

A comparative trial of hyposensitization in 1973 in the treatment of hay fever using Pollinex and Alavac-P

A. C. M. L. MILLER

E.N.T. Department, Belfast City Hospital, Belfast, Northern Ireland

Summary

A direct comparison was made in 112 hay fever patients of hyposensitization treatment with glutaraldehyde-pollen-tyrosine adsorbate (Pollinex) and with alum-precipitated pyridine extract (Alavac-P) which is an accepted form of treatment, its efficacy having been shown by a comparative trial against a placebo preparation.

No significant difference could be detected between the results of the two forms of treatment. Seventy-seven per cent of patients responded with improvement following treatment with the tyrosine adsorbed vaccine, and 81% of those receiving the alum-precipitated vaccine. Side effects from treatment, both local and general, were generally of an infrequent or mild nature for both vaccines.

Introduction

Our previously reported studies on hyposensitization treatment of hay fever have been aimed primarily at improving the safety and convenience to the patient of injection schedules, and we have developed two approaches. First, possible toxicological hazards of adjuvant materials have been reduced by use of a metabolizable adsorbant, tyrosine (Miller & Tees, 1974). Second, the allergenicity of the pollen extract has been reduced by treatment with glutaraldehyde, thereby enabling the number of injections to be decreased (Johansson *et al.*, 1974).

As a consequence of this work, a glutaraldehyde treated mixed grass pollen tyrosine adsorbate, Pollinex® (Bencard) has been made available in a three-dose form. The object of the currently reported trial was to assess the safety and effectiveness of this material by comparing it with an established formulation. Alavac-P was used as the comparison since its use in the treatment of hay fever has been established in a placebo controlled trial (Kerr & Murchison, 1973) where it was concluded that there was a significant difference in the incidence of symptoms in favour of this pollen adsorbate being an effective treatment.

Materials and methods

Patients

One hundred and twelve patients were selected on the basis of a history of seasonal

Correspondence: Dr A. C. M. L. Miller, E.N.T. Department, Belfast City Hospital, Belfast, Northern Ireland.

rhinitis of at least 2 years' duration, accompanied in some by seasonal asthma, and a positive skin prick test for grass pollens (Bencard B₂). Some had received hypsensitization treatment in previous years: those receiving corticosteroid treatment were excluded. The lower age limit was 9 years.

Patients were divided into two treatment groups approximately balanced in proportion with regard to sex, age, and previous hypsensitization.

Treatment

Two treatments were compared:

- (1) Glutaraldehyde modified grass pollen tyrosine adsorbate (Pollinex®, Bencard); administered to patients in group 1; three graded doses at weekly intervals to all patients.
- (2) Alum-precipitated pyridine extract (Alavac-P®, Bencard); administered to patients in group 2 in either of two schedules following manufacturers' recommendations for mildly sensitive or very sensitive patients.

Both materials are prepared from extracts of the twelve most commonly occurring grasses in the British Isles (bent, soft brome, cocksfoot, crested dogstail, false oat, meadow fescue, meadow foxtail, rye grass, meadow grass, Timothy, sweet vernal and Yorkshire fog). Doses given are summarized in Table 1.

Assessment

Side reactions following treatment were recorded. Patients were asked to complete a daily record card during the pollen season from May to July, the severity of symptoms being recorded according to a four point scale, together with the number of anti-

Table 1. Treatment schedules

Pollinex (group 1)		
Injection	Dose (Noon units)	
1	300	
2	800	
3	2000	
Alavac (group 2)		
	Mildly sensitive	Very sensitive
1	125	25
2	250	50
3	750	100
4	1750	200
5	3750	375
6	7500	750
7	12500	1500
8	25000	2500
9		5000

histamine tablets taken. Examination of the records at the end of the season was accompanied by careful questioning of the patient. The response to treatment was then assessed on a five-point scale as follows:

VG+, symptom free.

VG, very few symptoms, very much better than seasons without injection treatment.

MI, moderately improved—better than seasons without injection treatment.

SI, slightly improved—a little better than seasons without injection treatment.

NG, the same or worse than seasons without injection treatment.

Results were analysed statistically between different treatment groups using either a χ^2 or Fisher's Exact Test (2-tailed). A probability level of 5% or less has been taken to give a significant result.

Results

Of the 112 patients who entered the trial, sixty-six were treated with Pollinex (group 1), of whom fifty (76%) had previously received hyposensitization to grass pollens and sixteen were being hyposensitized for the first time. Similarly, of the forty-six patients who received Alavac-P (group 2), thirty-seven (80%) had been previously hyposensitized and nine were new to this form of treatment. All patients were sensitive to the grass pollens as shown by prick test and generally gave a positive skin test to at least one other allergen. Of those patients in group 1 28%, and of those in group 2 30%, suffered from pollen asthma as well as pollen rhinitis. The age, sex and hay fever history of all the patients is summarized in Table 2. Statistical testing showed the groups to be similarly balanced in every respect.

Six of sixty-six (9%) of those patients treated in group 1 had a mild generalized reaction of transient rhinitis or mild asthma but no patient had a severe generalized reaction. Mild generalized reactions occurred in seven patients in group 2. However, a further patient in group 2 had a generalized urticaria and swelling of arm, hand and face coming on 1 hr after the second injection and taking 2 days to subside completely. The course was thereafter terminated. Thus a total of eight of forty-six (17%) generalized reactions occurred with group 2, almost twice the incidence in group 1, although the difference does not approach statistical significance ($\chi^2 < 1$, $P > 0.3$).

Table 2. Basic patient data

		Pollinex (group 1)	Alavac (group 2)
Number of patients		66	46
Sex:	M	42 (64%)	27 (59%)
	F	24 (36%)	19 (41%)
Age (years):	Range	9-57	10-50
	Median	22	26
Hay fever history (years):	Range	2-24	2-45
	Median	9	9.5

Table 3. General reactions

	Pollinex (group 1)		Alavac (group 2)	
Previously hyposensitized	4/50	8%	3/37	8%
Not previously hyposensitized	2/16	12.5%	5/9	56%
Total	6/66	9%	8/46	17%

Table 4. Local reactions 1973

	Pollinex (group 1)		Alavac (group 2)	
Previously hyposensitized	14/50	28%	10/37	27%
Not previously hyposensitized	2/16	12.5%	4/9	44%
Total	16/66	24%	14/46	30%

Table 5. Results of treatment

	Pollinex (group 1)		Alavac (group 2)	
Previously hyposensitized	VG + 1 VG 17 MI 22 SI 2 MG 8	} 80%	VG + 2 VG 16 MI 10 SI 4 MG 3	} 80%
	Fifty patients		Thirty-five patients	
Not previously hyposensitized	VG + 0 VG 4 MI 7 SI 2 MG 3	} 69%	VG + 0 VG 3 MI 4 SI 0 MG 1	} 87.5%
	Sixteen patients		Eight patients	

The incidence of generalized reactions in those patients who had previously been hyposensitized and those not previously hyposensitized is shown in Table 3.

In those who had been previously hyposensitized it can be seen that the incidence (8%) is the same for the two groups. However, in those not previously hyposensitized a higher incidence of generalized reactions occurred in group 2—12.5% group 1, 56% group 2—but the difference does not quite reach statistical significance ($P = 0.058$, Fisher's Exact Test).

The data on local reactions of swelling, erythema and itch, none of which were serious, is shown in Table 4 and it can be seen that the overall incidence was sixteen of sixty-six (24%) in group 1 and fourteen of forty-six (30%) in group 2. The results have been subdivided within each group into those patients previously hyposensitized and those new to this form of therapy. It can be seen that a similar incidence—28% group 1, 27% group 2—is shown for those previously hyposensitized. However, for those not previously hyposensitized a higher incidence is shown for group 2—12% group 1, 44% group 2—but the difference is not significant.

The response to treatment is shown in Table 5. This assessment was made on all but three group 2 patients, one of whom had treatment terminated due to a general reaction, one was given only four injections and the third was not assessed. A further two patients in group 2 did not complete therapy—one completed only six of nine injections before mislaying the vaccine, and the second missed the final two injections of an eight dose schedule due to an intercurrent bout of influenza. However, both the patients have been assessed as having VG and VG+ responses for the season, respectively.

From Table 5, the categories VG+, VG and MI may be combined to indicate an overall good response. In group 1 an overall good response was shown by forty of fifty (80%) of previously hyposensitized patients and by eleven of sixteen (69%) of those not previously hyposensitized giving a fifty-one of sixty-six (77%) success rate for the whole group. The numbers of group 2 patients showing overall good response are twenty-eight of thirty-five (80%) in those previously hyposensitized, seven of eight (88%) in those not previously hyposensitized and thirty-five of forty-three (81%) for the whole group. None of the figures for any comparison between groups of different treatments reach statistical significance.

Discussion

Our earlier work indicated that treatment of hay fever patients with glutaraldehyde-grass pollen-tyrosine adsorbate provided a degree of clinical benefit of the same order as that provided by other formulations (Johansson *et al.*, 1974). The clinical benefit was accompanied by an induced pollen-specific IgG-antibody response of similar magnitude to those induced by unmodified pollen-tyrosine adsorbate or by Alavac-P. The current study extends these observations, being designed to check the effectiveness of the marketed product, Pollinex, which was developed from this earlier work. The established product, Alavac-P, was again used for comparison purposes.

Kerr & Murchison (1963), in a placebo-controlled trial of pyridine extracted alum-precipitated vaccine using a similar dosage schedule to that used in the present study, demonstrated that this formulation was effective in the treatment of hay fever. Subjective improvement was shown in 80% of patients, improvement being confirmed by patients' daily symptom charts. Evans (1967) reports that of 200 patients on alum-precipitated pyridine extracts, 82.5% responded favourably as measured by daily record card including drug usage. Knight & Tees (1968) recorded favourable clinical results in 62% of patients receiving Alavac-P. Blair, Ezeoke & Hobbs (1975) reported that 96% of patients benefited from treatments with Alavac-P. In these studies there were minimal side effects reported, either local or systemic.

Alavac-P has thus been established as a satisfactory form of treatment for hay fever and forms an acceptable standard of comparison for other treatments from the points of view of effectiveness and safety. The currently reported trial shows clinical

improvement in 81% of the Alavac treated group and in 77% of the Pollinex treated group. Local reactions were slightly more frequent in the Alavac group but, in general, were mild in nature. Similarly, the incidence of general reaction in the Alavac group was higher than in the Pollinex group, but again reactions were generally mild in nature. The only patient to discontinue treatment due to general reactions was receiving Alavac-p.

This trial shows that the effectiveness rate of Pollinex is similar to that of Alavac-p, but with the added convenience of only three doses, and a tendency to fewer side effects. Comparable rates of clinical effectiveness of Pollinex have been reported by Girard & Huguenin-Dumittan (1974) and Verstraeten *et al.* (1975).

Acknowledgments

I wish to thank Dr E. C. Tees of the Bencard Allergy Unit for advice with setting up the trial and for the supply of materials, and Miss J. Urwin for help with the statistical analysis of results.

References

- BLAIR, H., EZEKOE, A. & HOBBS, J.R. (1975) IgE, IgG and patient-self tests during slow hyposensitization to grass pollen. *Clinical Allergy*, **5**, 263.
- EVANS, R.G. (1967) Desensitization therapy in allergic diseases. *Excerpta Medica Symposium Whittington Hospital*, 19.
- GIRARD, J.-P. & HUGUENIN-DUMITTAN, S. (1974) Traitement de la rhinite saisonnière au moyen de complexes pollen-L-tyrosine. *Praxis*, **63**, 1554.
- JOHANSSON, S.G.O., MILLER, A.C.M.L., MULLAN, N., OVERELL, B.G., TEES, E.C. & WHEELER, A. (1974) Glutaraldehyde-pollen-tyrosine: clinical and immunological studies. *Clinical Allergy*, **4**, 225.
- KERR, J.W. & MURCHISON, L.E. (1963) A controlled trial of pollen adsorbate in the treatment of hay fever. *Scottish Medical Journal*, **8**, 485.
- KNIGHT, F.J.D. & TEES, E.C. (1968) Comparative vaccine treatments of hay fever. *Practitioner*, **201**, 774.
- MILLER, A.C.M.L. & TEES, E.C. (1974) A metabolizable adjuvant: clinical trial of grass pollen-tyrosine adsorbate. *Clinical Allergy*, **4**, 49.
- VERSTRAETEN, J.M., BAL, J., VAERENBERG, C., ROBIENCE, Y., SPINOIT, C., MAMPUYS, R. & DESCHÉPPER, P. (1975) Expérience clinique en Belgique pendant la saison pollinique 1973 avec un extrait de pollen adsorbé sur tyrosine. *Revue Française d'Allergologie*, **15**, 173.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.