CLINICAL STUDY SYNOPSIS

Title of the study: A double-blind comparison of Rhinocort® (budesonide) Aqua, MDI and placebo in the treatment of seasonal allergic rhinitis

Principal/coordinating investigator(s): James Day, Helen Ramsdale, Jorge Mazza, DW Moote, Piyush Patel, Michael Alexander, William Yang, Charles Frankish

Study site(s): Seven centres in Ontario, Canada

Publication (reference): None

Study period: August - September, 1991

Clinical phase: III

Objectives: To compare the relative effect of placebo and intranasal budesonide as an aqueous suspension and as a pressurized aerosol in the treatment of seasonal allergic rhinitis. The secondary objective was to investigate the systemic effects of the budesonide formulations in relation to placebo measured as 24-hour urinary cortisol excretion.

Study design: Double-blind, randomized, parallel-group design. Multicentre.

Number of patients (total and for each treatment): Three hundred and twenty-four (82 in the Aqua 400 μg group, 81 in the Aqua 256 μg group, 79 in the MDI group and 82 in the placebo group)

Diagnosis: A clinical diagnosis of ragweed-induced allergic rhinitis or rhinoconjunctivitis since at least the previous season.

Criteria for inclusion: Ragweed sensitivity verified by a positive skin prick test (a greater than 3 mm wheal response to a standard mixed ragweed extract). Age 12 or more.

Investigational drug: Rhinocort® Aqua was provided as an aqueous suspension at a

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concentration of 2 mg/mL, batch PL 200, or 1.28 mg/mL (batch RF 1B), in 10 mL glass vials with a mechanical pump. Each actuation delivered 100 μg or 64 μg of budesonide and contained 200 doses. The dosage was two actuations in each nostril in the morning.

Reference treatment(s): Budesonide pressurized aerosol, Rhinocort® was supplied in canisters fitted in nasal applicators. Each actuation delivered 50 μg of budesonide and each canister contained 200 doses (batch RA 189). The dosage was two actuations in each nostril twice daily. A placebo which was identical in appearance to Rhinocort® Aqua was used as a reference (batch DQC 51).

Duration of treatment: Three weeks.

Assessment methods: Symptom scores, overall assessment, 24-hour urinary cortisol.

Statistical methods: The mean values of the symptom scores for the individual symptoms as well as a mean combined nasal symptom score over the 1-week baseline and the 3-week treatment period were calculated. The primary efficacy variables were the three nasal symptom scores and the patient’s assessment of treatment efficacy. The change from baseline in the mean scores of the individual symptoms as well as mean combined nasal symptom score was subjected to t-tests and ANOVA, which was not based on ranked scores as stated in the protocol.

Global assessment of treatment efficacy, weekly use of Seldane® and change in laboratory assessments (urine cortisol etc) from baseline were analyzed with ANOVA on ranked scores. Compliance was subjected to an ANOVA.

In all ANOVA models mentioned above the factors centre and treatment were included. The possibility of an interaction between treatment and centre was considered in a preliminary analysis of the change in the mean scores of the nasal symptoms i.e. prior to testing for treatment effects. Since no effect of interaction was found, this factor was excluded in all subsequent ANOVA models. In all tests of significance two-tailed alternatives were considered. A p-value of <0.05 was considered statistically significant. P-values >0.10 were considered not significant and values in the interval 0.05< p<0.10 were considered nearly significant.

Summary of results: The study was conducted at seven different centres in Canada. Three hundred and twenty-four out-patients were enrolled in the study, 318 of these continued into the treatment period and 303 completed the entire study. The study comprised a 1-week baseline period followed by a 3-week treatment period, during which the patients were treated with two different doses of Rhinocort® Aqua (256 μg or 400 μg daily), or Rhinocort® MDI 400 μg daily or placebo. The primary variables were daily symptom scores and overall evaluation. The excretion of urinary cortisol was measured during the baseline period and again in the third week of treatment. Pollen counts were made throughout the study.

The study showed that budesonide, whether given as a water-based suspension or as a pressurized aerosol, considerably improves the symptoms of seasonal allergic rhinitis. In all active groups the reduction of all nasal symptoms differed significantly from the placebo group. There were no statistical differences between Rhinocort® Aqua 256 μg and Rhinocort® Aqua 400 μg nor were there any statistical differences between Rhinocort® Aqua 256 μg and the MDI group. The overall assessment of efficacy also strongly favoured active treatment. The use of antihistamines was considerably less in the active groups and the difference between the active groups and the placebo group was statistically significant. There were no statistical differences between any of the groups as regards urine cortisol and urinary creatinine.

There were only marginal differences in the incidence and nature of adverse events between the different Rhinocort® groups and also relative to the placebo group. The most frequently reported adverse events were headache, respiratory infection, pharyngitis and epistaxis.
Four patients discontinued because of adverse events: two patients in the Rhinocort® MDI 400 µg group, one patient in the Rhinocort® Aqua 256 µg group and one patient in the placebo group. There was one serious adverse event but causal relationship with the study medication was judged unlikely by the investigator.

Conclusion: Budesonide provides good alleviation of the symptoms of seasonal allergic rhinitis caused by ragweed whether given as a water-based suspension, Rhinocort® Aqua, or as a pressurized aerosol, Rhinocort®. Rhinocort® Aqua in the dosage 256 µg/day is as effective as Rhinocort® Aqua or Rhinocort® MDI in the dosage 400 µg/day. The incidence of adverse events during treatment with Rhinocort® Aqua is similar to that seen during treatment with Rhinocort® MDI. There is no evidence of an increased risk of suppressed cortisol production during treatment with Rhinocort® Aqua.