

TRIAL OF KETOTIFEN IN CHILDHOOD ASTHMA

A. V. PHERWANI* AND A. G. DESAI

Institute of Child Health

*J. J. Group of Government Hospitals and Grant Medical College,
Bombay - 400 008*

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Summary : An open trial of Ketotifen was conducted on 29 children suffering from asthma of varying duration. The drug was given orally in a dose of 1 mg twice a day. Children were followed up weekly for a period of 3 months. It was found beneficial (though the benefit was not statistically significant) in children having asthma of less than 2 years duration who were taking one drug regularly or were on occasional treatment. There was marginal effect in children taking salbutamol and theophylline together, but irregularly and no benefit in children taking prednisolone.

Key words:

Ketotifen

asthma

INTRODUCTION

There was no solution to prophylaxis against asthma until the development of Sodium chromoglycate (1,2). Though Sodiumchromoglycate is particularly helpful in children (3), its use is limited in this age group due to non-compliance due to the mode of administration of the drug i.e. by inhalation. Extensive studies discovered Ketotifen, a benzocyclohepatathiophene. It has powerful antihistaminic and antianaphylactic properties (4), inhibits antigen induced mediator release (9) and inhibits cyclic AMP phosphodiesterase in a manner similar to that of theophylline (7).

Different authors have given varying reports on the efficacy of Ketotifen in children (5,6,11,12). The present study was conducted to find out the effectiveness of Ketotifen in children suffering from asthma, at the Pediatric Asthma Clinic of the J.J. Group of Hospitals, Bombay,

MATERIAL AND METHODS

Twenty-nine children suffering from asthma were enrolled for the present study from March, 1982 to March, 1983. The selection was done on clinical grounds viz. witnessing an actual attack which improved with bronchodilator drugs. An informed written consent was obtained from the parents of all the patients.

Asthma was graded as severe when the heart rate was above 120/min, there was severe dyspnoea, wheezing, poor air entry and emphysema. Asthma was moderate when the heart rate was below 120/min, there was mild dyspnoea and wheeze and when rhonchii were heard without a stethoscope. Asthma was mild when rhonchii were heard only on auscultation.

Every child was subjected to a Mantoux Testing, x-ray chest, urine, stool, serum bilirubin, SGOT, SGPT, Blood urea and serum creatinine examination before, during and after the completion of the therapy. Absolute Eosinophil counts were done in 19 and serum IgE concentration in 21 cases. Asthma could be classified into extrinsic on the basis of IgE and/or skin testing for allergens in 22 cases. Pulmonary functions were done whenever it was possible to train the child (n=15).

Ketotifen was supplied in the form of Elixir, along with a 1 ml measure cup. Every child was instructed to take 1 ml of the drug after breakfast and after dinner. All the patients were followed up weekly as outdoor patients. Compliance was 100% and there were no drop-outs. At every visit the following parameters were noted: (1) Increase in the interval between attacks, (2) Improvement of symptoms, (3) Reduction in the dose of drugs, if any, and (4) Reduction in the severity of asthma. Parameters 1, 2, and 3 were dependent on the parents' and/or child's judgement and the results were analysed on yes or no basis. The last parameter was derived from physical examination by us as specified above. The data was analysed using 't' test whenever appropriate.

The children taken in the study were from our Asthma Clinic whose pattern of asthma was known to us. The children were maintained on their drugs but they did have exacerbations off and on. Therefore, some of the benefits of the drug may have been because the patient was seen in his non-attack period and vice versa, some of them may have been seen during an attack.

RESULTS AND DISCUSSION

Out of the 29 cases of asthma 65.5% (n=19) were males and 34.5% (n=10) were females. The children were between the ages of 2-12 years with a mean age of 7.5 years. All the cases except two had asthma for more than a year. 79.3% (n=23) had perennial, 3.4% (n=1) had seasonal, 6.93 (n=2) had recent onset asthma and 10.3% (n=3) could not relate their asthma to any time of the year. 65.5% (n=19) had severe, 24.1% (n=7) had moderate, 10.34% (n=3) had mild asthma. 48.3% (n=14) had asthma of recent onset i.e. of less than 2 years duration and 51.3% (n=15) were chronic asthmatics i.e. they had asthma for more than 2 years.

20.7% (n=6) were maintained on prednisolone, salbutamol and theophylline, while 3.4% (n=1) were taking prednisolone and salbutamol. 31.1% (n=9) were taking salbutamol and theophylline, 24.1% (n=7) were taking only salbutamol, 13.8% (n=4) were taking only theophylline and 6.9% (n=2) were on miscellaneous drugs.

The improvement in the various parameters is shown in Table I. It can be seen that 37.9% (n=11) showed improvement in all the parameters, 44.8% (n=13) did not show improvement in any parameter. The remaining 20.7% (n=5) showed improvement in less than 4 parameters. out of these 5 children. 3 showed improvement in 3 and 2 in 1 parameters. From the whole group (n=29), the interval between attacks increased in 48.5% (n=14), improvement in symptoms occurred in 37.9% (n=11), severity of attacks decreased in 48.3% (n=14) and drugs could be reduced in 44.8% (n=13).

Out of the 15 patients on whom PFT'S could be performed only 6.7% (n=1) showed an improvement in FEV1 of more than 30% after Ketotifen therapy. 73.3% (n=11) showed an improvement of less than 30% and 20% (n=3) showed deterioration, The FEV1 before and after therapy was 1147.67 and 1255.62 l/sec respectively. The difference is not statistically significant (t=0.63)

The above parameters were analysed in children taking prednisolone (mean dose, 16.89 mg/week) along with other drugs (n=7). 28.6% (n=2) had increased interval between attacks, 14.2% (n=1) had improvement in symptoms, 28.6% (n=2) could reduce the does of drugs and 28.6% (n=2) had decrease in the severity of symptoms.

In 9 children taking salbutamol and theophylline together, 11.1% (n=1) improved in all parameters. 44.4% (n=4) increased the interval between attacks and had improvement in symptoms and 33% (n=3) could reduce the dose of drugs and had a reduction in the severity of their attacks. 22.2% (n=2) showed no response. The mean dose/week of salbutamol before and in the last week of Ketotifen therapy was 21.17 and 17.38 *mgm* respectively. The difference is not statistically significant (t=0.578). Some improvement was seen in patients taking only one drug i.e. salbutamol (n=7) or theophylline (n=4) alone, where each of the above parameters improved in 63.6% (n=7) and did not improve in any parameter in 36.4% (n=4) of cases. However there was no significant reduction in the mean dose/week of theophylline before (966.55 *mg*) and in the last week (844.83 *mg*) of Ketotifen therapy (t=0.287). Of the two children who were on terbutaline one child improved in all parameters, while the other did not improve in any parameter.

TABLE I : Improvement in the various parameter after Ketotifen therapy.

<i>Parameter</i>	<i>% showing improvement</i>	<i>Number of patients 'n'</i>
Increased interval between attacks	48.3	14
Improvement of symptoms	37.9	11
Reduction in the doses of drugs	44.8	13
Decrease in the severity of attacks	48.3	14
Improvement in all parameters	37.9	11
Improvement in no parameter	44.8	13

We further analysed the effect of Ketotifen on children having asthma of recent onset (n=14) and found it to have some benefit in them. Children having asthma of less than 2 years were considered as recent asthmatics and the remaining as chronic (n=15). As shown in Table II, 42.83% (n=6) in the recent as compared to 20% (n=3) in the chronic group showed improvement in all the parameters and 35% (n=5) of the recent as compared to 60% (n=9) of the chronic group did not improve in any parameter. As shown in the table all the 4 parameters showed better improvement in the recent as compared to the chronic group.

All investigations done before, during and after the end of Ketotifen therapy were normal. Weight gain was seen in all except in 1 case. The only other side effect was

seen in a boy who developed tremors, itching, redness and scaling of the palms. The rash disappeared on stopping treatment and did not appear after restarting therapy; however the tremors persisted. No other side effects were encountered.

TABLE II : Comparison of different parameters between recent onset and chronic asthmatic children under treatment with Ketotifen.

Parameter	% of chronic asthmatics showing improvement (n=15)	% of recent asthmatics showing improvement (n=14)
Increased interval between attacks	33.33	57.14
Improvement of symptoms	26.66	50.00
Reduction in the doses of drugs	26.66	57.14
Decrease in the severity of attacks	26.66	64.28
Improvement in all parameters	20.00	43.83
Improvement in no parameter	60.00	35.00

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