CHILDHOOD ASTHMA, RESPONSE TO ORAL PROPHYLAXIS

Pages with reference to book, From 295 To 299

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Abstract

The value and efficacy of ketotifen as a prophylactic drug for childhood asthma was assessed for 1 year in 45 children. Sixty seven percent showed good response, 15.5% moderate and 17.7% poor response to ketotifen therapy. The side effects (sedation, dizziness, headache) were seen in 20% children which resolved without interruption of therapy. Ketotifen appeared to be an effective and safe oral prohhylactic drug for childhood asthma (JPMA 36: 295, 1986).

INTRODUCTION

Asthma is the most common cause of long-term respiratory disease in childhood.' It can result in considerable disability if appropriate treatment in not instituted. At least 20% of children wheeze as a result of asthma at some stage of childhood.[1] The incidence of asthma is reportedly less than 3% of the total population[2] Boys are affected twice as frequently as girls.[3]

In asthma, bronchial narrowing is due to a combination of factors such as bronchial muscle spasm. hypersecretion of mucus, and mucosal oedema.[4] This is due to a complicated interaction between tmmunological factors, reflex nervous changes, and underlying pathological damage.[5] There is extraordinary hyper-reactivity of tracheobronchial tree to various chemical mediators, (Histamine, SRS-A, Prostaglandins), which are activated or liberated by various insulting agents or events. [2] Since no permanent cure is available for asthma, probably the only way to enjoy a reasonably normal life is by preventing acute attacks. Ketotifen is a relatively new bonzocylonepta-thiophene which possesses pharmacological actions similar to those of disodium cromoglycate[2] and helps in prevention of asthmatic attacks.

Ketotifen is effective in preventing histamine induced bronchospasms,[67] Aspirin induced asthma[8] and appears to be as effective in most studies as disodium cromoglycate in inhibiting inhaled allergen induced broncho-spasm.[9]

Ketotifen exhibits marked antianaphylactic properties and specific antthistamine effect, besides exerting a powerful sustained-H 1 receptor blocking activity[10]. Oral administration, and twice daily dosage, has made it the drug of choice in the management of childhood asthma, especially for very young asthmatics who are unable to use a spinhaler, pressurized inhaler or nebulizer.

A prospective clinical study was done at National Institute of Child Health, to assess the value and efficacy of Ketotifen as prophylaxis against spontaneous attacks of childhood asthma and its effects on concomitant therapy required during these attacks.

MATERIAL AND METHODS

Forty five children, aged 4-14 years, having asthmatic attacks once monthly to more than once weekly, and regularly attending the clinic were selected for the study.

In every case, a detailed history was obtained, complete physical examination was done and peak

expiratory flow rate (PEFR) was measured in all children who co-operated. Investigations carried out included, Hb, total and differential leucocyte count, ESR liver function tests, urinalysis, stool examination and an X-ray Chest.

All these patients were observed for one month and asthmatic attacks were categorized as follows according to serverity of the attack. Severe: attacks of severe dyspnoea with severe respiratory distress, marked wheezing requiring steroids in addition to B_2 stimulants and Xanthines for relief. of symptoms.

Moderate: attacks of mild-moderate dyspnoea usually incapacitating enough to interfere with normal activities, requiring B_2 stimulants with Xanthines. Short course of steroid may be necessary for symptomatic control of some cases. Mild: attacks of mild dyspnoea not interfering with daily routine but requiring B_2 stimulants or Xanthines.

After the initial assessment, Ketotifen was started orally, 0.5 mg twice daily for children weighing less than 25 kg and 1mg twice daily for those above 25 kg.

Each asthmatic attack during the trial period was treated with salbutamol alone or in combination with theophylline or aminophylline, oral or intervenous (I.V.) depending upon the severity of the attack. I/V steroids followed by oral for 3 days were given whenever necessary. Antibiotics were given in cases of suspected infections. These children were assessed every 2 weeks for 3 months and then every month upto one year.

EFFICACY ASSESSMENTS

(a) Subjective assessments

Patients and mothers/attendants were questioned regarding the frequency, duration, severity of asthma attacks, and treatment given was evaluated and recorded as per the following scale; Feeding better, No change, Worse.

(b) Objective Assessments

The above subjective assessment was substantiated by clinical evidence of bronchospasm, prolonged expiration and PEFR. Signs of asthmatic attack, prolonged expiration, expectoration, wheezing, dyspnoea and severity, (as per protocol). Treatment given was also reviewed. Evaluation of the efficacy of Ketotifen was done as follows:--

(1) Very Good : 2/3 reduction in frequency, duration or severity of attack, and in concomitant therapy.
(2) Good: almost½ reduction in frequency, duration or severity, of attack, and in concomitant therapy.
(3) Moderate: almost1/3 reduction in frequency, duration or severity and in concomitant therapy.
(4) Ineffective: no significant change.

(c) Safety Assessment

Investigations listed above were repeated at 3 months and at one year. Adverse reactions were also recorded.

The study lasted over a period of 15 final months. A assessment was made at the end of the study.

RESULTS

Of 45 children 26 were males and 19 females. The mean age was 7.64 years (range 4-13 years), mean bodyweight and height were 20.7 kg (range 7.5 - 33.3 kg) and 113 cms respectively (range 76 - 145 cms).

The illness started under 7 years of age in 39 (86.6%). and a positive family history for asthma was present in 26 (57.7%).cases. Chest deformity was present in 11(24.4%) patients and 1 child had clubbing of nails (2.2%).

Forty five children completed 3 months, 21 six months and 10 one year trial. Thirty (66.6%) had very good or good response, 7 (15.5) moderate response, and 8 (17.7%) poor response to Ketotifen therapy (Table-I).

TABLE - I
Response to Ketotifen.

Duration of Therapy	Total Patients	V. Good	Good	Mode-rate	No Effect
3 Months	45	20 (44.4%)	10 (22.2%)	7 (15.5%)	8 (17.7%)
6 Months	21	12 (57.14%)	6 (28.5%)	3 (14.2%)	–
12Months	10	3 (30%)	6 (60%)	1 (10%)	–

The frequency and duration of attacks was reduced by 66.77 % and 74.1% respectively (Figures 1 and 2).

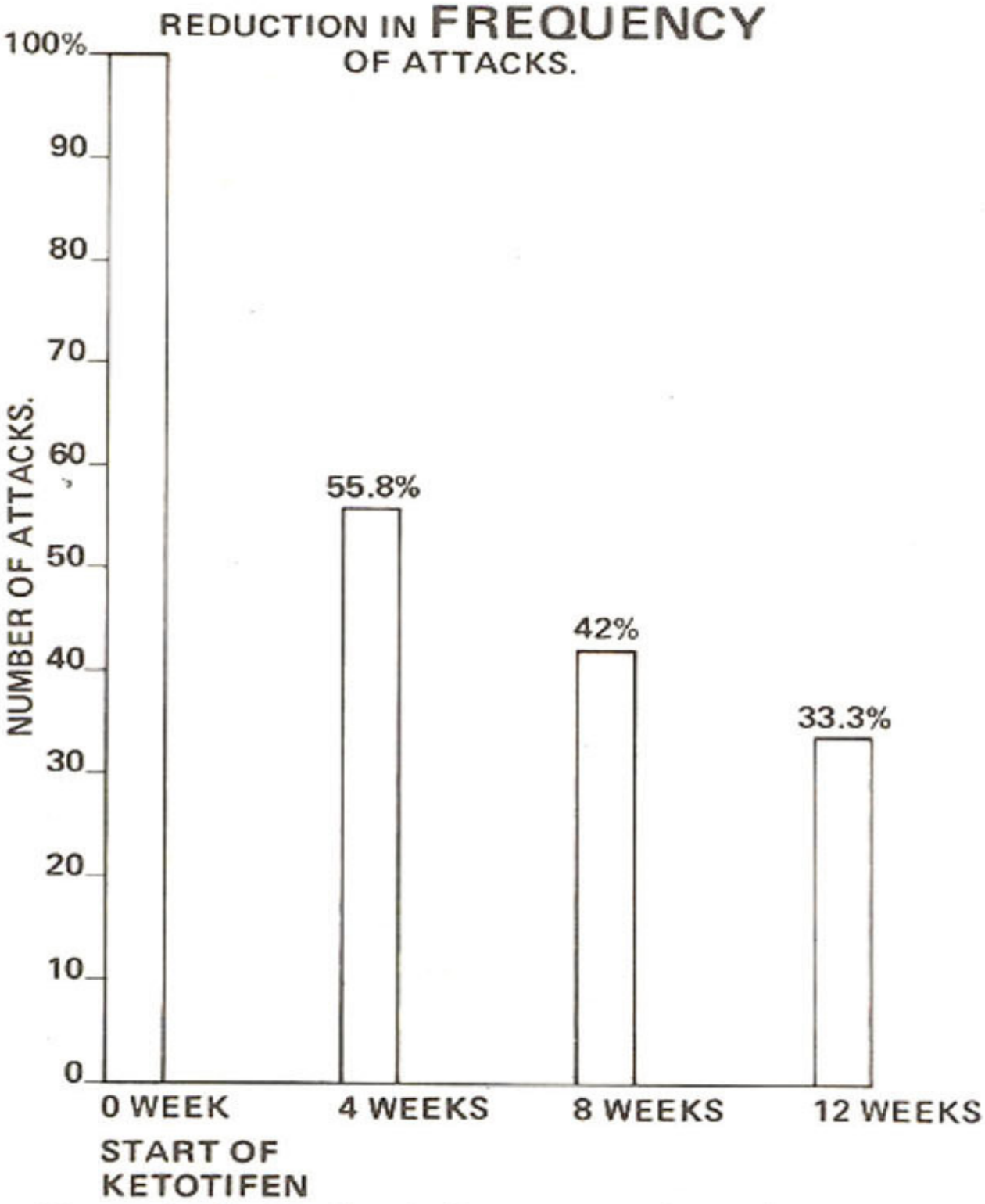

Figure 1. Reduction in frequency of attacks.

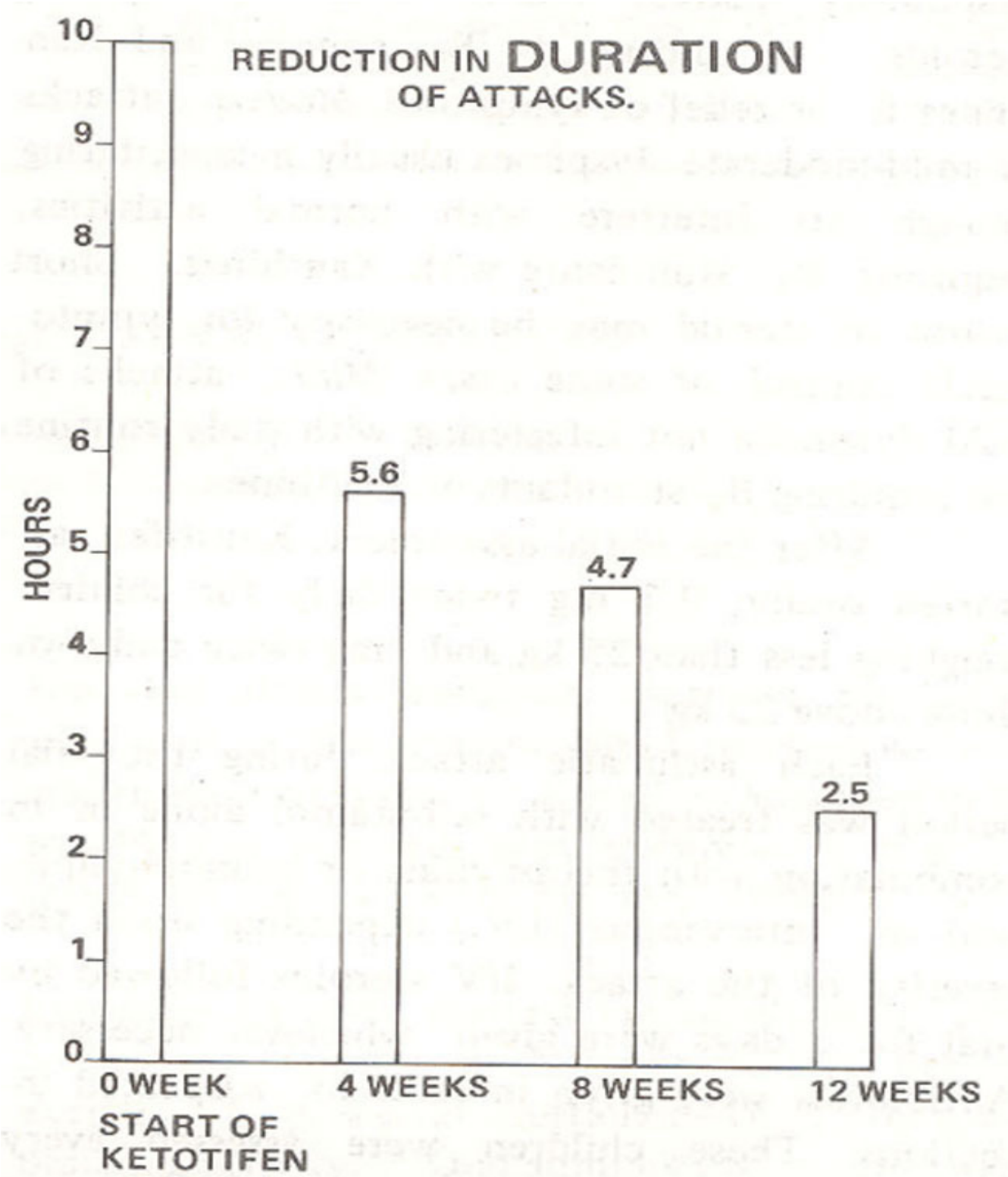

Figure 2. Reduction in duration of attacks.

PEFR improved in 16 (35.5%) children by (Figure 3).

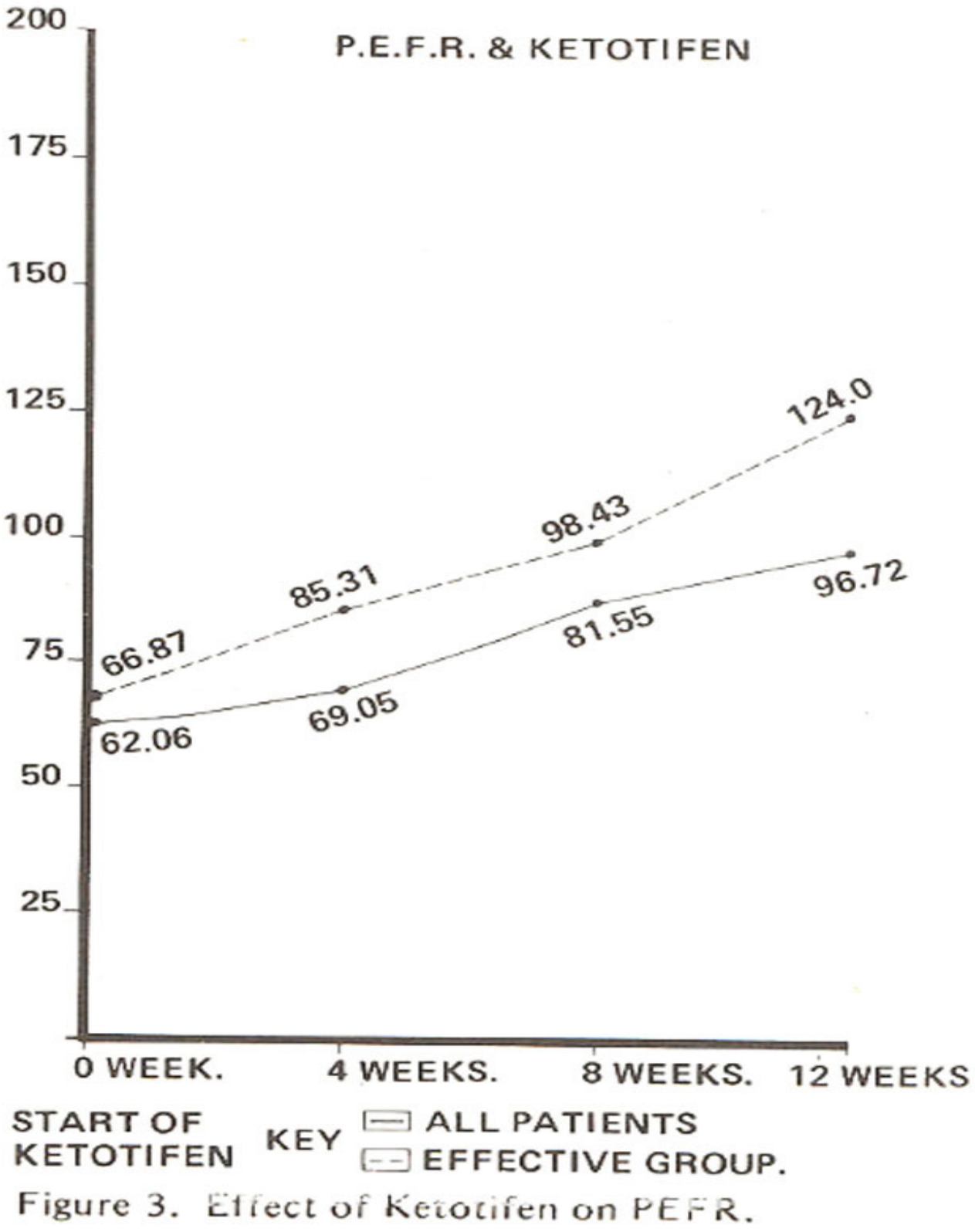

Figure 3. Effect of Ketotifen on PEFR.

The reduction in servity and concomitart therapy is shown in Figures 4, 5,6, and 7.

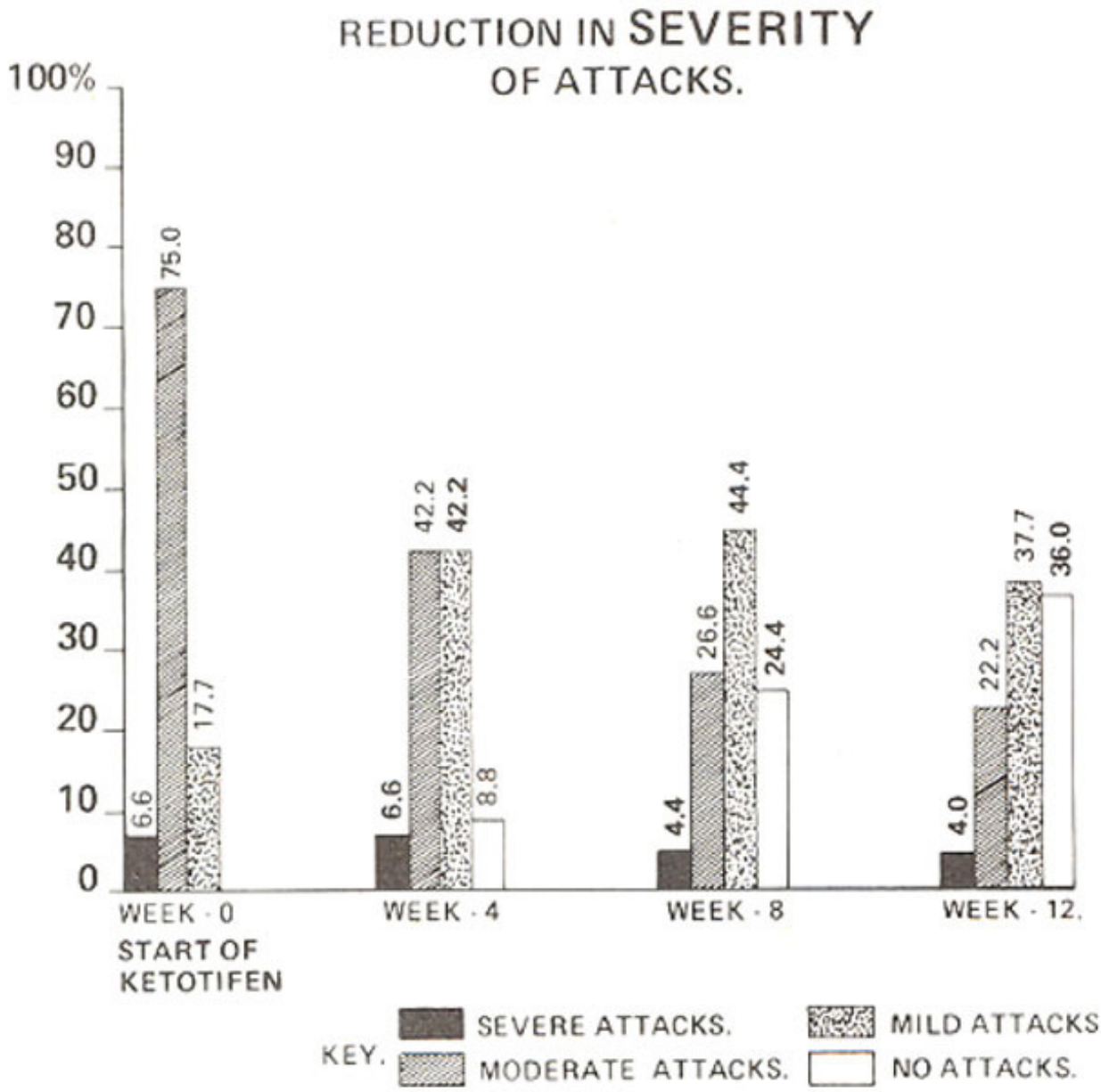

Figure 4. Effect of Ketotifen on severity of attacks.

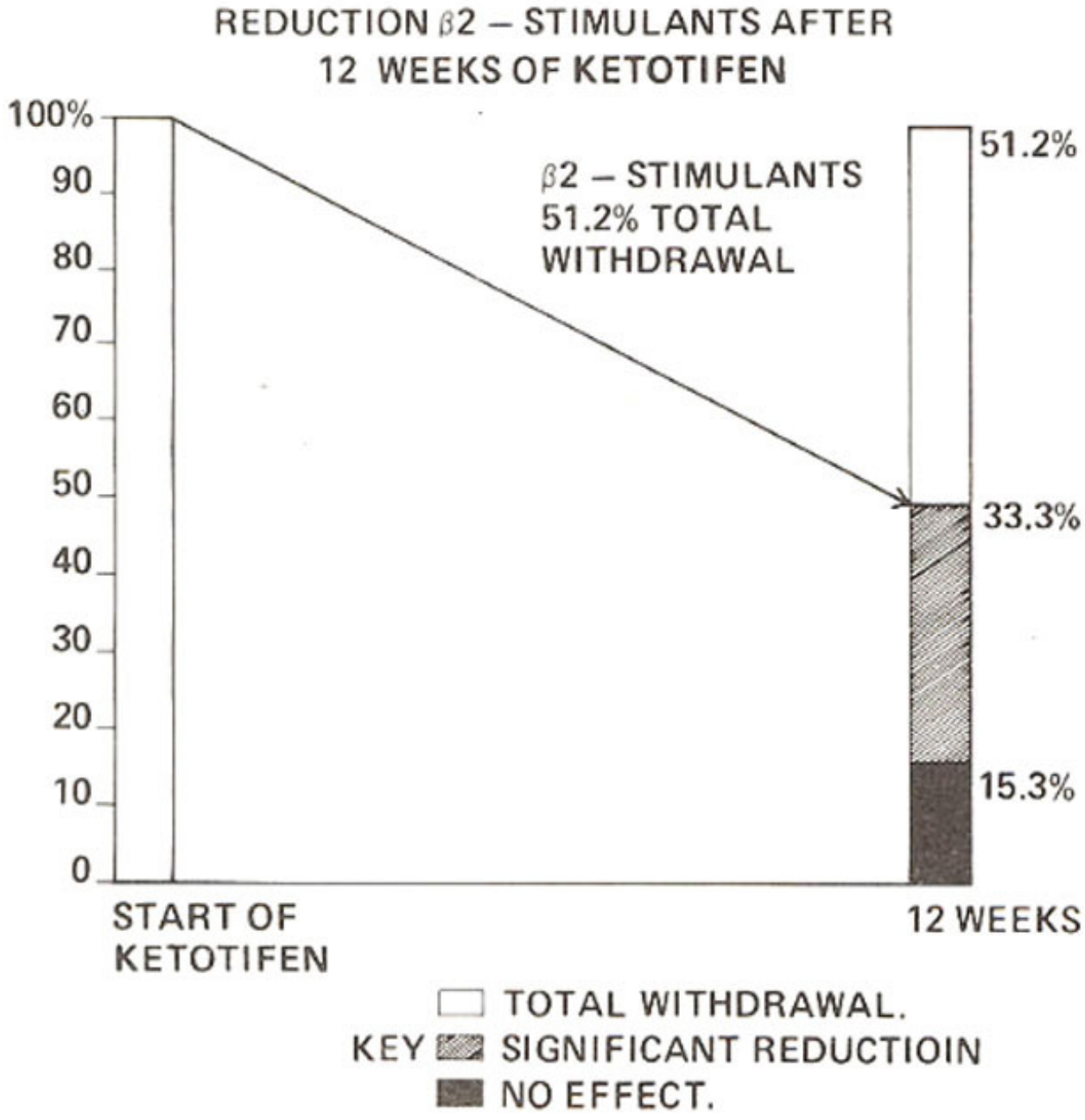

Figure 5. Effect of Ketotifen on B_2 stimulant intake.

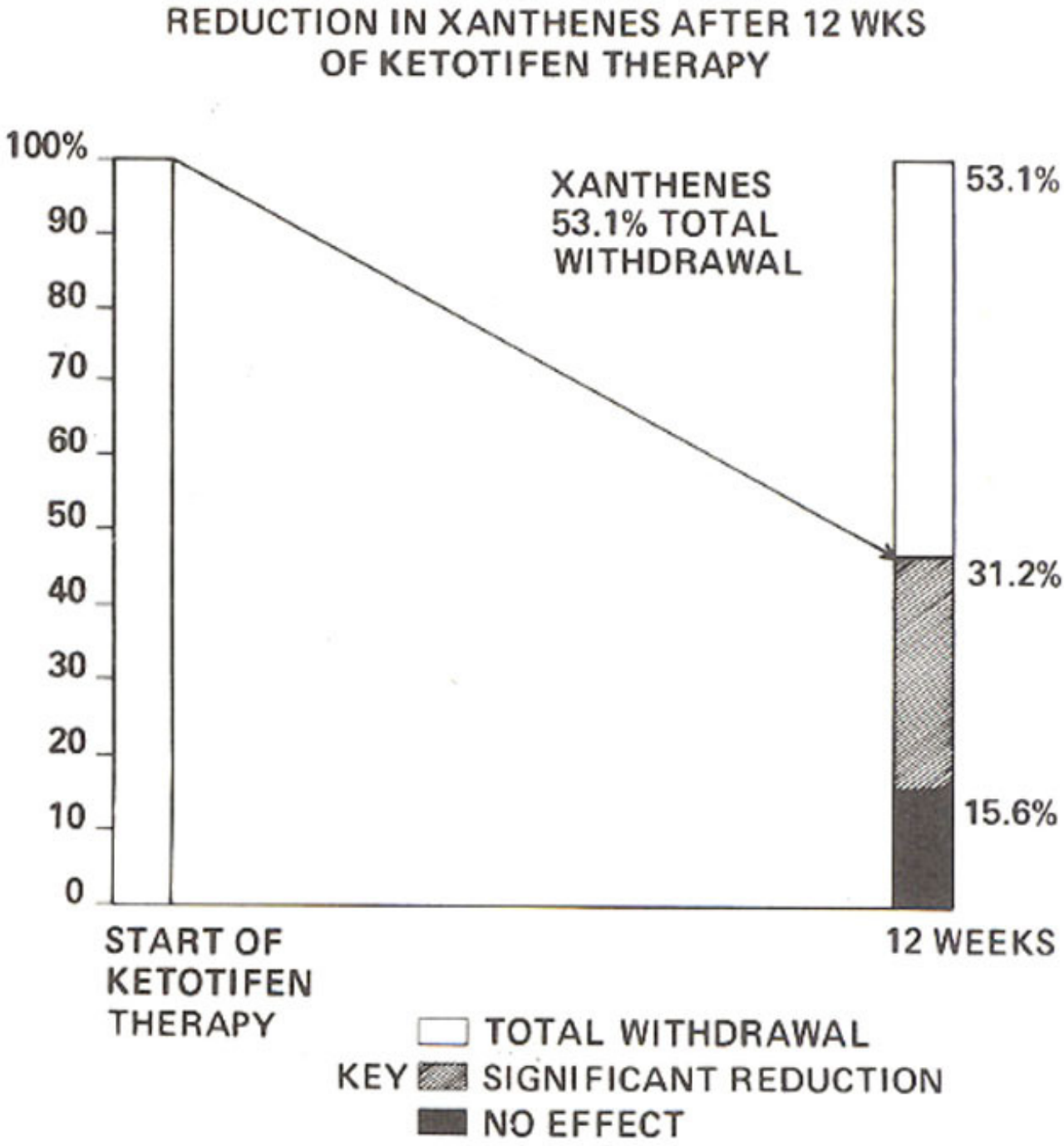

Figure 6. Effect of Ketotifen on xanthine intake.

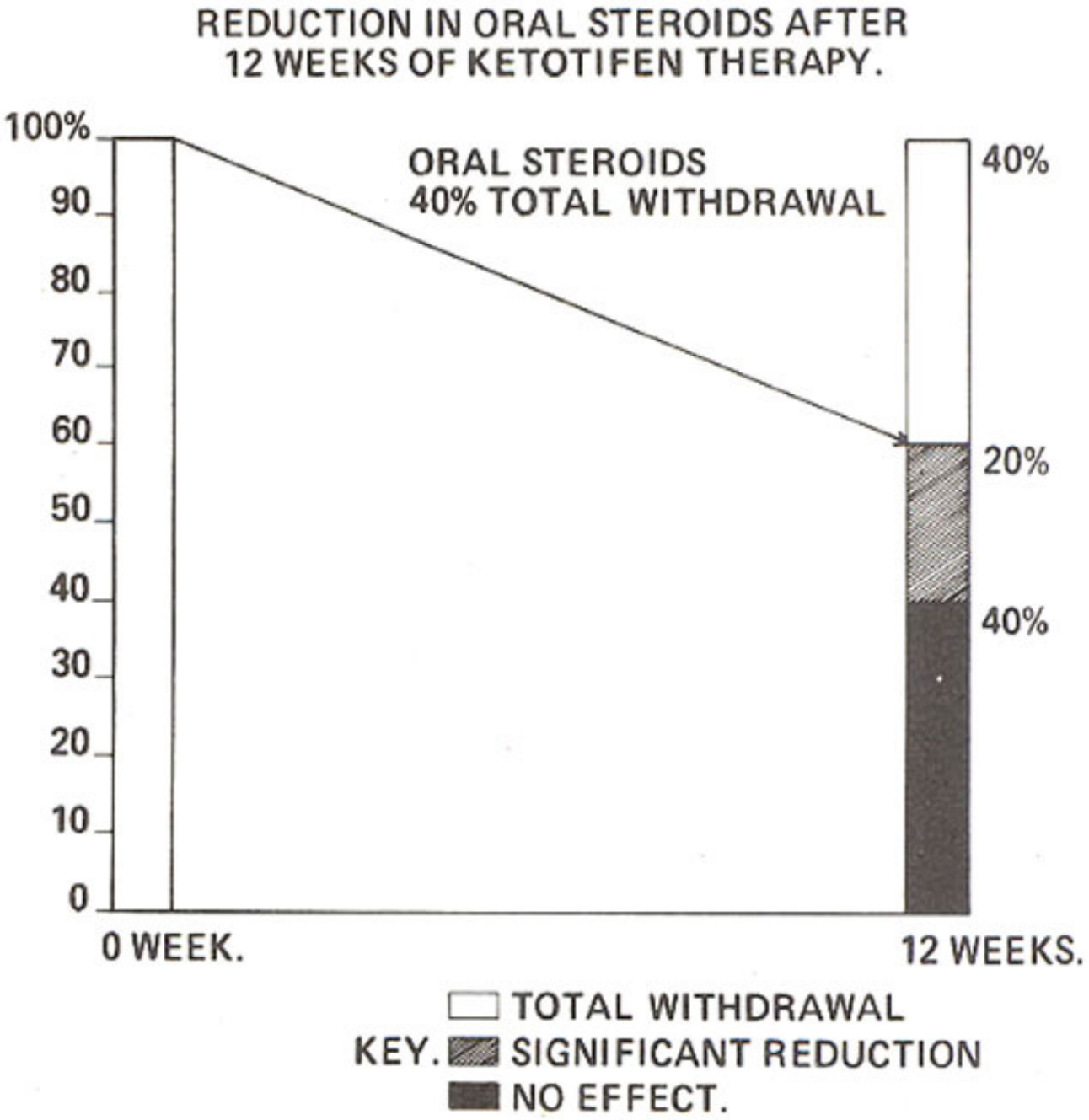

Figure 7. Effect of ketotifen on steroid intake.

Side effects seen in 9 (20%) children were sedation (7), dizzines (1) and headache (1), which resolved by the end of the 1st week without interruption of therapy. Even after 6-12 months of Ketotifen therapy, no significant side effects were observed.

DISCUSSION

Asthma is more common in male children and most of them have their initial symptoms before the age of 7 years[2] The frequency of asthma in boys was twice that in girls and 86.6% of children had their first

attack before the age of seven.
A family history was present in 57.7% children, showing an association between childhood asthma with a family history of this disease.[11]
Body weight of 77.77 % and height of 66.6 % children was below the 3rd centile.
Children with asthma may have growth retardation.[11]
Chest deformity[3,11] secondary to chronic hyperinflation, is one of the common complication of childhood asthma, if not managed properly and adequately. Chest deformity was present in 24.4% children in the present study.
Ketotifen was very effective in 66.6 % and quite effective in another 15.5 % of asthmalic similar findings have been reported in other studies.[12,15]
Ketotifen was effective in reducing the frequency[12,13] duration[13] and severity[14] of asthmatic attacks, as reported earlier.
Oral Ketotifen has a definite impact on the general well-being of the children. Asthmatic attacks are prevented, school performance is improved, and physical growth is accelerated.[16]
Although PEFR was improved in 16 (35.5%) children by almost 50%, it cannot be taken as a reliable index because it is difficult to measure PEFR in children and requires their full cooperation which in most cases is not possible.
Ketotifen appears to be a valuable advance in the long term management of childhood asthma. When given in adequate doses and for prolonged period it relieves respiratory symptoms and reduces or eliminates the need for concomitant therapy.

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