

# Oral Prophylaxis of Bronchial Asthma in Children

Pages with reference to book, From 90 To 93

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## Abstract

A prospective study was conducted on the efficacy of Ketotifen a benzocycloheptathiophene derivative, for oral prophylaxis of bronchial asthma in children.

Of 19 children who fitted the criteria for drug trial, the drug was very effective in reducing the number of attacks in 12 and moderately effective in 7 cases ( $P < 0.001$ ). Side effects of the drug were not severe enough to require withdrawal (JPMA 34: 90, 1984).

## Introduction

Bronchial asthma is a very distressing disease in children resulting in limitation of daily routine activity, poor school performance and growth retardation. Its prevalence in children is 13 % (Gobel, 1979). The cause of asthma is multifactorial including biochemical, autonomic and immunological factors. Histamin, serotonin and SRS-A released through immunologically mediated reaction produce bronchoconstriction by direct action on smooth muscles or indirectly by stimulation of vagal sensory receptors. As no permanent curative treatment is available prevention of asthma attacks is desirable. Sodium cromoglycate was the first asthma prophylactic drug but unfortunately it has to be given through inhalation requiring cooperation of the patient, hence, unsuitable for use in young children. Ketotifen, a benzocycloheptathiophene derivative, is an oral prophylactic drug for asthma which can be used easily and effectively (Craps et al., 1978; Kumagai and Tomioka, 1978; Marcelle and Lecomte, 1977; Girard and Cuevas, 1977). It has a mast cell stabilizing activity preventing release of histamin and serotonin but very little anticholinergic activity (Martin and Romer, 1978). To evaluate its efficacy in children, a prospective study was carried out at National Institute of Child Health, Jinnah Postgraduate Medical Centre, Karachi. The results of the study are presented.

## Material and Methods

Forty children reported at the study clinic. Their detailed medical history was taken. Height, weight and blood pressure were recorded. Peak expiratory flow rate (PEFR) was measured in those children who cooperated. Investigations like complete blood count (CBC), Urine examination, stool examination, Liver function tests (LFT) and X-Ray chest were done. They were observed for one month without ketotifen as controls before trial period of 3 months on it. Of these, 27 were selected for the study fulfilling the following criteria:-

- (1) At least one asthmatic attack per week.
- (2) At least one attack in a fortnight but every attack requiring steroids for control or the child having been on continuous steroid therapy for at least one month.
- (3) Regularity in attending the clinic.

These children visited the clinic at fortnightly intervals in between the asthmatic attacks. Their height, weight, pulse rate, blood pressure and measurements of PEFR were recorded on each visit.

Investigations like CBC, Urine examination, stool examination and LFT were also repeated on each visit.

After observing them for one month and obtaining the control values of mean number of asthmatic attacks, mean duration of the attacks and of other investigations, Ketotifen was started in a dose of 0.1

ml (0.04 mg) per Kg body weight twice a day. Each asthmatic attack during the trial period was treated with salbutamol syrup. Those not responding to bronchodilators were treated with intravenous hydrocortisone replaced by oral prednisolone which was tapered off and stopped in 3 days time if possible. Antibiotics were used only if an infection was suspected. The effectiveness of Ketotifen was judged using the following criterias

**Effective Group:**

(a) Very effective : Frequency and duration reduced to one third of the control stage and the attacks controlled by Sulbutamol.

(b) Moderately effctive: Frequency and duration reduced to less than half but more than one third of control stage and the attacks controlled by Salbutamol.

**Ineffective Group:**

Children not fulfilling the above criteria.

**Results**

Of these 27 children, 12 were males and 15 females. Their mean age was  $6.5 \pm 2.9$  years (Range 1½ to 11 years). The mean body weight was  $16.6 \pm 5.6$  Kg (Range 7.6 - 29.6 Kg) and mean height was  $109 \pm 18.8$  Cm (Range 70 - 137 Cm) (Table I).

**Table – I** **Body Weight And Height On Entry.**

Age	0 – 5 Years		6 – 10 Years		11 – 15 Years		Total	
Centiles	WT	HT	WT	HT	WT	HT	WT	HT
<3rd	5	5	9	3	0	0	14	8
3 – 10th	3	0	7	3	1	0	11	3
10-25th	0	2	0	9	1	1	1	12
25-50th	1	1	0	1	0	0	1	2
over 50th	0	1	0	0	0	1	0	2
<b>Total:</b>	<b>9</b>	<b>9</b>	<b>16</b>	<b>16</b>	<b>2</b>	<b>2</b>	<b>27</b>	<b>27</b>

Family history for bronchial asthma was present in 10 children. The fact that growth retardation is a common feature of bronchial asthma in children is supported by this study, 25 (90%) being under 10th centile and none over 50th centile. Similarly 23 (85%) children were under 25th centile for height. Nineteen (70.4%) were included in effective group. Ketotifen was very effective in 12 and moderately effective in 7 children in reducing mean number and duration of attacks (Fig.)

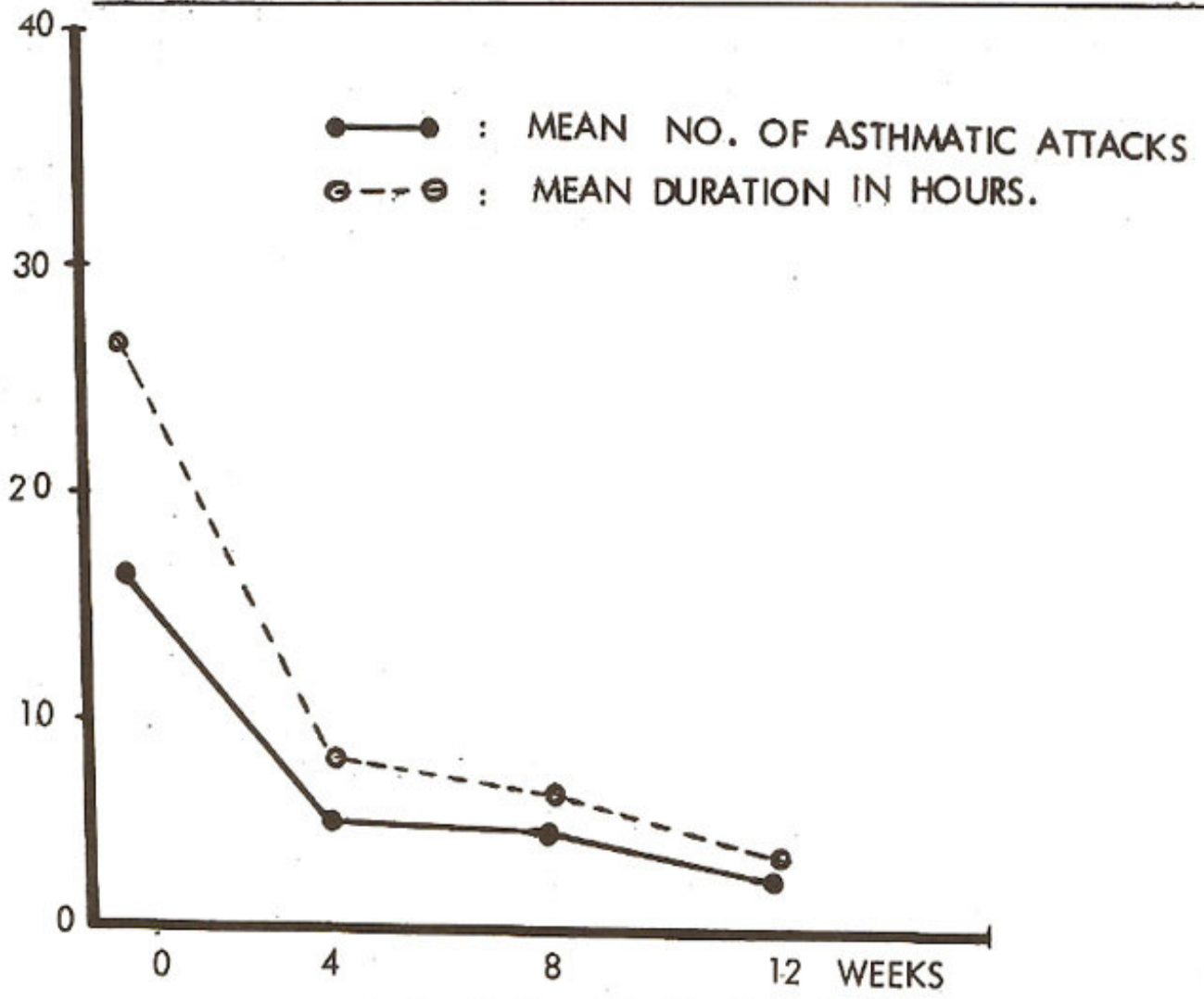


Fig. Mean Number and Duration of Asthmatic Attacks.

TTACKS.

significantly (P L 0.001). The mean number of attacks was reduced from  $163 \pm 11.5$  to  $1.4 \pm 1.8$  per month and the mean duration from  $28 \pm 17.1$  hours to  $1.6 \pm 3.7$  hours. The mean values of PEFV are given in Table II.

**Table II****Ketotifen And P E F R**

Month	All Cases (16)	(Group I) 'Effective' (II)	(Group II) 'Ineffective' (II)
(A) 0 month	88.4 ± 45.3	90 ± 37.4	85 ± 64.6
(B) 1st month	98.4 ± 50.4	112.3 ± 52.8	68.0 ± 29.5
(C) 2nd month	114 ± 52	130.5 ± 53.6	78. ± 24.9
(D) 3rd month	113.7 ± 63.4	132.7 ± 61.8	72 ± 48.7
S.E. between (A & D)	19.4	21.8	36
P. Value (A & D)	N.S.	N.S.	N.S.

It was increased in 16 children but increased only in 13 children. In 9 out of these 13 children it increased more than 50% of it's control value. Steroids were used only in 8 children. They were used continuously in 4 children, intermittently in another 4 children and during first month only in 3 children, by more than 5% of control in 9 (333%) and by over 10% in 8 (29.6%). No significant changes were recorded in pulse rate, blood pressure blood count and liver function tests. The side effects recorded were vomiting in one - self limited vertigo in one and irritability in one child. None of these were severe enough to withdraw the drug.

**Discussion**

Ketotifen was found to be effective in prophylaxis of bronchial asthma by other workers (Craps et al., 1978; Gobel, 1979 ; Stangi et al.,1980; Szezeklik et al., 1980). In this study it proved to be effective in just over 70% children. The reports of non-effectiveness of Ketotifen by Taylor and Ford (1979) and Wells and Taylor (1979) have not been substantiated by our study.

As reported earlier (Halvorsen. and Endsjo, 1980; Weheba, 1979; Gobel, 1978; Spicak, 1980)

Ketotifen was effective in reducing both the ion of asthmatic attacks.

These results are quite encouraging and important as Ketotifen being an oral prophylactic agent, can be given to children easily. Not only it relieved the distress and suffering of the children but also improved their general health as seen by increase in their body weight.

PEFR was not a reliable index of judging the efficacy of Ketotifen as not only it's measurements depend upon the cooperation of the children but also whether they come in acute attack or not. In our study though PEFR was increased in 13 (81.2%) children but statistically it was not significant.

Ketotifen is an effective and safe oral prophylactic drug for asthma from which a large number of children can derive benefit but a failure rate of about 3d% is likely; The parents should be appropriately informed before the drug is prescribed.

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