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WINNER OF THE 1995 AMERICAN RHINOLOGIC SOCIETY BASIC SCIENCE AWARD

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Brenda L. Chene, R.N., and Karen A. Klott, R.N.*

ABSTRACTS FROM THE WORLD RHINOLOGY LITERATURE

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RHINOLOGY AND NASAL ALLERGY
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Spectrum of Seasonal Allergic Rhinitis Symptom Relief with Topical Corticoid and Oral Antihistamine Given Singly or in Combination

Carter D. Brooks, M.D., Steven F. Francom, Ph.D., Bruce G. Peel, B.S.,
Brenda L. Chene, R.N., and Karen A. Klott, R.N.

ABSTRACT

Sixty ragweed-sensitive volunteers participated in a 2-week study that compared symptom profiles during treatment with antihistamine (loratadine, LOR) alone, topical corticoid (beclomethasone, BEC) alone, or the two drugs combined. For 5 days commencing shortly after the beginning of the ragweed bloom, patients took no treatment while we collected baseline data. They were then randomized to one of the three treatments, receiving that treatment for the balance of the 2-week study term. Twice each day they recorded the severity of congestion, eye symptoms, running and blowing, itching, and sneezing. At the end of the study they provided an estimate of overall symptom relief, which favored combined treatment (vs LOR $P = 0.001$, vs BEC $P = 0.042$). To gain an estimate of disease severity and treatment effectiveness over time, and to smooth out day-to-day variation, we divided symptom diary reports into three segments (days 2-4, 5-7, and 8-10) for

analysis. Combined treatment controlled symptoms better than antihistamine alone in nearly all study segments. Corticoid alone or combined with antihistamine provided similar control of congestion, running and blowing, and eye complaints. Combination therapy controlled itching and sneezing better, especially through the study segments 1 and 2. Patient preference for combined treatment seems to relate to control of itching and sneezing and rapid onset of effect. (American Journal of Rhinology 10, 193-199, 1996)

In several previous studies we have examined profiles of individual symptoms in allergic rhinitis and the selective effects of various treatments on these profiles. We showed that, compared to placebo, terfenadine suppressed sneeze, itch, and eye symptoms, benefitted congestion marginally, and failed to improve running and blowing. Of these, only control of sneezing appeared quickly after introduction of the drug in midseason.¹ Another study intended to establish minimal effective doses of oral methylprednisolone found, at 6 mg per day, significant suppression of congestion, postnasal drainage, and eye symptoms, but not itching, sneezing, and running.² These findings could be a clinical expression of the reported inability of systemic corticoid to prevent release of mediators from human mast cells.³

It appeared that the symptoms most responsive to antihistamine treatment responded least well to low dose corticoid and vice versa, providing a rational basis for combination of the two drug types for seasonal allergic rhinitis

From The Upjohn Research Clinics and Michigan State University College of Human Medicine, Department of Pediatrics and Human Development

This study was conducted in a clinic wholly supported by The Upjohn Company

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treatment. We have carried out preliminary studies documenting additive protection with combined antihistamine/corticoid treatment, and the equivalence of oral and topical corticoid when given as part of the combination.

Others have studied symptom control with combined antihistamine/topical corticoid treatment and have reported variable findings.⁴⁻⁷ Most reported a more modest increment of patient-perceived benefit with combined treatment than our preliminary studies led us to expect.

The goal of the study reported here was to compare profile and severity of individual symptoms, and overall patient perception of benefit during seasonal allergic rhinitis treatment with antihistamine (loratadine, Claritin, Schering-Plough, LOR) alone, topical nasal corticoid (beclomethasone, Vancenase AQ, Schering-Plough, BEC) alone, and the two drugs in combination. The study did not contain a concurrent placebo control group, but all study participants entered the treatment comparison from an untreated baseline observation period.

STUDY DESIGN AND EXECUTION

Subject Selection

Sixty subjects enrolled in and completed the study. Each treatment group contained 20 people; sex distribution in the LOR group was 10M/10F, whereas the BEC and the LOR/BEC groups both had 7M/13F. The three treatment groups were roughly comparable in age, height, and weight. All had reliable histories of seasonal rhinitis compatible with ragweed seasonal allergic rhinitis and strongly positive ragweed skin (prick) tests. Many had participated in previous studies and had provided records of the severity of their seasonal symptoms. None had evidence of significant complicating disease on history, physical examination, or screening laboratory testing; women had negative pregnancy tests on entry and again in mid-study. All alleged that they understood the design, demands, and risks of the study and signed their consent to participate. The Bronson

Hospital Human Use Committee reviewed and approved the study design and documents.

Treatment Schedule

In this community, ragweed typically begins to bloom around August 15. Subjects came under study observation on 18 August (Thursday) and were seen each Monday and Thursday through 1 September. From August 18 to 22 they used no treatment; this provided baseline information documenting seasonal allergic rhinitis severity at the beginning of the observation period. After 22 August they used their randomly assigned therapy, remaining on the same treatment through 1 September. At all visits we reviewed and verified hay fever symptom severity diaries, checked apparent study drug consumption, and inquired for possible treatment side effects or other medical events.

Table I shows the pollen counts obtained during the study confirming the appearance of reasonable levels by mid-August. (James L. McDonald, M.D., provided aeroallergen counts obtained from a roto-bar sampler located at an elevated urban site about one mile from the clinic where we ran the study.) Absolute counts never exceeded 169 grains per cubic meter, relatively low compared with prior years' experiences. However, they seemed to provide an adequate allergic stimulus, both in study subjects and nonstudy patients under our care.

Experimental Drug Treatment

We randomly allocated volunteers to three drug treatment groups consisting of:

1. Loratadine (Claritin, Schering-Plough) (LOR) 10 mg once a day, plus a placebo spray twice a day.
2. Beclomethasone (Vancenase AQ, Schering-Plough) (BEC) two sprays (about 84 mcg) each side of the nose twice a day, plus placebo LOR.
3. BEC twice a day plus LOR once daily.

During the treatment comparison, subjects took no other treatment that might affect their hay fever.

TABLE I

| Ragweed Pollen Grain Count in Particles Per CU Meter. Counts Made Using A Roto-bar Sampler Running Intermittently on a Downtown Rooftop | | | | | |
|---|-----------|---------------|---------------|-------------|---------------|
| Study Segment | Date | Ragweed Count | Study Segment | Date | Ragweed Count |
| | August 12 | 1 | 1 | August 23 | 83 |
| | August 13 | 6 | 1 | August 24 | 162 |
| | August 14 | 19 | 1 | August 25 | 169 |
| | August 15 | 14 | 2 | August 26 | 95 |
| | August 16 | 16 | 2 | August 27 | 144 |
| | August 17 | 40 | 2 | August 28 | 144 |
| | August 18 | 71 | 3 | August 29 | 116 |
| Baseline | August 19 | 27 | 3 | August 30 | 76 |
| Baseline | August 20 | 14 | 3 | August 31 | 67 |
| Baseline | August 21 | 59 | | September 1 | 45 |
| | August 22 | 23 | | September 2 | 19 |

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