

Nedocromil Sodium in the Management of Asthma in Patients of less than 18 Years of Age

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Abstract

Although Nedocromil sodium has been used extensively throughout the world, it has been available in Bangladesh for the last 12 months only.

Till now, very few studies have been carried out about efficacy and safety of Nedocromil sodium in pediatric age group below 12 years of age.

Objectives

1. To find out the role of Nedocromil sodium in the prevention of bronchial asthma in patients less than 18 years of age.
2. To find out efficacy of Nedocromil in the management of bronchial asthma in patients less than 18 years of age.
3. To find out the safety profile of Nedocromil in the management of Asthma.

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Brief review about Nedocromil sodium

Nedocromil was synthesized in 1965 as part of an attempt to improve upon the bronchodilator activity of khellin, a cromone derived from the plant *Amin visnaga*, which had been used by the ancient Egyptians for its spasmolytic properties¹. Although the parent compound lacks bronchodilating capability, Sodium Cromoglycate or Nedocromil was found to inhibit antigen induced bronchospasm as well as the release of histamine and other autocooids from sensitized mast cell². This is why the main use of Sodium Cromoglycate or Nedocromil is in the preventive treatment of bronchial asthma. When inhaled several times daily Sodium Cromoglycate or Nedocromil will inhibit both the immediate and the late asthmatic responses to antigenic challenge or to exercise. With regular use more than 2 to 3 month there is evidence of reduction of hyperresponsiveness to challenge with histamine or methacholine³.

Although Sodium Cromoglycate and Nedocromil have distinct properties, they have similar anti-

inflammatory actions. Their mechanism appears to involve the blockage of chloride channels, and they modulate mast cell mediator release and eosinophil recruitment. They also inhibit the early and late asthmatic response to allergen challenge and exercise – induced bronchospasm (EIB)⁴.

Nedocromil has some distinct advantages over Sodium Cromoglycate :

1. Nedocromil appears to be more potent than sodium Cromoglycate in inhibiting bronchospasm provoked by exercise, by cold dry air, and by bradykinin aerosol³.
2. Nedocromil was more effective than Sodium Cromoglycate in non-allergic patients using inhaled Corticosteroids⁵.
3. Nedocromil may have a modest effect in helping reduce the dose requirements for inhaled corticosteroids⁶.
4. It has distinct advantage over Sodium Cromoglycate in cough variant asthma. In

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cough variant asthma Nedocromil sodium is sometimes superior to inhaled Corticosteroids.

5. Dosing recommendations for both Sodium Cromoglycate and Nedocromil are for administration four times a day, although Nedocromil sodium has been shown to be clinically effective with twice daily dosing¹.

In addition Nedocromil has a strong safety profile as Sodium Cromoglycate³.

Methodology

It is a prospective study carried out in a private hospital and at Asthma Centre, IDCH, Dhaka Asthma patient up to 18 years age diagnosed as cough variant asthma, Intermittent severe or persistent asthma attending Asthma Centre, IDCH, Dhaka or a specific private Hospital (Nirupam Hospital Pvt. Ltd.) constituted the study population.

Patients diagnosed as asthma in whom clinical & laboratory findings excludes any specific lesion in the lung were taken as sample. Sample was collected consecutively over the months of February and March 1998.

The study was carried out over 6 months period after collection of each sample unit.

Sample was divided into 2 groups into group A and B. Group A was getting Nedocromil along with as per need Salbutamol Inhaler.

Nedocromil 2 puff 6 hourly was given for initial 1st month, then 2 puff 12 hourly was given as maintenance dose to group – a patient over 2 years of age. In less than 2 years age ½ dose was given initially and in maintenance period. Inhaled Corticosteroids (Beclomethasone) in low dose (according to patient age) or no preventer drugs was given to Group –B patient.

Patients were advised to attend the clinic for follow up at monthly interval for 6 months. At the end of 6 month results were compiled and analyzed.

During follow up of patient we divided the treatment outcome into 3 groups : (a) Full response (b) Partial response (c) No response.

(a) Full response means :

All the following criteria are present during follow up.

- I. Frequency of cough/wheeze/respiratory distress – almost nil.
- II. No coughing, wheezing or respiratory distress during playing or daily activities.
- III. No disturbance of sleep
- IV. Patient requires as per need salbutamol 1 time/day.

(b) Partial response means any one of the following 4 criteria are present

- I. Frequency of cough/wheeze/respiratory distress – occasional.
- II. Occasional coughing, wheezing or respiratory distress – during playing or daily activities.
- III. Occasional disturbance of sleep
- IV. Occasionally Patient requires as per need salbutamol ³ 1 time/day.

(c) No response means all the following 4 criteria are present.

- I. Frequency of cough/wheeze/respiratory distress – as before or increasing.
- II. Coughing, wheezing or respiratory distress during playing or daily activities – as before or increasing.
- III. Disturbance of sleep – as before or increasing
- IV. Patients requires as per need salbutamol ³ 1 time/day – as before.

9. All data were analyzed to find out the role of Nedocromil sodium in management of asthma as well as to find out the efficacy and safety profile of Nedocromil sodium. Chi-square test was used for statistical analysis of compiled data.

Results

60 patients were included in group –A and 90 patients were included in group B. But we failed to contact 11 patients of group A and 12 patients of group –B. Therefore we are now presenting the outcome of 49 patients of group – A and 78 patients of group B.

Table-I
Age Incidence

Group (n=49)			Group-B (n=78)		
Age	No	%	Age	No	%
0-2 yrs	6	12.2	0-2 Yrs	4	5.1
3-5	12	24.5	3-5	8	10.3
6-12	25	51.1	6-12	34	43.6
13-18	6	12.2	13-<18	32	41.0

Table-II
Sex incidence

Group-A (n=49)	No.	%	Group-B (n=78)	No	%
Male	29	59.2	Male	48	61.5
Female	20	40.8	Female	30	38.5

Table-III
Living Condition

Group-A (n=49)	No.	%	Group-B (n=78)	No	%
Urban	43	87.8	Urban	76	97.4
Rural	6	12.2	Rural	2	2.6

Table-IV
Family History

Group-A (n=49)	No.	%	Group-B (n=78)	No	%
Asthma	28	57.1	Asthma	36	46.2
Eczema	4	8.2	Eczema	2	2.6

Table-V
Associated condition

Group-A (n=49)	No.	%	Group-B (n=78)	No	%
Rhinitis	24	48.9	Rhinitis	29	59.2
Eczema	2	4.1	Eczema	2	2.6

Table-VI
Severity of asthma

Group-A (n=49)			Group-B (n=78)			P value
Type	No.	%	Type	No	%	
Intermittent mild	0		Intermittent mild	0		n.s.
Intermittent Moderate	0		Intermittent Moderate	0		n.s.
Intermittent Severe	12	24.5	Intermittent Severe	14	17.9	n.s.
Mild persistent	14	28.6	Mild persistent	10	12.8	<0.05
Moderate persistent	6	12.2	Moderate persistent	6	7.7	n.s.
Severe Persistent	8	16.3	Severe Persistent	20	25.6	n.s.
Cough variant asthma	4	8.2	Cough variant asthma	16	20.6	<0.05
Seasonal asthma	2	8.1	Seasonal asthma	12	15.4	<0.05
Exercise induced asthma	3	6.1	Exercise induced asthma	0	0	n.s.

Table-VII
Treatment outcome

Age (years)	Group-A (n=49)				Group-B (n=78)			
	No. of Patients	No Response	Partial Response	Full Response	No. of Patients	No Response	Partial Response	Full Response
<2	6 (12.2%)	3 (6.1%)	2 (4.1%)	1 (2.0%)	4 (5.1%)	0	2 (2.6%)	2 (2.6%)
2-5	12 (24.5%)	1 (2.0%)	7 (8.2%)	7 (14.3%)	8 (10.3%)	1 (1.3%)	2 (2.6%)	2 (6.4%)
6-12	25 (51.1%)	3 (6.1%)	7 (14.3%)	15 (30.6%)	34 (43.6%)	2 (2.6%)	12 (15.4%)	20 (25.6%)
13-<18	6 (12.2%)	0	1 (2.0%)	5 (10.2%)	32 (41.0%)	0	10 (12.8%)	22 (28.2%)

Table-VIII

Problem observed in group -A (n=49) patients

Drug defaulter	16 (32.6%) (Total)
1. Bitter taste	04 (8.2%)
2. Throat Irritation	02 (4.1%)
3. Nausea	02 (4.1%)
4. Coughing	01 (2.0%)
5. Headache	01 (2.0%)
6. Not available	04 (8.2%)
7. Costly	02 (4.1%)

Discussion

Cough is one of the commonest respiratory symptom. It may be the only presenting symptom of asthma⁷ and the earliest indication of worsening asthma⁸. Chronic cough may be defined as a cough

that persists longer than three weeks. Cough may be the only sign of the disease in children and may even be the precursor for the development of the disease^{9,10}.

Age incidence showed that in group -A, patients of 'less than 5 years of age' were more in number and in group B, patients of '13 to <18 years of age' were more. This was because our main aim was to find out the role of Nedocromil in preschool children age group patients. Rocchiccioli K & Pickering CAC⁹ reported in his double-blind crossover study that cold air induced bronchoconstriction in atopic asthmatics of preschool children, school children and adult could be prevented by pre-treatment with 4mg Nedocromil.

Sex incidence showed that no significant differences were observed between the groups. Male and female ratio was about 60:40, i.e. 3:2. Newaz S,

Ohio¹⁰ reported that in affluent society male children were more affected than female and in non-affluent society affected male and female ratio was same. He suggested a probable genetic factor might be responsible for these differences. As Dhaka is the main catchment area for this asthma centre and Dhaka City is the main affluent area of Bangladesh, male children were predominating than female. In this study living condition of the 2 groups were almost equal and patients were mostly coming from urban area.

Family history of asthma and associated condition were studied. It was found that there is no significant difference in group A & B. About 50% patients gave family history of asthma and/or allergic rhinitis. Asthma is highly correlated with atopy and there has been a recent unexplained increase in the prevalence of atopy in many population¹¹. Some recent studies suggested that bronchial hyperresponsiveness and a major locus controlling IgE production are both located in one or more genes on chromosome 5q31-q33¹⁰⁻¹¹. Even in the presence of an inherited predisposition, many other factors also affect the development of atopy and its effects in the individual patient. This study showed about 50% patients gave family history of asthma and/or allergic rhinitis could be correlated with the western studies¹¹⁻¹².

Nedocromil had been used more in mild persistent asthma and inhaled Corticosteroids were used more in severe persistent asthma and in cough variant asthma. Our aim was to use more Nedocromil sodium in cough variant asthma and seasonal asthma patients but unfortunately most of the cough variant asthma patients were unable to procure Nedocromil. We had not used Nedocromil in seasonal asthma because most of the patient gave history of asthma attack during cold season. Our study periods were during summer and rainy season.

Treatment outcome was analyzed and showed statistically no significant difference between the 2 groups. But apparently it was seen that Nedocromil was less effective in less than 2 years of age group. It was more effective in 2-5 years age group and it is as effective as group B in 6-12 years age group. In 13 - <18 years age group sample size of group - A was very small compared with group - B. But out of 6 patients 5 patients showed

complete response in patients treated with nedocromil. According to Expert Panel Report -2 Nedocromil sodium/sodium cromoglycate is the drug of first choice in childhood asthma whatever the severity of asthma¹³.

We had carefully evaluated the problems of Nedocromil sodium. In spite of full asthma education at the time of prescribing drugs out of 49 patients. 16 (32.6%) patients were irregular in taking Nedocromil sodium Inhaler. Out of these 16 patients, 4 (8.2%) patients were complaining of bitter taste, 2 (4.1%) patients were complaining about throat irritation, 2 (4.1%) patients complained of nausea 1 (2.0) patient felt headache after inhalation, 1 (2.0) patient were complaining of coughing during inhalation of drug, 4 (8.2%) patients said that it was not available regularly in their area (market), 2 (4.1%) patients were irregular to buy it due to monetary problem.

Conclusion

1. Nedocromil is a very effective drug over 2 years of age.
2. No significant side effect is observed over 6-month period.
3. Further study should be carried to see the efficacy for Nedocromil sodium in type matched and age matched bronchial asthma.

References

1. Shapiro GG, Konig P. Cromolyn or nedocromil sodium; a review Pharmacotherapy; 1985; 59 : 156-170.
2. Murphy S, Kelly HW. Cromolyn or Nedocromil sodium : a review of mechanisms and clinical use in asthma drug Intell. Clin. Pharm 1987; 21 : 22-35.
3. D'Alonzo ge, Nathan A, Henochowicz S, Morris RJ, Ratner P, Renard SI. Salmeterol xinafoate as maintenance therapy compared with albuterol npatients with asthma. JAMA 1994; 271 : 1412.
4. Nassif EG, Weinberger MM, Thompson R, Huntley W. The value of maintenance Theophylline In Steroid-Dependent Asthma. N Engl J Med 1981; 304-71.
5. Schwartz HJ, Blumenthal M, Brady R, Braun S, Lockey R, Myers D et al. A comparative

- study of the clinical efficacy of nedocromil sodium and placebo. How does Cromolyn or Nedocromil sodium compare as an active control treatment/Chest 1996; 109 : 945-52.
6. Petty TL, Rollins DR, Christopher K et al. Cromolyn or Nedocromil sodium is effective in adult chronic asthmatics. Am Rev Respir Dis 1989; 139 : 694.
 7. Mcfadden ER. Exertional dyspnoea as preludes to attack of bronchial asthma. N Engl J Med 1975; 292 : 555-559.
 8. Irwin RS, Curly FJ, French CL. Chronic cough : the spectrum and frequency of causes, key component of the diagnostic evaluation, and outcome of specific therapy. Am Rev Respir Dis 1990; 141 : 640-647.
 9. Rocchiccioli K, Pickering CAC. A double-blind crossover study to compare the effects of nedocromil sodium (4mg) and placebo given by pressurized aerosol in cold air bronchial challenge in asthmatic patients a preliminary report. Eur J Respir Dis 1986; 69 : 292-293.
 10. Newaz S. Concept of Asthma – An update. Proceeding of the '1st Workshop on Asthma' held in BCPS, Mohakhali, Dhaka 1996; 32-36.
 11. Cochrane GM, Jackson WF, Rees PJ. Asthma – Current perspective. Astra. 1996; 1 : 11-20.
 12. Global Initiative for asthma. Global strategy for asthma management and prevention NHLBI/WHO workshop report. National Institute of Health, 1995; (95-3659) : 11-23.
 13. Expert panel report-Z, guidelines for the diagnosis and management of asthma. National institute of health 1997; (97-4051) : 81-98.