

The Effect of "Cromolyn Sodium" on the Exercise Induced Bronchospasm of Asthmatic Children*

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The induction of increases in airway obstruction in asthmatics by exercise has been recognised for many years and studied extensively during the last 15 years.¹⁻⁴ This abnormal response to exercise can be inhibited or prevented by the administration of a bronchodilator, but its pathogenesis is unknown.⁵

Cromolyn Sodium or disodium cromoglycate is known also as Intal, Aarane, or Lomudal. This medicine is neither a bronchodilator nor an antihistaminic. It seems to prevent the release of chemical mediators of the allergic response following reaginic antigen-antibody reaction.⁶ Since its introduction into clinical use by Altounyan⁷ in 1967, its effect on bronchial asthma has been widely studied.

It has been shown that Cromolyn Sodium prevents bronchospasm produced by exercise and experimental inhalation of allergens.⁸⁻¹⁰ Its effect upon exercise response is subject to criticism for the following reasons:

Some of the studies include a limited number of patients. In others only adults have been investigated; and Cromolyn Sodium was administered with isopreterenol in some studies. In still others the procedures used to produce exercise-induced bronchospasm (EIB) were not well standardized.

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The purpose of this study is to find the effect of Cromolyn Sodium on standardized exercise-induced bronchospasm in asthmatic children only.

Materials and Methods

Thirty four patients with bronchial asthma who were attending the Allergy Division of Hacettepe Children's Hospital, for their recurrent and reversible airway obstruction episodes, were studied.

There were 16 girls and 18 boys. Their ages varied between 9-18 years. The severity of their asthmatic conditions ranged from mild to severe. All of them had positive skin test results with inhalant allergens. All subjects had complete physical examinations at the beginning of the study and their chest X-rays were taken.

Cycloergometer exercise tests were performed as follows:

All subjects rode a cycloergometer for 5 minutes against a load standardized at a level sufficient to increase the heart rate to 180 beats per minute, or at least 500 KgM per minute per square meter, as previously described by Pierson and associates.¹¹

Testing was performed during the same period of the day in order to avoid possible circadian variations in exercise tolerance of the patients. Subjects were asked to omit their medications 24 hours prior to testing. If the subjects had any symptoms on the testing day, exercise was postponed until they were asymptomatic.

Exercise induced bronchospasm is a phenomenon that not only varies among different atopic children with similar vital capacities but also varies from day to day in the individual asthmatic patient. Thus this study was designed to allow each subject to serve as his own control.

Each subject was given two exercise periods at two hour intervals on the same day. The first exercise period was accepted as the control. Before exercise, resting forced vital capacity (FVC) and forced expiratory volumes in one second (FEV₁) were measured using a Collins pulmonet spirometer. Then, cycloergometer exercise tests were given to each patient as described above.

After cycloergometer exercise tests, forced expiratory volume in one second were measured immediately afterwards, as well as 5, 10, 15 and 20 minutes later. After a two hour resting period, all subjects were given second exercise tests.

Sixty minutes and 15 minutes prior to the second exercise period, patients were given two doses of 20 mgm, Cromolyn Sodium inhalation using its special spinhaler.

Measurements of resting FVC and FEV_1 were repeated, then the subjects underwent the second exercise period and all procedures were repeated as in the first exercise period.

Results and Discussion

In 6 out of 34 asthmatic patients there was no fall in FEV_1 during the 20 minutes after the cycloergometer exercise tests were applied. 28 out of 34 patients showed more than 10 % fall in FEV_1 after exercise, compared with those of resting FEV_1 values.

The fall of FEV_1 after cycloergometer-exercise tests without Cromolyn Sodium is summarized in Table I. six patients had no fall in FEV_1 , 12 of them had 10 to 24 % and 16 of them had a 25 to 55 % fall on FEV_1 .

TABLE I

Number of Patients	The Fall of FEV_1 after Exercise (% of the Resting FEV_1 Values)
6	No Fall
12	10 - 24
16	25 - 55

After two inhalations of Cromolyn Sodium the following results were obtained from 28 patients who had exercise-induced bronchospasm without Cromolyn Sodium, (Table II). Twenty two of these patients had no fall in FEV_1 ; the other 6 patients showed a 10 % fall in FEV_1 . These 6 patients were in the group of patients who had more than a 25 % decrease in the FEV_1 without Cromolyn Sodium.

TABLE II

Number of Patients	The Fall of FEV_1 after Exercise with Cromolyn Sodium
22	No Fall
6	10 %

Table III shows the comparison of mean values of FEV_1 of 28 patients with and without Cromolyn Sodium at rest and at various times after exercise.

TABLE III

	Mean values of FEV_1 of 28 patients			
	Rest	Immediately following exercise	5 minutes later	10 minutes later
Before Cromolyn Sodium	1842,86	1714,29	1446,43	1517,86
After Cromolyn Sodium	1848,21	2019,64	1882,14	1871,43
P	$P > 0,05$	$P < 0,05$	$P < 0,05$	$P < 0,05$

The effect of Cromolyn Sodium on the mean values of FEV_1 patients with EIB is shown on Figure 1. The straight line indicates the mean values of FEV_1 for the 28 patients without Cromolyn Sodium. The broken line shows the mean values of FEV_1 with Cromolyn Sodium.

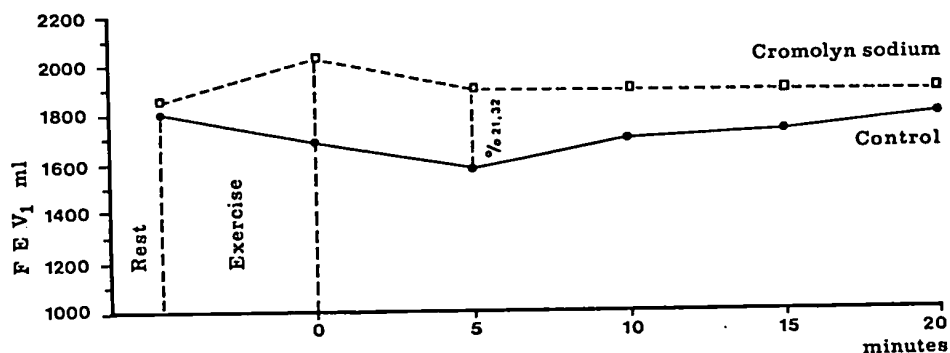


Figure 1

The effect of Cromolyn Sodium on the mean values of FEV_1 , in 28 patients who showed EIB

Cromolyn sodium did not effect the resting FEV_1 and there were no significant differences between the mean values of FEV_1 before and after exercise with Cromolyn Sodium.

The maximum fall in FEV_1 was observed 5 minutes following the exercise without medication. The mean fall was 21.32 %. This was found to be statistically significant ($p < 0.05$). For calculation of the therapeutic effect of Cromolyn Sodium the values of FEV_1 at 5 minutes post exercise were accepted and the effect of Cromolyn Sodium was found to be statistically significant.

Figure 2 shows results of similar studies in the 6 patients who had no exercise-induced bronchospasm. As can be seen there is no significant bronchospasm in these cases and Cromolyn Sodium did not affect these patients significantly.

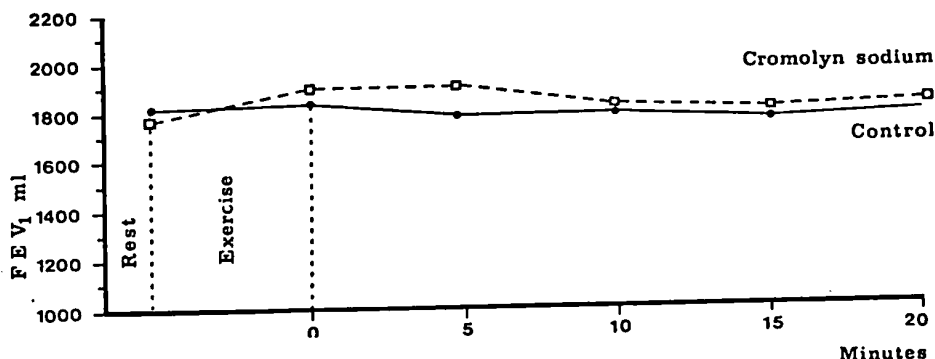


Figure 2

The effect of Cromolyn Sodium on the mean values of FEV_1 , in 6 patients who did not show EIB

These data confirm the impression of others that Cromolyn Sodium is effective in modulating EIB.^{8,10} The few studies failing to show a beneficial effect was probably due to the following reasons:

1. Cromolyn Sodium was not given just prior to exercise.¹²⁻¹³
2. Intrinsic asthmatics were included.¹⁴
3. A treadmill exercise challenge which can produce very severe bronchospasm was given.⁹

Summary

34 patients with bronchial asthma were given Cromolyn Sodium just prior to exercise to prevent bronchospasm. Cromolyn sodium completely prevented exercise-induced bronchospasm in 80 % of the patients tested. The rest of the patients were partially protected.

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