

Treatment of chronic urticaria with a β_2 -adrenergic stimulant

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Summary

Twenty-four patients with chronic urticaria resistant to conventional therapy were treated orally with terbutaline, a specific β_2 stimulant. This therapy was much more effective than antihistamines. At the dose of 1.25 mg three times a day, there were few side effects. The efficacy was independent of the IgE levels; it seemed greater in idiopathic cases than in cholinergic or pressure induced urticaria.

Introduction

The ideal treatment of chronic urticaria lies in the removal or the avoidance of aetiological factors. However, most often they are difficult to identify or to avoid so that in many cases the only possible treatment is symptomatic. Classically, this consists of antihistamines, corticosteroids and sedatives, none of them being satisfactory. Because of their side effects, corticosteroids should be avoided for long term use in this benign disease. On the other hand, chronic treatment with antihistamines may be incompatible with normal social activities because of their main side effect: drowsiness.

An increasing body of evidence indicates that mast cells play a major role in the genesis of most cases of chronic urticaria (Warin & Champion, 1974).

Experimental data further demonstrate that β -adrenergic agents, such as isoprenaline and its derivatives, have an inhibitory effect on the mast cells' degranulation, which leads to the liberation of the chemical mediators of the allergic reaction. Beta-adrenergic stimulants thus appear as potential anti-allergic agents (Bourne, Lichtenstein & Melmon, 1972). In the present study, we report our experience in the treatment of chronic urticaria with a specific β_2 stimulant, terbutaline, known for its good tolerance in the treatment of asthma.

Material and methods

Patients

Twenty-four patients with at least 6 months of chronic urticaria were included in

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Table 1. Characteristics of patients

Age	Sex ratio	Duration of the disease
10-47 years	Male: 12	6-24 months
Mean: 30	Female: 12	Mean: 14

this study because of unresponsiveness to conventional therapy or corticosteroid dependence (Table 1). Their ages ranged between 10 and 47 (mean 30) years. There were twelve males and twelve females. The duration of the urticaria ranged from 6 to 24 months (mean 14). The clinical diagnosis was based on a complete laboratory investigation, a systematic search for a causative agent in the anamnesis and an exclusion diet.

The present series comprises sixteen idiopathic, five cholinergic and three pressure urticaria cases. Four patients were atopic as indicated by the medical history, their serum IgE concentration and the existence of positive RAST tests to common pneumallergens.

Treatment schedule

Terbutaline was administered orally at the dose of 1.25 mg three times a day. Corticosteroids or antihistamines were stopped at the beginning of the assay. An extra dose of 2.5 mg of terbutaline was recommended when the first symptoms of hives appeared.

Clinical evaluation

The patients were examined at 2-weekly intervals over 2 months. At the end of this period, three different physicians evaluated the treatment on the following parameters: itching, eruption (frequency, number and size of the weal and flare eruptions) and the blocking effect at the beginning of a crisis. For each of these symptoms a score was rated as indicated in Table 2. Similar criteria were used to assess the clinical effect of antihistamines (Dexchlorpenizamine, Cyproheptadine) on the same patients.

Statistical methods

The efficacy of terbutaline was compared to that of antihistamines by variance analysis.

Table 2. Evaluation of effect of β_2 -adrenergic stimulant

Score x = 0	No effect	1	Slight improvement
2	Improvement	3	Marked improvement
4	Complete remission		

Symptoms:	Erythema	Itching	Attacks	Score
	$\frac{x_1}{4}$	$\frac{x_2}{4}$	$\frac{x_3}{4}$	$\frac{x_1 + x_2 + x_3}{12} =$

Statistical analysis by F test.

Table 3. Comparison of antihistamines and terbutaline in the treatment of chronic urticaria

Subjects investigated	No. of cases	Antihistamines				Terbutaline			
		Erythema	Pruritus	Attacks	Total score	Erythema	Pruritus	Attacks	Total score
All patients	24	0.22 $\pm$ 0.14*	0.30 $\pm$ 0.16	0.22 $\pm$ 0.17	0.27 $\pm$ 0.16	0.67 $\pm$ 0.3†	0.5 $\pm$ 0.3	0.63 $\pm$ 0.36†	0.65 $\pm$ 0.3†
Idiopathic Urticaria	16	0.218 $\pm$ 0.15	0.36 $\pm$ 0.16	0.25 $\pm$ 0.2	0.27 $\pm$ 0.17	0.734 $\pm$ 0.26†	0.59 $\pm$ 0.27†	0.63 $\pm$ 0.11†	0.65 $\pm$ 0.2†
Cholinergic urticaria	5	0.2 $\pm$ 0.1	0.12 $\pm$ 0.14	0.16 $\pm$ 0.14	0.17 $\pm$ 0.11	0.55 $\pm$ 0.14†	0.41 $\pm$ 0.22	0.5 $\pm$ 0.17	0.5 $\pm$ 0.13†
Pressure urticaria	3	0.33 $\pm$ 0.14	0.37 $\pm$ 0.17	0.25 $\pm$ 0.14	0.33 $\pm$ 0.14	0.58 $\pm$ 0.5	0.58 $\pm$ 0.52	0.58 $\pm$ 0.5	0.58 $\pm$ 0.5
Atopic patients	4	0.25 $\pm$ 0.12	0.31 $\pm$ 0.12	0.25 $\pm$ 0	0.27 $\pm$ 0.10	0.75 $\pm$ 0.11†	0.50 $\pm$ 0.22†	0.67 $\pm$ 0.21†	0.69 $\pm$ 0.04†
Non-atopic patients	20	0.22 $\pm$ 0.13	0.36 $\pm$ 0.11	0.22 $\pm$ 0.12	0.27 $\pm$ 0.11	0.66 $\pm$ 0.12†	0.56 $\pm$ 0.10†	0.57 $\pm$ 0.16†	0.608 $\pm$ 0.13†

* Mean score $\pm$ s.d.; † $P = 0.05$; ‡ $P = 0.01$.

Results

Terbutaline treatment was much more active than antihistamines (Table 2). Its action was more pronounced on the eruption than on itching or on blocking attacks. Idiopathic cases responded better than other cases. Terbutaline was equally active in atopic or non atopic patients. Although an improvement was observed in ten cases after the first day of treatment, a beneficial effect was generally observed after 2 weeks' therapy. The maximum therapeutic effect was noted 1 month after the beginning of the treatment. At that time, four patients entered into complete and lasting remission. In twelve out of fifteen cases terbutaline was able to inhibit the progress of the urticarial eruption when taken at the beginning of the symptoms. The only side effect, palpitations, was observed in one case, on the first day of treatment.

Discussion

The aim of the present communication is to report a clear-cut effect of terbutaline on the main symptoms of chronic urticaria. As a result of this treatment, the frequency, number and size of the weal and flare eruptions were considerably reduced. Itching was similarly decreased but in some cases it persisted despite the absence of eruptions. Furthermore, when taken at the beginning of the symptoms, terbutaline was able to block a forthcoming crisis. Most patients noted an improvement after 1 week of therapy but the maximum therapeutic effect was obtained after 1 month. The treatment was equally effective in atopic and non-atopic patients, however a greater efficacy was noted in idiopathic rather than in cholinergic or pressure-induced urticaria. At the dose of 1.25 mg three times a day, side effects were reported in one case only, these being palpitations.

Our data thus suggest that terbutaline, a β_2 -adrenergic stimulant, may be considered as a useful and safe anti-allergic agent. Beta₂-adrenergic stimulants are now widely used in the management of asthma owing to their potent bronchodilator activity (β_2 receptor stimulation) without major cardiac acceleration (β_1 receptor stimulation) (Bergmann, Persson & Wetterlin, 1969; Elgefors & Wilhemsen, 1971). The anti-allergic activity of these substances is shown by their protective effect on mast cell degranulation (Perper, Sanda & Lichtenstein, 1972). The therapeutic effect of terbutaline in the management of chronic urticaria might be secondary to its action either on the dermal mast cells or on the cutaneous vascular system (Shereff *et al.*, 1975). It is worth noting that the use of sympathicomimetics in urticaria is not new. Indeed, it is well documented that epinephrine is efficient in the treatment of acute urticaria (Kram *et al.*, 1975); its use in a long term therapy is evidently contra-indicated because of its side effects and the short duration of its action.

References

- BERGMANN, J., PERSSON, H. & WETTERLIN, K. (1969) Two new groups of selective stimulants of adrenergic beta-receptors. *Experientia*, **25**, 899.
- BOURNE, H., LICHENSTEIN, L. & MELMON, K. (1972) Pharmacologic control of allergic histamine release *in vitro*: evidence for an inhibitory role of 3',5'-adenosine monophosphate in human leukocytes. *Journal of Immunology*, **108**, 695.
- ELGEFORS, B. & WILHEMSEN, L. (1971) Effects of a new stimulator of beta-receptors, terbutaline on ventilation capacity, lung resistance, heart rate and blood pressure. *European Journal of Clinical Pharmacology*, **3**, 209.
- KRAM, J., BOURNE, H., MAIBACH, H. & MELMON, K. (1975) Cutaneous immediate hypersensitivity in man. Effect of systematically administered adrenergic drugs. *Journal of Allergy and Clinical Immunology*, **56**, 387.

- PERPER, R., SANDA, M. & LICHTENSTEIN, L. (1972) The relationship of *in vitro* and *in vivo* allergic histamine release: inhibition in primates by cAMP active agents. *Internal Archives of Allergy*, **43**, 837.
- SHEREFF, R., HARWELL, W., LIEBERMAN, P., ROSENBERG, E. & ROBINSON, H. (1975) Effect of beta-adrenergic stimulation and blockade on immediate hypersensitivity skin test reaction. *Journal of Allergy and Clinical Immunology*, **52**, 328.
- WARIN, R. & CHAMPION, R. (1974) Basic mechanisms. In: *Urticaria*, p. 19. Saunders Company Ltd., Philadelphia.

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