A Comparative Study of the Clinical Efficacy of Nedocromil Sodium and Placebo*

How Does Cromolyn Sodium Compare as an Active Control Treatment?

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Nedocromil sodium and cromolyn sodium are the only two currently available nonsteroid anti-inflammatory agents for treatment of asthma. Clinical differences between the two agents remain under continuous investigation with reports differentiating the two on the basis of atopy of the patient and reversibility of bronchoconstriction. This study investigated the efficacy of nedocromil sodium (4 mg, qid) for treatment of mild-to-moderate asthma in comparison to placebo using cromolyn sodium (2 mg, qid) as an active control treatment. Patients were primarily allergic asthmatics (with at least 15% reversibility) previously maintained on a regimen of regular bronchodilator therapy. During a 2-week run-in period, the patient's slow-release theophylline therapy was removed, and the patients were randomized to treatment after deterioration of asthma control (asthma symptom summary score of 3 for 7 of the 14 days). After 8 weeks of treatment, patients were returned to as occasion requires bronchodilator therapy, as per the 2-week baseline period. The results demonstrate that patients treated with nedocromil sodium showed statistically significant improvements during the primary time period (mean weeks 3 through 8) over placebo-treated patients as evidenced by all indexes of asthma symptoms, pulmonary function measurements, and decreased bronchodilator reliance (p<0.05). Patients treated with cromolyn sodium demonstrated similar improvements over placebo-treated patients. Comparisons between nedocromil sodium and cromolyn sodium showed the two agents to be comparable in this group of primarily allergic patients with reversible disease. Between-group differences were noted for 3 of the 13 variables (nighttime asthma, FEV1, and forced expiratory flow rate between 25% and 75% of the FVC) in favor of cromolyn sodium when the data were pooled during the primary time period. The number of patients missing 1 or more days from work/school/regular activity due to asthma was significantly fewer compared with placebo, and favoring nedocromil sodium over cromolyn sodium. No differences were observed among the three treatments for adverse events. This study demonstrated that in primarily allergic patients with reversible airways disease, nedocromil sodium and cromolyn sodium are both significantly more effective than placebo for treatment of mild-to-moderate asthma.

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**Key words:** anti-inflammatory; asthma; cromolyn sodium; Intal; nedocromil sodium; pulmonary function; quality of life; Tilade

Nedocromil sodium is a chemically distinct anti-inflammatory agent for treatment of mild-to-moderate asthma. Specifically, nedocromil sodium is the disodium salt of a pyranoquinoline dicarboxylic acid, which is a nonsteroid compound. Only one other nonsteroid anti-inflammatory agent is currently available for treatment of asthma in the United States:

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asthmatics with at least a 15% reversibility of bronchoconstriction.

Other comparative studies between these two agents have demonstrated that nedocromil sodium appears to have a broader spectrum of action than cromolyn sodium. Specifically, this is supported by challenge studies in sensitive asthmatic patients, animal models of asthma, and in vitro tests on a variety of leukocytes involved in the inflammatory response seen in asthmatic patients.\textsuperscript{1} Nedocromil sodium has been shown to be equally effective in blocking the bronchoconstrictive response to allergens, specifically mast cell-related mechanisms,\textsuperscript{2} and exercise challenges.\textsuperscript{3} However, differences between the two agents favoring nedocromil sodium over cromolyn sodium have been determined for nonspecific challenges, including adenosine,\textsuperscript{4,6} sulfur dioxide,\textsuperscript{7,8} sodium metabisulfite,\textsuperscript{9,10} and cold air.\textsuperscript{11} The clinical relevance of these comparative tests remains under investigation.

To date, two clinical efficacy studies comparing nedocromil sodium and cromolyn sodium have been reported, both of which favor nedocromil sodium over cromolyn sodium in patients with chronic reversible airways disease maintained on a regimen of corticosteroids.\textsuperscript{12,13} In these clinical trials, however, most of the patients were nonallergic, and patients had moderate-to-severe disease as based on their reliance on concomitant inhaled and oral corticosteroid therapy. Therefore, previous studies have not specifically investigated the comparative efficacy of nedocromil sodium and placebo using cromolyn sodium as an active control treatment group in mild-to-moderate allergic asthmatic patients who respond well to cromolyn sodium. This study was designed as a double-blind, group comparative trial that investigated the relative efficacy of these two nonsteroid, anti-inflammatory agents for treatment of primarily allergic mild-to-moderate asthma.

**Materials and Methods**

**Study Design**

From 12 different treatment centers, patients participated in a 14-week, double-blind, placebo-controlled trial that included a 2-week run-in, 2-week baseline, 8-week treatment phase, followed by a 2-week follow-up (washout) period. Prior to run-in, the reversibility of airway obstruction was determined (at least a 15% improvement in PEFR) after a short-acting $\beta_2$-agonist aerosol. After the 2-week run-in, patients were randomized to one of three treatments groups: (1) nedocromil sodium, 4 mg qid; (2) placebo qid; or (3) cromolyn sodium, 2 mg qid. On initiation of the baseline period, patients discontinued their use of all maintenance bronchodilators and only were permitted rescue bronchodilator therapy for the following 2 weeks. After the 2-week baseline period, patients were randomized to treatment if the sum of daytime and nighttime asthma was 3 or greater for at least 7 of the 14 baseline days. Patients who qualified for study entry if they showed a 15% decrease in PEFR (reversible) during baseline. After successful completion of the 8-week treatment period, patients were removed from the test treatment and maintained on as occasion requires (pm) bronchodilator treatment alone as per the baseline period.

During the 14-week study, patients were seen at the clinic on 12 separate occasions: entry, after run-in, after baseline, weekly intervals during the treatment period, and at the end of the 2-week follow-up.

**Patients**

Three hundred six patients between the ages of 18 and 70 years were randomized to treatment: 103 received nedocromil sodium, 99 received placebo, and 104 received cromolyn sodium. Almost all patients had an allergic component to their disease (nedocromil sodium, 86%; cromolyn sodium, 85%; placebo, 86%) as determined by clinical history and skin testing. Patients receiving immunotherapy continued to receive the same dose throughout the study. Prior to entry into the study, all patients were maintained on a regimen of daily slow-release theophylline and, at least, pm inhaled or oral $\beta_2$-agonists. Use of inhaled/oral corticosteroids, cromolyn sodium, or antihistamines during the 4 weeks prior to the study was reason for exclusion. Possibility of pregnancy also was reason for exclusion.

**Efficacy Variables**

On entry into the study, patients began daily diary card recordings of asthma symptoms, morning and evening peak flow rates, use of study medication, and use of concomitant medications. Asthma symptoms included daytime asthma and cough that were recorded using a five-point scale (0=none; 1=mild; 2=moderate; 3=severe; 4=very severe). Nighttime asthma was recorded on a four-point scale (0=slept well; 1=mild symptoms; 2=moderate symptoms; 3=severe symptoms, awake most of the night). The primary efficacy variables during the 8-week treatment phase included the mean asthma summary score (defined as the mean for daytime asthma, nighttime asthma, and cough), peak expiratory flow rate (PEFR), and use of concomitant medications. Changes in PEFR were recorded in the morning and evening and scored as the best of three maneuvers. Patients also recorded the number of days missed from work/school/usual activities.

During each of the 12 clinic visits, patients underwent pulmonary function tests: PEFR, FEV\textsubscript{1}, forced expiratory flow rate between 25% and 75% of FVC (FEF\textsubscript{25-75}), and FVC. After the baseline period and again after 2, 5, and 8 weeks of treatment, physicians monitored the patient’s overall severity of asthma on a five-point scale (1=none; 5=severe asthma).

At the end of the 8-week treatment period, both the patients and physicians rated treatment effectiveness as one of five categories: very effective, moderately effective, slightly effective, not effective, and made condition worse. Adverse events were recorded at each of the eight clinic visits during the treatment phase.

The study protocol was approved by the Institutional Review

| Table 1—Demographic Characteristics and Patient Withdrawals |
|------------------|------------------|------------------|------------------|
|                  | Nedocromil       | Placebo          | Cromolyn         |
|                  | Sodium           | Sodium           | Sodium           |
| Age, yr          |                  |                  |                  |
| Mean             | 30.2             | 40.4             | 40.6             |
| Range (yrs)      | 19-69            | 18-69            | 18-70            |
| Sex              |                  |                  |                  |
| Male             | 61               | 56               | 61               |
| Female           | 42               | 43               | 43               |
| Duration of asthma, yr |        |                  |                  |
|                  | 20.2             | 19.5             | 18.1             |
| Allergic asthma, % | 86              | 86               | 85               |
| Withdrawals      | 0                | 10               | 3                |

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Board of each center, and each patient signed a written informed consent form before entry into the study.

Statistical Analysis

Statistical analysis was done by grouping the 14-week trial into six 2-week analysis periods: baseline, treatment weeks 1 to 2, 3 to 4, 5 to 6, 7 to 8, and follow-up. Additionally, the data were analyzed for weeks 3 through 8, the protocol defined primary time period. For pretreatment comparability within clinics, binary variables (sex, etc) were analyzed using Fisher’s Exact Test. Quantitative variables (e.g., age, duration of asthma) were analyzed using a two-sample t test, and clinician assessment of asthma was analyzed using the Wilcoxon rank-sum test. Pretrial analyses across clinics used the Mantel-Haenszel test for binary variables, two-way analysis of variance for quantitative variables, and extended Mantel-Haenszel test for clinician assessment of asthma. Within-clinic comparisons for the treatment phase used analysis of covariance for ranks for nonparametric analysis. Clinician and clinic opinions of treatment were analyzed with the Wilcoxon rank-sum test. Across-clinic analyses used a two-way analysis of covariance and a stratified randomization covariance analysis of ranks for parametric and nonparametric methods, respectively. These tests were performed for diary card data, pulmonary function tests, and clinician assessment of asthma. Across-clinic analysis of clinician and clinic opinions of treatment utilized the extended Mantel-Haenszel test.

Patients who required prednisone or who were withdrawn due to lack of treatment efficacy were classified as treatment failures. Data from these patients were included in subsequent analyses using values representative of the worst possible response: i.e., symptom score maxima, lowest PEFR measurements, and highest clinician severity score possible. Pulmonary function values were determined as a percentage of the failed patient’s maximum fall from baseline using the following formula: 100% - (x% + 10%), where x equals the maximum recorded fall from baseline. The additional 10% was included to give the projected worst possible response had the patient remained in the study.

Results

Of the 306 patients randomized to treatment, no between-group differences were observed among the three groups of patients (Table 1). Most patients in all three treatment groups had allergic asthma: nedocromil sodium, 86%; placebo, 86%; and cromolyn sodium, 85%. As also shown in Table 1, 13 patients withdrew from the study: none in the nedocromil sodium group, 10 in the placebo group, and 3 in the cromolyn sodium group. Reasons for patient withdrawals in the placebo group included the following: treatment failure (n=4), intolerance to treatment with the study drug (n=3), moved from the area (n=1), intercurrent illness (n=1), unavailable for follow-up (n=1). In the cromolyn sodium group, reasons for withdrawal included the following: intolerance to study drug (n=1), intercurrent illness (n=1), and noncompliance (n=1). The cromolyn sodium-intolerant patient complained of severe throat irritation and was withdrawn after 4 weeks. Twenty-eight patients were considered treatment failures: nedocromil sodium, 8 patients; placebo, 16 patients; and cromolyn sodium, 4 patients. Unless withdrawn from the study, these patients remained in the statistical analysis.

Study medication compliance was monitored on patient daily diary cards. Overall, patient compliance, as recorded, was good with no differences among the three groups. Two patients used nedocromil sodium at a reduced dose; one patient taking placebo and one patient taking nedocromil sodium reduced their dose during the last 2 weeks of the study, and one patient taking cromolyn sodium used an increased dose during weeks 1 to 2 of treatment.

Primary Efficacy Variables

The results for the mean asthma summary score (mean of daytime, nighttime, and cough) are shown in

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21730/)

**Figure 1.** Mean asthma summary score. Reflecting the mean of daytime asthma (range, 0 to 4), nighttime asthma (range, 0 to 3), and cough (range, 0 to 4), the mean asthma summary score indicated a single overall variable for asthma severity. Solid squares = nedocromil sodium; diamonds = cromolyn sodium; filled triangles = placebo; asterisk = p ≤ 0.001, nedocromil sodium and cromolyn sodium vs placebo.

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21730/)

**Figure 2.** Use of concomitant rescue bronchodilators: mean daily doses of immediate-release theophylline and short-acting inhaled β2-agonist. Following the withdrawal of slow-release theophylline therapy at the start of the baseline period, all three treatment groups demonstrated increases in rescue bronchodilator therapy. Compared with placebo, reliance on rescue medication significantly decreased with either active treatment. Solid squares = nedocromil sodium; diamonds = cromolyn sodium; filled triangles = placebo; asterisk = p ≤ 0.001, nedocromil sodium and cromolyn sodium vs placebo.
Figure 1. The removal of maintenance oral bronchodilators during the baseline period resulted in an increase in asthma symptoms and an increase in prn bronchodilator therapy (Fig 2). Within the first 2 weeks of treatment, the use of nedocromil sodium restored asthma symptoms to run-in levels, and significant between-group differences in favor of nedocromil sodium over placebo were achieved and maintained for treatment weeks 3 through 8 (p<0.01; see Table 2 for individual asthma symptom scores). The significant improvements in asthma symptoms were evident despite concurrent reduction in rescue bronchodilator therapy compared with placebo-treated patients (Fig 2). Patients treated with cromolyn sodium also showed significant improvements over placebo for the asthma summary score during the entire 8-week treatment period (p<0.01). No statistically significant differences were determined for the asthma summary score between nedocromil sodium and cromolyn sodium (Fig 1).

With the withdrawal of the patients' maintenance bronchodilator therapy during baseline, daily PEFR measurements decreased. Both morning and evening peak flow rates had returned to run-in levels within 2 weeks of starting treatment with nedocromil sodium and remained significantly (p<0.05) improved compared with placebo throughout the trial (Fig 3). Again, these changes were evident despite increasing use of rescue bronchodilator therapy in the placebo group. Patients treated with cromolyn sodium also demonstrated significantly higher morning and evening PEFR rates over placebo-treated patients (Fig 3). No be-

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**Table 2—Diary Card Asthma Symptoms**

<table>
<thead>
<tr>
<th></th>
<th>Slow-Release Theophylline Withdrawal Baseline</th>
<th>Treatment Weeks</th>
<th>Follow-up</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Run-in</td>
<td>1-2</td>
<td>3-4</td>
</tr>
<tr>
<td>Daytime asthma (range 0-4)</td>
<td>Jedocromil sodium</td>
<td>1.78</td>
<td>2.12</td>
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<tr>
<td></td>
<td>Placebo</td>
<td>1.73</td>
<td>2.15</td>
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<tr>
<td></td>
<td>Cromolyn sodium</td>
<td>1.69</td>
<td>2.19</td>
</tr>
<tr>
<td>Nighttime asthma (range 0-3)</td>
<td>Nedocromil sodium</td>
<td>0.93</td>
<td>1.19</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>0.85</td>
<td>1.22</td>
</tr>
<tr>
<td></td>
<td>Cromolyn sodium*</td>
<td>0.98</td>
<td>1.35</td>
</tr>
<tr>
<td>Cough (range 0-4)</td>
<td>Nedocromil sodium</td>
<td>1.30</td>
<td>1.52</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>1.15</td>
<td>1.41</td>
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<tr>
<td></td>
<td>Cromolyn sodium</td>
<td>1.27</td>
<td>1.59</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Disease severity (range: 0=none, 4=very severe)</th>
<th>Baseline</th>
<th>Wk 2</th>
<th>Wk 5</th>
<th>Wk 8</th>
<th>Follow-up</th>
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<tbody>
<tr>
<td>Nedocromil sodium</td>
<td>2.28</td>
<td>1.97</td>
<td>1.85</td>
<td>1.76</td>
<td>2.08</td>
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<tr>
<td>Placebo</td>
<td>2.29</td>
<td>2.40</td>
<td>2.31</td>
<td>2.29</td>
<td>2.39</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td>2.38</td>
<td>1.93</td>
<td>1.73</td>
<td>1.66</td>
<td>2.00</td>
</tr>
</tbody>
</table>

*For nighttime asthma, statistically significant differences in favor of cromolyn sodium over nedocromil sodium were achieved (p≤0.05) for weeks 1 to 2, 3 through 8, and 7 to 8.
between-group differences were noted when comparing diary card PEFR for patients treated with nedocromil sodium or the active control, cromolyn sodium.

Clinic pulmonary function testing revealed significant improvements over placebo in those patients treated with nedocromil sodium or cromolyn sodium (p<0.05) for PEFR, FEV$_1$, and FEF$_{25-75}$ (Table 3). Nonparametric analyses of these data demonstrated significant between-treatment differences favoring cromolyn sodium over nedocromil sodium for the pooled mean data for treatment weeks 3 through 8 for FEV$_1$ and FEF$_{25-75}$.

During the baseline period, there were no between-group differences in the clinician’s evaluation of asthma severity (Table 2). However, after 2 weeks of treatment with either nedocromil sodium or cromolyn sodium, significant improvements were observed over placebo-treated patients (p<0.001). No significant differences between nedocromil sodium- and cromolyn sodium-treated groups were noted.

Patients also recorded the number of days missed from work/school/regularly scheduled activities. As shown in Figure 4, during the 8-week treatment period, 25 patients in the placebo group reported missing one or more days from work/school/regularly scheduled activities. In contrast, only six patients in the nedocromil sodium group missed 1 or more days (p<0.01 compared with placebo). A total of 14 patients treated with cromolyn sodium missed 1 or more days from regularly scheduled activities (p<0.05 compared with placebo).

At the conclusion of the 8-week treatment period, the patients and physicians evaluated the overall efficacy of treatment. Both patients and physicians favored the use of nedocromil sodium or cromolyn sodium over placebo (p<0.001). No differences were observed between nedocromil sodium and cromolyn sodium.

Adverse events were collected at each clinic visit during the treatment period. There were no serious side effects reported for any of the three test treatments. The two most common adverse events were unpleasant taste (nedocromil sodium, 14%; placebo, 4%; cromolyn sodium, 2%) and bronchospasm (nedocromil sodium, 4%; placebo, 12%; and cromolyn sodium, 2%). Table 4 lists the adverse events attributed
to the test medications that were reported with an incidence of at least 3%.

**Discussion**

The results from this study demonstrate the efficacy and safety of nedocromil sodium for treatment of mild-to-moderate allergic asthma as compared with placebo treatment. When comparing nedocromil sodium with the active control, cromolyn sodium, the two agents appeared clinically similar. Statistically, 3 of 13 variables favored cromolyn sodium over nedocromil sodium when analyses utilized the pooled data for treatment weeks 3 through 8 (the protocol defined primary time period). The clinical significance of these differences was not apparent. Other differences between the two agents included the number of asthma-related absences from work, school, or other regular activity which favored nedocromil sodium (6 patients) over placebo (25 patients) and cromolyn sodium (14 patients) and the incidence of a transient unpleasant taste upon inhalation (14% in the nedocromil sodium group compared to 2% in the cromolyn sodium group). The difference in taste raises questions regarding possible unblinding of the study and potential compliance issues. However, subanalyses of nedocromil sodium “tasters” in two studies have shown no interference with results due to taste, and the taste can be substantially reduced by the use of spacer devices and holding chambers or even by telling the patient to use a rinse or mint following inhalation.

Our data are consistent with other reports in the literature demonstrating comparable efficacies for nedocromil sodium and cromolyn sodium in sensitive asthmatic patients challenged with specific allergens, including house dust mite, pollen, and cat dander. The two drugs also have been shown to inhibit mast cell-mediated allergic responses, measured using in vitro systems, with similar relative potencies. Given these results and those from allergen challenges showing comparable levels of protection with both agents, it is not surprising that in the selected population of allergic patients included in this study, nedocromil sodium and cromolyn sodium performed comparably.

Other studies comparing the relative efficacies and potencies of nedocromil sodium and cromolyn sodium have shown differences between these agents. The distinguishing feature of these studies is an involvement of nonallergic or non-mast cell-mediated mechanisms. For example, when nedocromil sodium or cromolyn sodium is administered prior to an allergen challenge, the early and late asthmatic responses are inhibited. However, when administered after the early response has occurred, nedocromil sodium, but not cromolyn sodium, inhibits the late asthmatic reaction. The fact that nedocromil sodium may regulate the late bronchoconstrictive response that occurs after mast cell degranulation has occurred suggests a separate anti-inflammatory activity of the drug that is absent with cromolyn sodium.

One possible difference in anti-inflammatory activity may involve regulatory effects on eosinophils. A report by Warringa et al. showed that nedocromil sodium inhibited the chemotaxis of eosinophils isolated from either nonallergic donors or allergic asthmatic patients. In these participants, nedocromil sodium inhibited the chemotactic responses regardless of the time of treatment; and the inhibitory effects of nedocromil sodium were evident for both activated and activated eosinophils. For eosinophils collected from allergic asthmatics, nedocromil sodium inhibited chemotaxis regardless of whether the cells were isolated prior to allergen challenge or 3 h after allergen challenge (and the associated early response), providing an in vitro model of the previously discussed work of Pelikan and Knotnerus. A more powerful anti-inflammatory activity for nedocromil sodium on eosinophils also is suggested by review of an earlier in vitro study done by Bruinzeel and colleagues, who investigated the comparative efficacies of nedocromil sodium and cromolyn sodium on eosinophil chemotaxis normally induced by lipid-like and protein-like mediators. Specifically, nedocromil sodium, but NOT cromolyn sodium, inhibited platelet activating factor- and leukotriene B4-induced chemotaxis of eosinophils. Collectively, these studies support a more direct and effective eosinophil-targeted anti-inflammatory activity of nedocromil sodium as compared with cromolyn sodium. Bronchial biopsy specimens in patients with relatively mild asthma have shown nedocromil sodium and beclomethasone dipropionate, but not albuterol (all administered 2 puffs, qid), to reduce the number of activated eosinophils.

Differences between nedocromil sodium and cromolyn sodium also are seen in pharmacologic comparisons involving nonallergen challenges (eg, sulfur dioxide, sodium metabisulfite, adenosine monophosphate). In many instances, nedocromil sodium has been shown to block these challenges at lower relative doses than cromolyn sodium. It recently was suggested that these observations may relate to different potencies of the two agents on specific chloride channels involved in the activation of a variety of inflammatory cells and sensory nerves.

It is interesting that the results of this study are in direct opposition to those of the earlier reported placebo-controlled comparison of nedocromil sodium and cromolyn sodium by Lal et al. In that European multicenter trial, all efficacy variables favored nedocromil sodium over cromolyn sodium with statistically significant differences (p<0.05) determined for daytime asthma, nighttime asthma, and nighttime use of rescue bronchodilators. The major difference between
the two studies lies in the makeup of the patient groups: the study reported herein included predominantly allergic patients whose asthma previously was well controlled with sustained-release theophylline whereas the European study included predominantly nonallergic asthmatics who had been maintained on a regimen of inhaled corticosteroids and bronchodilators prior to the start of the study. These observations suggest that differences between the two drugs may become apparent in two situations: first, when there is a nonallergic component to the patient's disease, and second, when the patient's asthma becomes more severe—either acutely or chronically. The latter may explain the stronger effect of nedocromil sodium on asthma-related absences observed in this study, assuming that an asthma-related absence represents an acute increase in disease severity. It also may explain why nedocromil sodium, unlike cromolyn sodium, has been shown to provide added clinical benefit to the more severe asthmatic patient who requires high doses of inhaled corticosteroids or even oral steroids.26,27

In conclusion, this study clearly shows that nedocromil sodium and cromolyn sodium exert similar levels of clinical improvement for patients with mild-to-moderate asthma who have an allergic component to their disease. When considering the building evidence of literature reporting similar mechanisms of action for these agents on the mast cell-driven asthmatic responses, patients with primarily mast cell-mediated asthma, as evidenced by the allergen-triggered early asthmatic response, will find little or no difference between nedocromil sodium and cromolyn sodium therapy. Therefore, patients responding well to cromolyn sodium therapy should not necessarily be switched to nedocromil sodium therapy in hopes of seeking better control of their disease. However, we should also consider that this type of patient (i.e., the patient with mild-to-moderate allergic disease who presents predominantly with symptoms that respond to maintenance bronchodilators) may show similar levels of improvement with any anti-inflammatory agent. Careful assessment of the published literature supports this suggestion showing that inhaled corticosteroids will produce similar levels of improvement to those observed with nedocromil sodium or cromolyn sodium in this study, when the patients have relatively mild allergic asthma.25 As evidenced by other studies in the literature, however, in patients whose disease extends beyond the mast cell-driven early asthmatic response and involves other inflammatory cells (e.g., eosinophils)—i.e., the patients who do not respond optimally to cromolyn sodium—it is likely that nedocromil sodium will confer greater clinical benefit.

APPENDIX
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