Calcium Glycerophosphate Nasal Spray Reduces Rhinitis Symptoms.

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ABSTRACT

Rationale: Many patients with rhinitis remain symptomatic and/or intolerant of treatment. Recently, Baines *et al*. (2014) reported that ALP is elevated in neutrophilic asthma, leading us to hypothesize that a topical spray of calcium glycerophosphate (CGP), an ALP inhibitor, might be useful in treating rhinitis.

Methods: This study was approved by the Drexel University Human Research Protection Committee. Seven subjects (42 ±7 YOA, 2M, 5 F) with target composite run-in scores ≥ 5 (0=no symptoms to 3=severe symptoms) for rhinorrhea, itching, congestion, and sneezing were treated with intranasal CGP (30 mg per nostril, b.i.d., as a spray) over 3 weeks. Subjects scored AM and PM pre and post treatment rhinorrhea, itching, congestion and sneezing for the three week period of the study. Results, including pulmonary function tests, were assessed weekly and data analyzed by analysis of variance for repeated measures.

Results: The mean pre-treatment composite score was 6.929 ± 4.2. The score declined significantly ($p<0.0001$) over the period of the study, to 2.80±0.635 (AM, pre), 2.03 ± 0.617 (AM, post), 3.17±0.757 (PM pre) and 2.30±0.605 (PM, post). There were no changes in pulmonary function or blood chemistry over the period of the study.

Conclusions: These data demonstrate that intranasal CGP effectively reduces the symptoms of rhinitis. The molecule is classified as "generally recognized as safe" by the FDA. As a normal metabolic intermediate, it is unlikely to have significant abuse liability, even when used over a long period of time. These properties make it an attractive candidate for rhinitis treatment.

INTRODUCTION

Many patients with rhinitis remain symptomatic and/or intolerant of treatment. Recently, Baines *et al*. (2014) reported that alkaline phosphatase is elevated in neutrophilic asthma, leading us to hypothesize that a topical spray of calcium glycerophosphate (CGP), an alkaline phosphatase inhibitor, might be useful in treating rhinitis.

METHODS

The Drexel University Human Research Protection Committee approved this study. Sixteen subjects (6 M, 10 F, 38.9 ± 4.61 YOA) were recruited for this study. Of these, three subjects (3 M) failed to meet the target composite run-in scores ≥ 5 (0=no symptoms to 3 = severe symptoms) for rhinorrhea, itching, congestion, and sneezing, and two (1M, 1F) failed to complete the study. Eleven subjects (39.1 ± 4.86 YOA, 2 M, 9 F) completed the study. Subjects were tested for allergen sensitivities; of the eleven subjects completing the study, seven subjects reacted to from 1 to 26 different allergens, while the remaining four subjects showed no identifiable allergen sensitivities. Two subjects (both F) had a history of asthma, and one subject (M) had been previously diagnosed with COPD.

Treatment consisted of intranasal CGP (30 mg per nostril, b.i.d., as a spray) over 3 weeks. Subjects scored AM and PM pre and post treatment rhinorrhea, itching, congestion and sneezing for the three-week period of the study. Results, including pulmonary function tests, were assessed weekly and data analyzed by analysis of variance for repeated measures, followed by Sidak's multiple comparison test, or by a post-test for linear trend. All statistical analyses were performed using the Prism 6.0 software package. All values given in this report are mean ± SEM

RESULTS

The morning and evening composite subject scores for rhinorrhea, itching, congestion and sneezing are presented in Figure 1. The mean pre-treatment composite score was 7.37 ± 0.441. Both the pre- and post-treatment scores were significantly ($p<0.0001$) lower than the run-in scores at each time point. Both the AM and PM post-treatment scores were significantly lower than the pre-treatment scores at each time point.

The cumulative number of sprays per subject, as recorded by the subjects in their daily diary, is shown in Table 1. Two-way analysis of variance showed that dosing did not differ between subjects, nor did it differ with time.

Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and peak expiratory flow (PEF) were used to evaluate pulmonary function at run-in, and on days 7, 14 and 21 of treatment. FEV1 did not change over the course of the study, and was 2.88 ± 0.27 liters at run-in and 2.85 ± 0.26 liters at day 21. Similarly, PEF was 6.15 ± 0.53 L/sec at run-in and 6.04 ± 0.56 L/sec at day 21. On the other hand, as shown in figure 2, FVC increased significantly, by about 165 ± 91 mL, over the course of the study. Interestingly, the greatest increase in FVC (0.59L, 17%) was in the one patient previously diagnosed with COPD. FEV1/FVC decreased slightly but significantly, as a consequence of the increase in FVC.

As shown in Table 2, 21 days of intranasal CGP treatment had no significant effect on any of the blood chemistry parameters measured. However, it is noteworthy that WBC was slightly decreased at Day 21 as compared to run-in ($p = 0.096$, one-tailed paired Student's t-test).

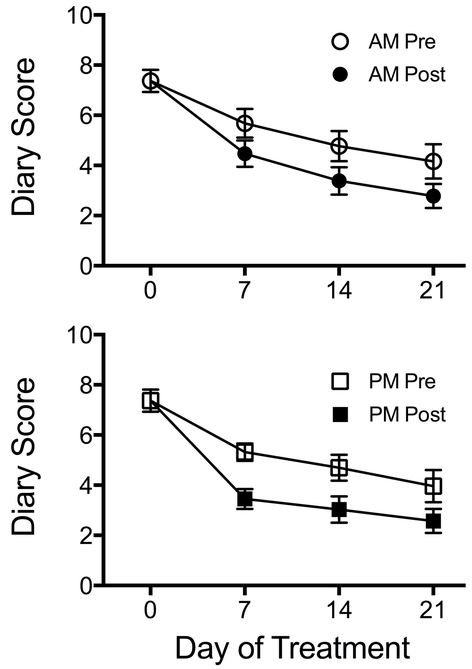

Figure 1. Mean pre- and post-treatment diary scores for symptoms. Both pre-and post-treatment scores were significantly ($p< 0.0001$) lower than the run-in score for each of the treatment days. The pre- and post-treatment scores were significantly different for each time point for both A.M. ($p < 0.05$) and P.M ($p < 0.01$), as determined by analysis of variance for repeated measures followed by Sidak's multiple comparison test.

Day	Cumulative Sprays (Mean ± SEM)
7	13.3 ± 0.79
14	14.4 0.77
21	13.7 ± 0.94

Table 1. Subjects recorded the number of sprays per day in their diary. The cumulative number of sprays per week did not differ during the course of the study

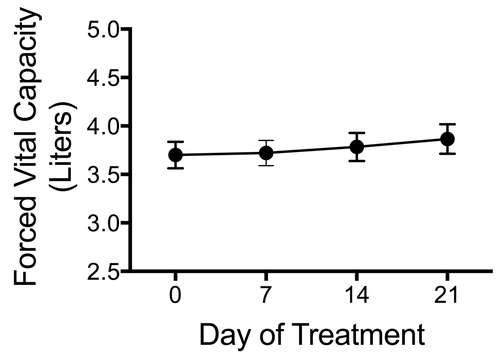

Figure 2. There was a small but statistically significant linear trend to increase FVC over the time course of the study. Slope = 0.0280, p =0.0112

	Run-In	Day 21		Run-In	Day 21
WBC	7.40 ± 0.63	6.65 ± 0.57	**Chloride**	101 ± 0.76	101 ± 0.69
RBC	4.54 ± 0.07	4.52 ± 0.09	**CO_2**	25.0 ± 0.80	24.8 ± 0.58
Hbg	13.2 ± 0.28	13.1 ± 0.38	**BUN**	12.4 ± 1.80	14.0 ± 0.58
Hct	39.7 ± 0.87	39.4 ± 0.89	**Calcium**	9.45 ± 0.11	9.53 ± 0.12
PLT	263 ± 28.7	263 ± 27.3	**Total Bilirubin**	0.43 ± 0.08	0.44 ± 0.08
Total Protein	7.12 ± 0.19	6.88 ± 0.14	**Alk Phos**	66.4 ± 6.81	63.4 ± 7.47
Albumin	4.36 ± 0.14	4.30 ± 0.12	**AST**	24.7 ± 5.19	26.4 ± 7.75
Glucose	98.2 ± 6.85	87.2 ± 6.81	**Phosphorus**	3.49 ± 0.13	3.7 ± 0.15
Sodium	138 ± 0.78	138 ± 0.49	**ALT**	19.6 ± 4.77	19.1 ± 5.53
Potassium	4.05 ± 0.07	4.04 ± 0.09			

Table 2. Blood chemistry values did not differ between run-in and day 21

DISCUSSION

These data demonstrate that intranasal CGP effectively reduces the symptoms of rhinitis. The marked decrease in scores over the course of the study suggests that the symptomatic relief is not a temporary effect consequent to washing irritants away from the nasal passages, but results from a longer-lasting effect.

The symptomatic relief is unlikely the consequence of a change of seasons, or differing allergen sensitivities. Patients were enrolled in the study over a 14-month period, and exhibited a wide range of sensitivities, yet the diary scores remained remarkably consistent between subjects. Furthermore, a sister study conducted in New Mexico (data presented separately) produced much the same results, despite being performed at a different time, by different investigators, and in a part of the country having a very different ambient allergen profile as compared to Philadelphia.

The small increase in FVC is intriguing and bears further investigation. While the average increase in FVC was small, it suggests that treatment may improve pulmonary compliance. It is important to note that this was a 21 day study, and neither the diary-score nor the FEV data have reached plateau. It seems reasonable to speculate that both parameters may continue to improve.

Calcium glycerophosphate is classified as "generally recognized as safe" by the FDA. As glycerophosphate is a normal metabolic intermediate, it is unlikely to have significant abuse liability, even when used over a long period of time. Twice daily use as a nasal spray not only provided symptomatic relief, but also may have a mild effect on pulmonary function. These properties make calcium glycerophosphate an attractive candidate for rhinitis treatment.

REFERENCES

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