DISODIUM CROMOGLYCATE IN ALLERGIC BRONCHIAL ASTHMA: A REPORT ON TWENTYONE PATIENTS

Gulsena Masood and Nabiha W. Hasan

Abstract

An open trial of Disodium Cromoglycate (INTAL) was carried out in twentyone patients of allergic bronchial asthma of extrinsic and intrinsic type over a period of four weeks. On inhalation of one capsule six hourly, nineteen patients showed a significant symptomatic improvement. The attacks were completely prevented in sixteen of these. Ten patients were followed up for periods ranging from six months to one year and in all these the improvement was found to be maintained.

Introduction

Intal was introduced in 1965 as a substance which, if inhaled before the challenge, could effectively prevent the asthmatic response to inhaled antigen in sensitized individuals (Howell and Altounyan, 1968). It was first reported as a specific anti-allergic drug primarily on the basis of its ability to block immediate type of allergic reaction in human lung by inhibiting de-granulation of MAST CELLS. Inhibition of certain Arthus—Type reactions have also been reported. In addition the drug has been found to reduce the air-way obstruction induced by exercise. However it is ineffective if inhaled a few minutes after provocation. It's value, therefore, is only in prevention of allergic asthmatic attacks. The effect of inhalation of one capsule is expected to last about six to eight hours. Results of several double-blind clinical trials (Pepys, 1968; Robertson et at., 1969; General Practitioner Research Group, 1969) confirm the efficacy of Intal in this condition.

This product was made available in Pakistan in 1974. It was decided to conduct a trial for evaluating its role in prophylaxis of allergic bronchial asthma.

Patients and Method

A total of twentyone patients of allergic bronchial asthma were studied from November 1974 to December 1975. The trial lasted for four weeks. The dose was one capsule inhaled every six hours. During this period a symptomatic assessment was made and recorded once a week. After the initial four weeks, a long term follow-up was conducted in those patients who continued to use it. They were asked to report the progress atleast once a month, and to write or ring if attendance in person was not possible. Ten out of twentyone were thus followed for six months to one year.

Department of Medicine, Fatima Jinnah Medical College and Sir Ganga Ram Hospital, Lahore.

Criteria for Diagnosis of Allergic Bronchial Asthma

(*a*) Bronchial asthma was considered to be allergic in nature if one or more of the following criteria were fulfilled:

1. Identifiable Allergen
2. Seasonal incidence
3. Upper Respiratory tract allergy
4. Other allergic manifestations
5. Positive family history

Age and Sex distribution, duration of Asthma is shown in tables I and II.

Table I: Age and Sex Distribution

Age Groups	*No. of Patients*	*Male*	*Female*
15-25 years	6	2	4
25-35 ,,	3	1	2
35-45 ,,	3	1	2
45-65 ,,	9	3	6

Table II: Duration of Asthma

Duration of Asthma in years	*No. of Patients*	*Male*	*Female*
0-3 Years	6	1	5
3-5 ,,	5	2	3
5-10 ,,	2	1	1
10-20 ,,	7	2	5
Over-20 ,,	1	—	1

Grading of Severity of Asthma

This was based on the average number of asthmatic attacks suffered per month during the previous six months (Table III).

Table III: Grades of Severity

Grade	*Number of attacks per month*	*No. of Patients*
I (Mild)	1—2	8
II (Moderate)	Upto 4	4
III (Severe)	Upto 8	6
IV (Very Severe)	More than 8 to almost daily.	3

Administration of Intal

One capsule was inhaled through SPINHALER every six hours. If a six hourly schedule was not considered practical, the patients were told to inhale one capsule in the morning, one at mid-day, one in the evening and one at night. The method of inhalation was demonstrated

individually and every patient was supervised during the first few inhalations. They were particularly advised to ensure that the entire contents of the capsules were inhaled at one sitting. Whatever bronchodilators were in use by the patient were continued until such time that the patient decided to give them up, having derived adequate benefit from Intal inhalations.

Side Effects

None of the patients experienced bronchospasm during the inhalation. Except for slight irritation of throat and a transient unpleasant taste, no side effects were complained of. None of the patients considered these as reason enough for discontinuation of treatment.

Results

Since this was an open trial, an attempt was made to improve the reliability of assessment of response by taking into account three different therapeutic effects:

(*i*) Symptomatic improvement
(*ii*) Prevention of attacks
(*iii*) Sparing effect on steroid dose

Symptomatic Improvement

This was recorded once a week on record charts according to the grading scale described below:

A	*B*	*C*	*D*	*E*
Much better	Little better	The same	Little worse	Much worse

The above grading was recorded in accordance with the symptoms observed, such as, cough and sputum, wheeze, tightness of chest, sleep, breathlessness on exertion and frequency of asthma attacks.

Symptomatic improvement began in nineteen of 21 patients within first two weeks of treatment and was maximum by the end of fourth week; when all of the nineteen patients were showing grade A improvement in all symptoms. Many commented that for the first time in several years they felt free of chest symptoms.

Prevention of Attacks

Out of twentyone studied, the asthmatic attacks were totally prevented in sixteen. In three these were reduced by 50%. While in two there was no reduction in the number of attacks; though both considered the attacks to be milder during the trial period.

Sparing Effect on the Dose of Steroids

Seven patients under study had been taking steroids during the previous six months or more. In two of these, steroids were stopped completely during Intal therapy, and no recurrence of attacks was noted during the succeeding six months at follow up. In three the dose could be reduced by 50%. In one the dose could be reduced by 25%. In one, the same dose of steroid had to be continued to keep the patient free from attacks.

Long Term Follow-up

Ten out of twentyone patients were followed for six months, and five for one year. They have continued to use Intal at lower dosage (two capsules a day) increasing it if a break-through wheeze occurred. The improvement shown in the initial four weeks was maintained. Five of these patients have learnt to use Intal before the challenge and can, for the first time, undertake dusty journeys without fear of respiratory discomfort.

Discussion

The inhibitory effect of intal on allergen inhalation tests was observed by Pepys et al. (1968) in ten patients and is the subject of their paper.

These authors found that Intal inhibited all allergic reactions produced by the inhalation of the appropriate allergen in these asthmatic patients. Five of these gave immediate (reagin mediated) asthmatic reactions; three had allergic bronchopulmonary aspergillosis who gave both immediate and late asthmatic as well as febrile reactions, two were bird fanciers who gave late asthmatic and febrile reactions to avian precipitins.

A double blind clinical trial carried out on eleven patients of allergic bronchial asthma was reported by Robertson, Epstein and Warrell (1969). In nine of these there was symptomatic improvement as well as an increase in peak expiratory flow. Other lung function tests also improved significantly.

Another double blind cross over sequential trial extending over six weeks in ten severely disabled asthmatics was reported by Howell and Altounyan (1968). They assessed the severity from the various respiratory symptoms in these and found Intal plus Isoprenaline very effective. In a clinical trial (double blind) conducted by the General Practitioner's Research Group (1969), similar conclusions were drawn. A total of fiftyseven patients were studied, after breaking the code it was found that twentynine had received

Intal and twenty eight placebo. There were statistically significant differences in all individual respiratory symptoms as well as in the number of attacks between the two groups. They considered Intal a worth-while treatment.

Our results compare favourably with those so far reported. Since Intal is recommended as a preventive treatment, we have taken into consideration the reduction in number of asthma attacks during the trial. The complete protection in 76.19% of patients is gratifying. As regards the sparing effect of Intal on steroid dosage, out of the twentyone studied, only seven had been taking steroids. Out of these in two the steroids were withdrawn completely without causing deterioration, where as a reduction in dose by 50% in three and by 25% in one could be achieved with Intal. It is suggested that this additional advantage of Intal be studied in trials on larger number of patients of allergic bronchial asthma who have been on steroids. These patients develop obesity and proneness to chest infections from long-term use of steroids. These two side-effects are particularly undesirable in patients with air way obstruction. Intal could be of considerable value in this group of asthmatics.

The introduction of an effective prophylactic treatment for allergic bronchial asthma has given a new dimension to the management of this very disabling condition. So far the use of anti-histamines and specific desensitization have both produced unsatisfactory results. Intal has several advantages; it is easy to take, free of side effects, effective if inhaled a few minutes before the challenge and there is no tolerance after its prolonged use.

The only objection could be to its cost. But if we calculate the cost and risks of treatment, inconvenience of hospitalization and time lost from work or studies in patients with bronchial asthma, it is obvious that Intal is a worth while treatment specially for severe asthmatics. Allergic bronchial asthma accounts for 2-5% admissions to our acute medical wards. Majority of these patients are admitted as emergencies, requiring infusion of aminophylline. The average stay in hospital is from one to two weeks in mild cases and more than three weeks in severe cases. Thus the condition is responsible for considerable morbidity.

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