

Clinical aspects of allergic disease

Evaluation of a non-chlorofluorocarbon formulation of cromolyn sodium (Intal) metered-dose inhaler versus the chlorofluorocarbon formulation in the treatment of adult patients with asthma: A controlled trial

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Background: Cromolyn sodium is a nonsteroidal inhaled anti-inflammatory agent for the treatment of asthma. As with other pressurized aerosol medications, the metered-dose inhaler (MDI) formulation currently contains chlorofluorocarbon (CFC) propellants. Because of their harmful effects on the environment CFCs are now generally banned from production and use. Alternative propellants under production for MDIs include derivatives of hydrofluoroalkane (HFA). This study uses HFA-227 in an MDI formulation of cromolyn sodium.

Objectives: The objectives of the study were (1) to examine the efficacy and safety of an HFA formulation of cromolyn sodium (Intal) MDI and (2) to compare the HFA formulation with the CFC formulation.

Methods: A multicenter, randomized, double-blind, placebo-controlled, parallel study with two active groups (HFA-cromolyn sodium [$n = 113$] and CFC-cromolyn sodium [$n = 107$]) and a placebo-treated group ($n = 105$).

Results: Patients treated with either formulation of cromolyn sodium MDI showed a statistically significant ($p < 0.05$) improvement of 12% to 18% compared with placebo in symptom summary score, daytime asthma symptoms, and albuterol use. No statistically significant differences were observed in pulmonary function. Patient and physician opinions of overall effectiveness favored HFA-cromolyn sodium over placebo ($p = 0.01$), with no other significant between-treatment differences. No statistically significant differences existed among groups in the incidence of treatment-related adverse events.

Conclusion: The HFA formulation of cromolyn sodium MDI is a well-tolerated and active alternative treatment for asthma patients aged 12 years and more. (*J Allergy Clin Immunol* 1998;101:7-13.)

Key words: Chlorofluorocarbon, cromolyn sodium, hydrofluoroalkane, metered-dose inhaler, Montreal Protocol, ozone

Abbreviations used

CFC:	Chlorofluorocarbon
FEF _{25-75%} :	Forced expiratory flow during midportion of FVC
FVC:	Forced vital capacity
HFA:	Hydrofluoroalkane
MDI:	Metered-dose inhaler
PEFR:	Peak expiratory flow rate
PFT:	Pulmonary function test

Cromolyn sodium is an inhaled antiinflammatory agent for the treatment of asthma. Clinical studies have shown this nonsteroid medication, available as a nebulizer solution and as a metered-dose inhaler (MDI), to control the symptoms and bronchial hyperresponsiveness associated with asthma and to reduce the number of acute exacerbations (and associated costs), with few reports of adverse events.¹⁻⁶ Like other pressurized aerosol medications, the MDI formulation of cromolyn sodium currently contains chlorofluorocarbon (CFC) propellants. During recent years, CFCs have been criticized for their harmful effects on the environment, especially depletion of the stratospheric ozone layer. The production and use of CFCs were banned by international treaty (the Montreal Protocol) in 1987. More than 100 countries signed the Montreal Protocol, which targeted complete cessation of CFC consumption by 1996. Interestingly, the United States had banned nonmedicinal uses of CFCs in 1978, almost a decade earlier than the Montreal Protocol. Exemptions to the national and international bans were made for MDIs, to allow time for comparative clinical trials of alternative propellants, as required by worldwide regulatory agencies including the Food and Drug Administration in the United States.

Alternative formulations of medications to treat asthma are available, including dry powder inhalers and nebulizer solutions. These formulations are CFC free. However, despite the availability of these alternatives, the MDI remains the most commonly prescribed, regularly used, and patient-preferred device for the treat-

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ment of asthma. Many patients are comfortable with this type of inhaled delivery system: it is compact, easy to carry, and for many patients, relatively easy to use (although regular education and checking of technique is recommended). MDIs account for only 0.5% of annual CFC consumption worldwide.⁷ Nevertheless, in response to the national and international bans, manufacturers of MDIs have been assessing non-CFC propellants as alternative delivery systems. The reformulation of MDI medications that use acceptable non-CFC propellants will allow patients with asthma and other pulmonary disorders to continue to use the type of inhaled medications with which they are familiar.

Thus far, the most promising alternative propellants for MDIs are derivatives of hydrofluoroalkane (HFA), and clinical studies of asthma medications have focused on HFA-134a (tetrafluoroethane) and HFA-227 (heptafluoropropane). These agents lack chlorine and thus have no ozone depletion potential and negligible global warming potential.⁸⁻¹⁰ Preclinical studies have demonstrated the acceptability of these propellants in terms of pharmacology, toxicology, and safety.¹¹

Rhône-Poulenc Rorer has developed a formulation of cromolyn sodium MDI that contains HFA-227. The study reported here was intended (1) to evaluate the efficacy and safety of the HFA-cromolyn sodium, compared with placebo and (2) to compare HFA-cromolyn sodium with CFC-cromolyn sodium, in patients 12 years of age and older with mild-to-moderate asthma.

To our knowledge, this is the first reported clinical study of a nonsteroidal antiinflammatory asthma medication formulated with an HFA propellant.

METHODS

Study population

Patients in the study were 12 years of age or older and had mild-to-moderate asthma. All patients had used as-needed β_2 -adrenergic agonist bronchodilator, administered by MDI, to control asthma symptoms, at least three times per week for the month preceding the screening visit (visit 1), and they had an FEV₁ between 50% and 90% of the predicted normal value, with 15% reversibility of FEV₁ (or 25% of forced expiratory flow during midportion of forced vital capacity [FEF_{25-75%}]) after inhaled β_2 -agonist.

Excluded from the study were patients with clinically significant respiratory disorders, current or recent smokers, patients with a history of life-threatening asthma exacerbations, patients with seasonal allergic asthma, and patients who were currently participating in another investigational drug study or had participated in one within 1 month of the screening visit. Also excluded were patients who used any of the following medications within stated periods before screening: (1) inhaled corticosteroids within 4 weeks of visit 1, or oral or parenteral steroids for more than 10 days during the 3 months before screening; (2) albuterol or other MDI bronchodilator within 6 hours; immediate-release theophylline, ipratropium bromide, oral or nebulized β_2 -agonists, or salmeterol within 12 hours; or sustained-release theophylline within 48 hours of visit 1; or (3) cromolyn sodium or nedocromil sodium within 2 weeks of visit 1.

Signed informed consent was obtained from each patient.

Study design

This was a multicenter (22 sites), randomized, double-blind, placebo-controlled, parallel group study. After screening, patients entered a 2-week baseline period during which they were permitted only as-needed albuterol MDI. During this time, all patients maintained daily diary records of the severity of their daytime and nighttime asthma symptoms; their use of albuterol and other medications; morning and evening peak expiratory flow rates (PEFRs) measured with a hand-held peak-flow meter; and a description of any adverse events. Nighttime symptoms were scored each morning on awakening as follows: 0 = no symptoms; 1 = symptoms on awakening only; 2 = symptoms that caused one instance of awakening during the night or causing patient to awaken early; 3 = symptoms that caused two or more instances of awakening during the night and that caused patient to awaken early; 4 = symptoms that kept patient awake most of the night; 5 = symptoms that kept patient awake all night. Daytime symptoms (cough, wheeze, chest tightness, and breathlessness) were recorded each evening on a scale of 0 to 5 (0 = no symptoms; 1 = symptoms for one short period during the day; 2 = symptoms for 2 or more short periods during the day; 3 = symptoms for most of the day but not affecting normal activities; 4 = symptoms for most of the day and affecting normal activities; 5 = symptoms so severe that the patient could not perform normal activities or sleep). Clinic visits were scheduled at regular 2-week intervals and included review of diary cards and measurements of pulmonary function by spirometry (FEV₁, forced vital capacity [FVC], FEF_{25-75%}, and PEFR). Before the baseline period and at the end of the double-blind treatment period, blood and urine samples were taken for blood chemistry and hematology evaluation and urinalysis. Patients were eligible for randomization after the baseline period if they had displayed appropriate levels of asthma symptoms, defined as a total asthma symptom score of at least 28 (out of a total possible score of 140), and with no more than 8 symptom-free days during the 14-day baseline period. Eligible patients were randomized to one of three treatment groups: HFA-cromolyn sodium, CFC-cromolyn sodium, or placebo, each treatment consisting of two puffs (2 mg) four times daily for 12 weeks. Patients continued using albuterol MDI as rescue medication for the duration of the study.

Medications

Patients in each of the three groups were instructed to take two puffs of study drug four times daily (early morning, lunchtime, dinnertime, and bedtime). Each actuation of cromolyn sodium MDI (HFA or CFC formulation) delivered 1 mg of drug through the mouthpiece. Therefore, patients in the active treatment groups received a total daily dose of 8 mg cromolyn sodium. The placebo MDI contained only HFA-227 and excipients in the same concentrations as the active treatment HFA inhaler. The HFA- and CFC-canisters were similar in shape and appearance.

In addition to their study medications, patients were permitted to take the following medications during the study: (1) inhaled albuterol in response to asthma symptoms; (2) antibiotics for bacterial infections; (3) antihistamines, topical cromolyn sodium, or nasal and ocular vasoconstrictor agents for allergies; (4) nasal corticosteroids for allergies if the daily dose was stable throughout the study or if taken as a 14-day regimen by patients who developed allergic nasal symptoms during the study; (5) continued immunotherapy for patients who had been on a stable maintenance dose for at least 3

TABLE I. Characteristics of study populations

Characteristic	HFA-Cromolyn sodium	CFC-Cromolyn sodium	Placebo	<i>p</i> value
No. patients	123	122	120	
Age (yrs)				
Mean	29.8	31.6	32.7	0.28
Range	12-71	12-76	12-74	
Sex				
Male	60	57	54	0.84
Female	63	65	66	
Duration of asthma (yrs)				
Mean	14.7	17.2	16.4	0.32
Range	1-48	0.5-76	1-68	
Asthma medications used during 3 months before trial (%) patients				
Short-acting bronchodilator	100	100	100	
Inhaled steroids	1.6	4.9	3.3	
Cromolyn sodium/nedocromil sodium	13.0	7.4	9.2	
Theophylline	4.1	5.7	6.7	
Mean measurements of randomization				
Symptom summary score (0-10)	3.56	3.58	3.52	
Albuterol use (puffs/day)	3.76	4.05	4.10	
FEV ₁ (% of predicted normal value)	77.2	75.7	73.2	

months prior to screening; and (6) mucolytics and expectorants as needed.

Efficacy variables

The primary efficacy variable was the symptom summary score (defined as the sum of daytime asthma and nighttime asthma scores). Secondary variables included pulmonary function tests (PFTs) performed at biweekly clinic visits, use of as-needed albuterol, daytime and nighttime asthma symptom scores, and morning and evening PEFs recorded in patients' diaries. The primary time period was the entire 12-week treatment period. Data were also examined at 2-week intervals (diary variables) or at each visit to assess the time course of response.

Opinions of treatment effectiveness

At the end of the treatment period, the patient and physician each rated his or her opinion of the overall effectiveness of the treatment in controlling the patient's asthma by using the following scale: 1 = very effective, 2 = moderately effective, 3 = slightly effective, 4 = had no effect, and 5 = made condition worse.

Statistical methods

The study was designed to have 100 evaluable patients per treatment group. This estimate was based on detecting a difference of 0.3 points in the mean symptom score, assuming a standard deviation of 0.65 points, a type I error of 0.05, and power of 90%.

The three treatment groups were assessed for demographic and baseline comparability with the Cochran-Mantel-Haenszel test (for categorical data) and an analysis of variance (for continuous data) with treatment and center as the stratifying variables. Efficacy measures were analyzed by using a parametric analysis of covariance with the treatment value as the response variable and the baseline value as the covariate. If the overall three-treatment group test was statistically significant

($p < 0.05$), pairwise comparisons were made. Patient and physician opinions of treatment efficacy were assessed with the Cochran-Mantel-Haenszel test.

Adverse events were categorized according to a modified version of the terminology of the World Health Organization dictionary, and the association between the adverse event rates and treatment was assessed with Fisher's exact test.

Patients were classified as treatment failures if they required disallowed concomitant medications, if they withdrew for any reason involving the worsening of their asthma symptoms, or if treatment had no effect. Data from patients who withdrew from the trial for reasons other than treatment failure were included in the statistical analysis up to the point of withdrawal. Data from patients who withdrew from the trial because of treatment failure were included up to the time of withdrawal, and after withdrawal, data used were the individual's worst recorded values.

RESULTS

Demographics and screening characteristics

A total of 650 patients at 21 centers were screened for entry into the study, and 366 were randomized to treatment. The demographics of the study population and baseline measurements are shown in Table I. The severity of asthma at the start of the study was similar among the three treatment groups, as reflected by the use of anti-asthma medications during the 3 months before the screening visit and by baseline measurements (see Table I).

A total of 325 patients completed the entire 12 weeks of treatment (HFA-cromolyn sodium, 113; CFC-cromolyn sodium, 107; placebo, 105). Forty-one patients withdrew after randomization, 22 because of an adverse event (HFA-cromolyn sodium, 3; CFC-cromolyn sodium, 9; placebo, 10). A total of 37 patients were

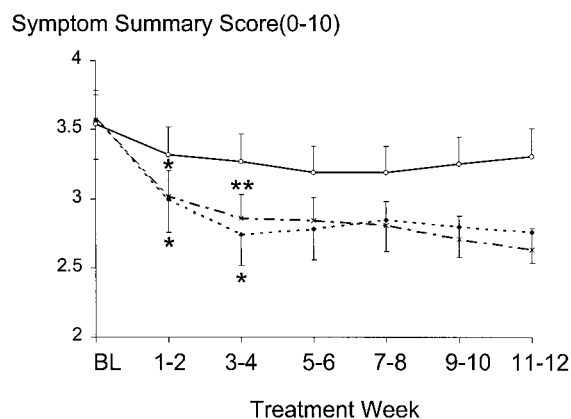


FIG 1. Biweekly mean symptom summary scores (daytime plus nighttime symptom scores; range, 0 to 10) for the three treatment groups (circles, placebo; x, HFA-cromolyn sodium; diamonds, CFC-cromolyn sodium). * $p < 0.05$; ** $p < 0.01$, compared with placebo.

classified as treatment failures (HFA-cromolyn sodium, 9; CFC-cromolyn sodium, 12; placebo, 16).

Diary card variables

Over the 12-week treatment period, patients treated with either formulation of cromolyn sodium had milder symptoms than did patients in the placebo group, with statistically significant differences from the placebo group determined for treatment weeks 1 to 2 and 3 to 4 (Fig. 1). There were no statistically significant differences between the symptom scores for the two active treatment groups. The overall reduction in symptom scores during the 12-week treatment period is shown in Figure 2. During the treatment period, patients in both cromolyn sodium groups reduced their symptom scores by approximately 20% (HFA: baseline score, 3.56; weeks 1 to 12 score, 2.85; $p = 0.042$ versus placebo; CFC: baseline score, 3.58; weeks 1 to 12 score, 2.84; $p = 0.042$ versus placebo) compared with a reduction of 9% in the placebo group (baseline score, 3.52; weeks 1 to 12 score, 3.21). These changes paralleled trends in daytime and nighttime asthma symptoms (see Fig. 2). Daytime asthma symptoms decreased with all three treatments, but the reductions were greater in the two cromolyn sodium groups throughout the trial. Within 2 weeks of starting treatment, daytime symptom scores decreased by 18% in patients treated with HFA-cromolyn sodium (baseline score, 1.99; week 2 score, 1.64; $p = 0.013$ versus placebo) and by 15% in the group treated with CFC-cromolyn sodium (baseline score, 1.99; week 2 score, 1.70; $p = 0.044$ versus placebo). During the same period, daytime symptom scores in the placebo group decreased by approximately 8% (baseline score, 2.07; weeks 1 to 2 score, 1.91). Overall, during the 12 weeks of treatment, patients in the HFA- and CFC-cromolyn sodium groups reduced their respective daytime asthma symptom scores by approximately 23% (weeks 1 to 12: HFA, 1.54; $p = 0.018$ versus placebo; CFC, 1.57; $p =$

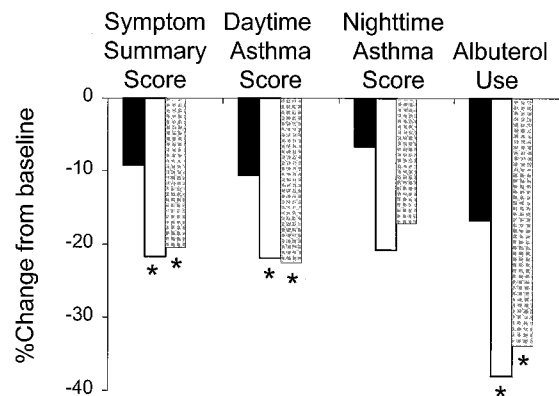


FIG 2. Mean percent changes from baseline for the three treatment groups (filled columns, placebo; open columns, HFA-cromolyn sodium; shaded columns, CFC-cromolyn sodium), over the 12-week treatment period, for the symptom summary score, daytime symptoms, nighttime symptoms, and albuterol use. * $p < 0.05$, compared with placebo.

0.036 versus placebo), compared with a 11% reduction in the placebo group (weeks 1 to 12, 1.86). Patients using cromolyn sodium also reported fewer nighttime symptoms, although comparisons with placebo did not reach statistical significance until the last 2 weeks of the trial. At treatment weeks 11 to 12, the mean nighttime symptom scores for the cromolyn sodium groups (HFA, 1.24; CFC, 1.21) were approximately 20% less than the baseline scores (1.57 for both), whereas patients treated with placebo reported no change in the severity of their symptoms (baseline score, 1.44; weeks 11 to 12, 1.42). Compared with placebo, the differences were statistically significant ($p = 0.05$).

Compared with placebo, both cromolyn sodium groups reported greater morning PEFs during the treatment period. The differences in morning PEFs between patients treated with HFA-cromolyn sodium and those treated with placebo reached statistical significance at treatment weeks 1 to 2 (HFA, 416.1 ml; CFC, 406.2 ml; placebo, 389.9 ml; $p = 0.011$, HFA versus placebo) and weeks 3 to 4 (HFA, 423.1 ml; CFC, 407.1 ml; placebo, 393.8 ml; $p = 0.022$, HFA vs placebo). Although these improvements were maintained throughout the trial, peak flow rates in the placebo group gradually increased, resulting in loss of the statistically significant between-treatment differences. No significant differences in evening PEFs were observed at any time during treatment, although trends toward higher peak flow rates with cromolyn sodium were observed.

The improvements in asthma symptoms and peak flow rates in the two active treatment groups were paralleled by decreased use of rescue albuterol, and between-treatment differences in albuterol use were statistically significant for all biweekly periods (Fig. 3), compared with placebo. Again, there were no statistically significant differences between the HFA-cromolyn and the CFC-cromolyn sodium groups. Overall, patients treated

TABLE II. Pulmonary function variables at baseline and during the primary treatment period

Treatment	Baseline	Treatment weeks 1-12
FEV ₁ (L)		
HFA-cromolyn sodium	2.83	2.95
CFC-cromolyn sodium	2.74	2.80
Placebo	2.62	2.66
FVC (L)		
HFA-cromolyn sodium	3.92	4.01
CFC cromolyn sodium	3.81	3.83
Placebo	3.61	3.68
FEF _{25-75%} (L/sec)		
HFA-cromolyn sodium	2.30	2.46
CFC-cromolyn sodium	2.15	2.28
Placebo	2.16	2.18
PEFR (L/min)		
HFA-cromolyn sodium	430.8	449.4
CFC-cromolyn sodium	409.2	421.8
Placebo	401.4	412.8

FEF_{25-75%}, forced expiratory flow during mid-portion of FVC; FVC, forced vital capacity.

with cromolyn sodium reduced their albuterol use by approximately 35% (Fig. 2; HFA: baseline score, 3.68; weeks 1 to 12 score, 2.45; $p = 0.011$ versus placebo; CFC: baseline score, 4.05; weeks 1 to 12 score, 2.53; $p = 0.011$, versus placebo), compared with a reduction of approximately 16% in the placebo group (baseline score, 4.10; weeks 1 to 12 score, 3.44).

Spirometry at clinic visits

Pulmonary function measurements are shown in Table II. No statistically significant differences were determined, relative to placebo, for any PFT measurements for treatment weeks 1 to 12, although the treatment effect for FEF_{25-75%} approached statistical significance ($p = 0.085$) with a 7% and 6% increase from baseline in the HFA- and CFC-cromolyn sodium groups, respectively, compared with a 0.9% increase in the placebo group. No significant between-group differences were determined in comparisons of the two active treatments.

Opinions of treatment effectiveness

Physicians rated the treatment as moderately or very effective for 57% of the patients treated with HFA-cromolyn sodium compared with 37% of the placebo-treated patients and 48% of the patients treated with CFC-cromolyn sodium. The mean scores for treatment effectiveness among physicians were: 2.64 and 2.73, respectively, for patients treated with HFA- or CFC-cromolyn sodium compared with 3.04 for patients in the placebo group. Compared with placebo, the treatment difference was statistically significant for the HFA-cromolyn sodium group ($p = 0.002$). Treatment differences did not reach statistical significance for the comparison of the two cromolyn sodium groups ($p = 0.494$) or the comparison of the placebo and CFC-cromolyn sodium groups ($p = 0.071$).

Albuterol use(puffs/day)

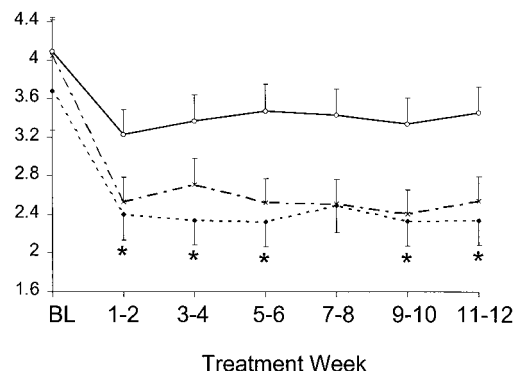


FIG 3. Biweekly mean scores for albuterol use (puffs per day) for the three treatment groups (circles, placebo; x, HFA-cromolyn sodium; diamonds, CFC-cromolyn sodium). Compared with placebo, between treatment differences for both propellant formulations of cromolyn sodium were statistically significant (* $p < 0.05$) at all time points, except weeks 7 to 8.

Approximately 64% of the patients in the HFA-cromolyn sodium group rated their treatment as moderately or very effective. This was in comparison with 54% of patients in the CFC-cromolyn sodium group and 45% of placebo-treated patients. The mean scores for opinions of treatment effectiveness were 2.45 and 2.56 for the HFA- and CFC-cromolyn sodium groups, respectively, compared with 2.91 for the placebo group. Comparisons of the active treatments with placebo were statistically significant ($p = 0.004$, HFA-cromolyn sodium versus placebo; $p = 0.047$, CFC-cromolyn sodium versus placebo). Between-treatment differences were not statistically significant for the comparison of the cromolyn sodium groups ($p = 0.703$).

Adverse events

Eighty-one percent of the patients reported at least one adverse event during the treatment period, and event rates were similar among the three treatment groups (HFA-cromolyn sodium, 100 patients (81%) reported adverse events; CFC-cromolyn sodium, 97 patients (80%) reported adverse events; placebo, 100 patients (83%) reported adverse events). Approximately 10% of patients reporting adverse events had at least one event that was probably treatment-related. The three most common treatment-related events were headache (HFA-cromolyn sodium, 2%; CFC-cromolyn sodium, 2%; placebo, 3%), pharyngitis (HFA-cromolyn sodium, 2%; CFC-cromolyn sodium, 2%; placebo, 1%), and chest tightness (HFA-cromolyn sodium, 0%; CFC-cromolyn sodium, 3%; placebo, 1%). There were no statistically significant differences among the three treatment groups in the incidence of treatment-related events.

Of the 22 withdrawals attributed to adverse events (HFA-cromolyn sodium, 3; CFC-cromolyn sodium, 9; placebo, 10), only two were judged to be treatment related. One patient in the CFC-cromolyn sodium group

withdrew after 2 days of treatment because of pharyngitis and increased asthma symptoms. One patient withdrew from placebo treatment after 31 days because of sleeplessness.

There were no clinically significant changes for laboratory variables in any treatment group.

DISCUSSION

This placebo-controlled study showed that HFA-cromolyn sodium inhalation aerosol reduces asthma symptoms and decreases rescue medication use in patients with mild-to-moderate asthma. HFA-cromolyn sodium was not significantly different from the currently used CFC formulation, either in activity or tolerability. It is noteworthy that asthma symptoms in both active groups were reduced by more than 20%, and at the same time albuterol use among these patients declined by more than 33%, compared with the use during the baseline period. This is precisely the treatment goal for mild-to-moderate asthma patients as described by both national and international guidelines: that is, fewer symptoms with less reliance on inhaled rescue medications.¹²⁻¹⁴

All three treatments were well tolerated, with no significant between-treatment differences for adverse events. No significant bronchoconstrictive, central nervous system, or gastrointestinal effects were reported for the placebo containing the HFA propellant, nor did any patient treated with the placebo-HFA report an unpleasant taste. Both physicians and patients found HFA-cromolyn sodium to be more effective than placebo.

A commonly held perception is that cromolyn sodium requires 2 to 4 weeks of continuous treatment before maximum clinical effect is evident. This perception exists despite the fact that a single dose of the drug prevents mast cell degranulation and subsequent allergic symptoms.¹⁵⁻¹⁷ In this study, differences from placebo reached statistical significance for both formulations of cromolyn sodium within the first 2 weeks of therapy for daytime symptoms, overall symptoms, and albuterol use.

Interestingly, although there were trends toward milder nighttime asthma symptoms and improved pulmonary function measurements with the two active treatments, statistical significance was not achieved. In part this may reflect a placebo effect, and in part it may reflect the broad range of patients included in the study. The trial included asthmatic patients who had FEV₁ measurements between 50% and 90% of the predicted normal value at the screening visit. The question that arises with such a broad range of FEV₁ values is whether a patient with an FEV₁ of 60% of the predicted normal value at the start of the trial may have a higher potential for improvement, particularly in terms of PFTs, than a patient with an FEV₁ that is 80% of that predicted. For the latter patient, asthma symptoms and, particularly, the use of a bronchodilator to treat asthma symptoms, may be more reliable indicators of treatment efficacy. Other studies²⁻⁴ have shown cromolyn sodium to im-

prove nighttime asthma symptoms in patients with mild-to-moderate asthma.

In summary, our results show that HFA-cromolyn sodium can provide similar clinical benefit to the currently used CFC formulation, with a comparable tolerability profile. To our knowledge, this is the first published controlled study comparing HFA and CFC formulations of a nonsteroidal antiinflammatory asthma medication.

Many practitioners and patients rely on cromolyn sodium MDI because of its established efficacy and exceptional safety profile. Our findings confirm the clinical history of the CFC formulation of cromolyn sodium as a well-tolerated and active therapy for treating patients with mild-to-moderate asthma¹⁻⁶ and provide reassurance that the new formulation will not alter the clinical benefit or the level of patient comfort obtained with the drug.

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