the extract in the placebo emulsions. The emulsions were prepared by passing the materials through a 24 gauge double-hub needle for at least 100 strokes. Each patient received a total of 0.24 ml. of emulsion in the triceps muscle, as suggested by Salk.¹ A relatively low dosage of the extract (1000 protein nitrogen units) was administered to those receiving the active emulsion.

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*Obtained from Hollister-Stier Laboratories, Atlanta, Ga.

†A sterile material containing 6 parts Light White Mineral Oil NF XI and 1 part Manide Mono-Oleate (Arlacel A) obtained from Hollister-Stier Laboratories, Atlanta, Ga.

TABLE I. DAILY SCORING ACCORDING TO SYMPTOMS AND MEDICATIONS

SYMPTOMS	MEDICATION	SCORE
None	None	0
Mild	None	1
Moderate	1 or 2 tablets with good relief	2
Moderate	More than 2 tablets or use of nebulizer with moderate or good relief	3
Severe	More than 2 tablets or use of nebulizer with poor or moderate relief	4
Severe	No relief from maximum medications	5

Each patient was given a randomly selected number by one of the investigators. Placebos were randomly assigned to half of the numbers and active emulsions to the rest. None of us knew which material the patients received. The emulsions were administered on Oct. 16 and 17, 1962.

Sera were obtained before treatment and at 6 and 14 weeks post treatment for determination of hemagglutinating antibody titers. The titers were determined according to the method of Arbesman and co-workers,² except that mountain cedar pollen extract was used as the antigen. A fourfold change in titer was required to be considered significant.

UNTOWARD REACTIONS

Of the patients who received the active emulsion, 3 (18 per cent) had marked local swelling, heat, pain, erythema, and minimal pruritus beginning within a few hours and persisting not more than 4 days. One of these patients had previously received aqueous extract for 5 years, and the other 2 had received aqueous extract for 1 month in February, 1962. Minimal local pain was experienced by 5 patients who were given the active emulsion and by 4 who received the placebo emulsion. There were no cysts or nodules.

CLINICAL EVALUATION AND RESULTS

The patients maintained daily records concerning the type and severity of symptoms and number of medications used. A daily score was calculated for each patient on the basis of information in Table I. All patients were seen by the same physician at least monthly. The daily scores were tabulated from Dec. 1, 1962, through Feb. 28, 1963.

The mean season score for those who received the active emulsion was 156 compared to 175 for those who received the placebo emulsion. Statistical analysis with the *t* test and nonparametric test indicated no difference between the 2 groups.

The subjective response of the patients to the emulsion therapy according to whether they had had any previous therapy is shown in Table II.

HEMAGGLUTINATING ANTIBODY STUDIES

Of the 17 patients who received active emulsion, 9 demonstrated a fourfold rise in hemagglutinating antibody titers (Table III). Six reported that they had a good season, as did 5 of the 8 who did not have a rise in titer.

In the placebo group, 2 of 4 with increased titers and 5 of 13 without a rise in titer had a good season.

Only 6 patients had received no previous therapy. Of the 4 who were given active emulsion, 3 had a rise in titer and clinical improvement. The other patient had no significant change in titer and no clinical improvement. Of the 2 who were given placebo emulsions, neither had clinical improvement, but 1 had an increase in titer.

DISCUSSION

A relatively small amount of pollen extract (1000 protein nitrogen units) was used in the active emulsion. Only 700 protein nitrogen units of mountain

TABLE II. PATIENTS' EVALUATION OF EMULSION THERAPY

SUBJECTIVE RESPONSE	PREVIOUS THERAPY							
	NONE		LESS THAN 3 MONTHS AQUEOUS		MORE THAN 3 MONTHS AQUEOUS		AQUEOUS AND EMULSION	
	A*	P†	A	P	A	P	A	P
Type of season								
Good	3	0	1	3	4	3	3	1
Bad	1	2	2	2	3	4	0	2
Compared to last season								
Better	3	0	1	3	1	6	1	0
Same	1	0	2	2	5	1	1	1
Worse	0	2	0	0	1	0	1	2

*Number of patients who received active emulsion.

†Number of patients who received placebo emulsion.

TABLE III. HEMAGGLUTININATING ANTIBODY RESPONSE

ACTIVE EMULSION				PLACEBO EMULSION			
PATIENT	PRE-TREATMENT TITER	POSTTREATMENT TITER		PATIENT	PRE-TREATMENT TITER	POSTTREATMENT TITER	
		6 WEEKS	14 WEEKS			6 WEEKS	14 WEEKS
J C	1:1	1:8	1:2	D A	1:4	1:8	1:32
D D	Neg	1:2	1:4	A A	1:2	1:8	1:4
C D	1:1	1:16	1:16	D B	1:128	1:128	1:32
E F	Neg	1:32	1:2	H B	1:2	1:8	1:32
P G	1:1	1:16	1:4	E B	1:1	1:8	1:4
A G	Neg	1:4	1:2	M E	Neg	1:8	1:8
R H	1:1	1:16	1:2	E G	1:32	1:4	1:2
A H	1:4	1:32	1:2	M G	1:16	1:16	1:4
G H	1:4	1:256	Neg	P H	1:32	1:32	1:128
L H	1:64	*	1:512	L L	1:4	1:4	1:4
E J	1:32	1:64	1:1024	J M	1:8	*	1:4
H M	1:8	1:32	1:2	G P	1:8	1:64	1:1
N M	1:64	1:128	1:2	M R	1:4	1:128	Neg
L P	Neg	1:8	1:4	C S	1:4	1:1	1:2
J S	1:16	1:256	1:8	M T	1:16	*	1:4
V S	1:32	1:16	1:2	B T	1:2	*	1:4
R W	1:2	1:32	1:4	M W	Neg	1:16	1:64

*Not done.

cedar pollen extract were administered in a water-in-oil emulsion to 13 patients at this hospital in November, 1961.³ All but 1 reported a favorable response. This excellent clinical result prompted this double-blind study.

Friedlaender⁴ has commented on the difficulties of using the double-blind technique in evaluating therapeutic response in allergic disease. Viral infections which occurred during the winter months further complicated the clinical evaluation of this study. Response to therapy may also be influenced by the amount of air-borne pollen present. Except for 8 days of extremely high pollen counts in December, 1961, the total counts for this and the previous season were similar.⁵ However, 9 patients (53 per cent) who received the placebo emulsion reported fewer symptoms than during the previous season (Table II).

Most of our patients had received previous aqueous therapy, and 6 had been given emulsion repository therapy the previous season. This could have contributed to the high incidence of benefit from the placebo treatment. In the previously untreated group there was, in general, a good response to the active emulsion and poor response to the placebo.

The patients who received the active emulsion had a better mean score than the placebo group. However, the difference was not significant at the 5 per cent level. In a somewhat similar study, Friedlaender and Friedlaender⁴ reported a small statistical difference between the group given an emulsion containing ragweed extract and another group given a placebo emulsion. The active emulsion contained either 2500 or 5000 protein nitrogen units of ragweed pollen extract. Sherman and associates⁶ found definitely superior results in patients treated with emulsions which contained ragweed pollen extract compared to those treated with placebo emulsions. They separated their patients into groups according to their skin reactivity to ragweed pollen extracts. The patients who received 2500 or 5000 protein nitrogen units had seasons similar to those who received only 1000 units. The patients who received 10,000 protein nitrogen units had the best season, but their counterparts who received the placebo also had symptoms which were the least severe of the entire placebo group.

It is doubtful that the failure to demonstrate a clear difference in our treated group, as compared to the placebo group, can be attributed solely to our use of low-dosage extract.

SUMMARY

A double-blind repository emulsion study for mountain cedar pollinosis was accomplished during the pollen season of 1962-1963. The active emulsion contained 1000 protein nitrogen units of pollen extract. Thirty-four patients participated in the study, and only 6 had not received prior therapy.

The group that received the active emulsion had a better mean score than the placebo group, but the difference was not statistically significant. The previous aqueous or emulsion therapy may have contributed to the apparent benefit from the placebo treatment.

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