

Comparison of a glutaraldehyde-modified pollen-tyrosine adsorbate with an alum-precipitated pollen vaccine in the treatment of hay fever

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Summary

Nineteen patients with hay fever symptoms received nine weekly injections of a pyridine-extracted alum-precipitated grass pollen vaccine (Alavac P). The results were compared with a group of twenty patients who received a three injection series of a glutaraldehyde-modified pollen-tyrosine vaccine (Pollinex). In both groups 65% had a subjective improvement in their symptoms and no significant difference in symptom scores was obtained throughout the pollen season. In the Pollinex group a lower incidence of systemic side effects was recorded.

Introduction

Many patients with troublesome hay fever find that oral antihistamines do not give adequate relief of symptoms without producing the side effects of sedation and restriction of physical activities such as driving. Topical preparations are often of limited value in these patients and there is consequently a continuing interest in pre-seasonal hyposensitization therapy, first introduced by Noon in 1911. The original technique involved multiple injections of an aqueous extract of grass pollen which, although it gave satisfactory results, had a number of drawbacks including the large number of injections, the need for repetition at each pollen season and a high incidence of both local and general reactions during the administration of the course. In recent years various preparations have been marketed which are more acceptable to patients.

The introduction of the pyridine-extracted alum-precipitated pollen vaccine reduced the number of injections and produced fewer side effects than previous preparations (Fuchs & Strauss, 1959). Controlled trials have clearly shown that this vaccine is effective in hay fever when compared with placebo (Kerr & Murchison, 1963) and gives a result at least equivalent to the prolonged aqueous course (Frankland & Noelp, 1966).

In 1974 grass pollen-tyrosine adsorbate was introduced and was shown to be effective when compared with pyridine-extracted alum precipitate (Miller & Tees,

1974). A further modification of pollen-tyrosine adsorbate with glutaraldehyde has been shown to be immunologically active, producing an increase in IgG, and the clinical efficacy of this preparation has not been impaired using a dosage schedule reduced to three injections (Johansson *et al.*, 1974).

This study was undertaken to compare the clinical effectiveness of glutaraldehyde modified grass pollen-tyrosine (Pollinex) with pyridine-extracted alum precipitate (Alavac P) in a controlled trial.

Materials and methods

The patients were in the age range 14–50 years and had been referred to the clinic with severe hay fever symptoms which had proved resistant to oral or topical therapy. All had a definite seasonal history of rhinitis of at least 2 years' duration, with positive skin reactions to prick testing with grass pollen extract and a number had, in addition, symptoms of pollen asthma. Thirty-nine patients consented to participate in the trial and were randomly allocated into two groups:

Group I

Nineteen patients (twelve male and seven female). They received nine weekly injections of Alavac P starting with a dose of 25 Noon u and approximately doubling the dose at each injection until 5000 u were administered in the final injection.

Group II

Twenty patients (eleven male and nine female). They received three weekly injections of Pollinex starting with 300 Noon u and progressing to 800 in the second and 2000 u in the final dose.

All completed the injection course but two were lost to follow-up after moving out of the area and one other failed to complete the scoring card.

The participants were not informed of the differences in the number of injections in the two groups and inter-patient contact at the treatment area was minimized. Side effects to the injections were noted by the nursing staff and, when required, a physician not involved in the trial was consulted. The patients were provided with monthly symptom cards to keep a record of the presence and severity of symptoms from 1 May to 31 August 1975. The symptoms charted were: eyes, watering and itching; nose, streaming, sneezing and stuffiness; throat, itching; chest, wheezing. A space was left for one additional symptom which was included at the patient's discretion.

A scoring system was devised with a scale ranging from 0 to 3 to indicate the severity of the symptom recorded. Since eight different symptoms were listed the maximum possible daily score for an individual was twenty-four. Also recorded on the chart was the amount of additional therapy required to control symptoms and information such as the number of days spent outside the local area. Regular reminder letters were sent out to stimulate completion of the score cards. In September, the patients were reassessed and gave a subjective impression of the preceding season. The symptom score cards were then collected and analysed.

The Glasgow pollen count was measured from May to August using a Hirst Volumetric Spore Trap and local weather conditions were noted. This information was not readily accessible to the public, although a retrospective count was available on the telephone weather service. All subjects resided within a 10 mile radius of the Western Infirmary, Glasgow, where the pollen count was recorded.

Results

The pollen counts were recorded and found to be slightly higher than in the previous two pollen seasons (Allen, 1975), confirming the adequacy of the pollen challenge. Pollen spores were first detected sporadically in mid-May in small concentrations, but consistent counts were not obtained until the first week in June which was therefore regarded as the start of the pollen season.

Effect on symptoms

The combined weekly symptom score for both groups reflected the prevailing pollen counts throughout the season (June, July, August) and on comparing the groups no significant difference was obtained in the mean weekly symptom scores during this period (Fig. 1). In May, however, the Alavac P group had significantly lower symptom scores ($P < 0.05$, Mann Whitney U test).

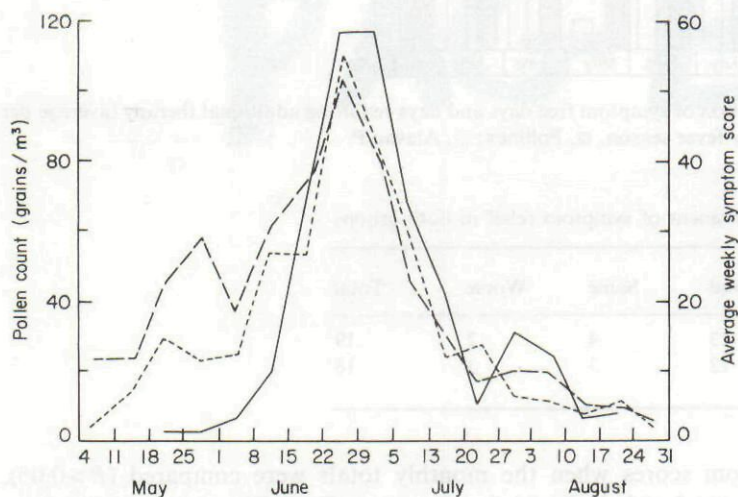


Fig. 1. Symptom scores and pollen count variation throughout the 1975 season in both groups of hay fever patients. —, Pollen count; ----, Alavac P; — · —, Pollinex.

The number of days recorded free from symptoms was considered, and again no significant difference was obtained during the months of pollen exposure (Fig. 2a). Figure 2b compares the number of days in both groups on which additional therapy was required. Although the Alavac group appeared slightly more favourable, this difference was not statistically significant ($P > 0.05$, Mann Whitney U test). In the follow-up assessment 53% of the Pollinex group and 59% of the Alavac group claimed that less additional oral or topical therapy was required during the season. The subjective assessment of the hay fever symptoms is shown in Table 1. Sixty-five per cent of patients in both groups claimed to have improved in spite of the higher pollen counts during the season.

Effect on pollen asthma

Nine patients in group I and ten in group II had a clearly associated history of asthma restricted to the pollen season. Once again the response was similar with no significant

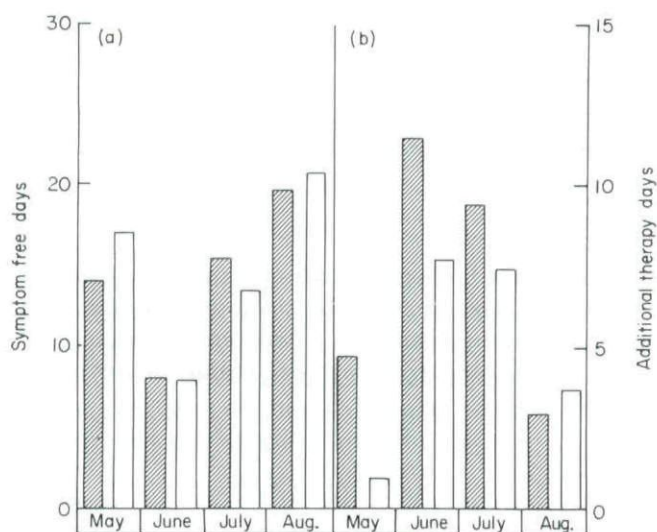


Fig. 2. Monthly distribution of symptom free days and days requiring additional therapy (average per patient) during 1975 hay fever season. ▨, Pollinex; □, Alavac P.

Table 1. Subjective assessment of symptom relief in both groups

	Improved	Same	Worse	Total
Pollinex	13	4	2	19
Alavac P	12	3	3	18

difference in symptom scores when the monthly totals were compared ($P > 0.05$). Four patients in group I (Alavac) and five in group II (Pollinex) felt a subjective improvement in their asthmatic symptoms compared with the previous season.

Side effects

Fourteen patients in each group had local reactions at the injection site which were not troublesome.

In the Pollinex group, four patients recorded systemic reactions which were considered mild and included: hay fever symptoms, palpitation, lightheadedness and wheezing, headache and wheezing.

Ten patients in the Alavac group had systemic symptoms during the injection course. Three were of a severe nature requiring emergency medical treatment: generalized itch and asthma, generalized itchy erythema, widespread urticarial eruptions and asthma.

One patient had a moderately severe asthmatic reaction and the remaining six patients had mild systemic upset: one with hay fever symptoms, three with lightheadedness, one with general malaise, one with mild generalized erythema.

There was therefore a higher incidence of side effects recorded in the Alavac group although this difference was not statistically significant ($\chi^2 = 3.20$, $0.05 < P < 0.1$).

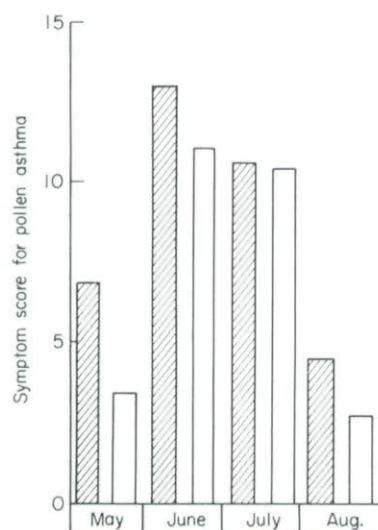


Fig. 3. Mean monthly symptom scores for pollen asthma during 1975 hay fever season (average per patient). ▨, Pollinex; □, Alavac P.

Discussion

Pre-seasonal hyposensitization is generally accepted as an effective treatment of hay fever when compared with placebo. In this trial Pollinex was compared with a well established hyposensitization programme using a pyridine-extracted alum-precipitated pollen vaccine.

Based on the pollen count, the hay fever season started during the first week in June and lasted until the third week in August. During this period the symptom scores showed that the severity of symptoms was directly related to the pollen count. In May, however, twelve (63%) in the Pollinex group, and twelve (70%) in the Alavac P group had typical hay fever symptoms with the symptom scores being significantly higher in the Pollinex group during this month. This observation is of considerable interest as no grass pollen was counted until 17 May and the count remained low until early June with a range of 1–5 cm. The main pollen in the atmosphere during May was birch and sensitization to this pollen may have been a factor in the causation of these early symptoms in both groups. There is a possibility that the grass pollen count in the domestic environment of those patients affected was higher than that counted but patients in both groups were scattered randomly throughout the locality and the number of days spent outside the area in both groups was identical.

Pollinex appears to offer a distinct advantage in its freedom from systemic side effects which only occurred in four patients and were mild compared with the ten patients in the Alavac group, four of whom had moderate or severe reactions. This concurs with the findings of Johansson *et al.* (1974) who also found a low level of toxicity with glutaraldehyde-modified pollen-tyrosine.

The lack of response in over 30% of patients of both groups suggests that further consideration be given to the optimum dosage schedule of allergen injected and the low toxicity in the tyrosine group gives scope for the further study of this problem.

Pollinex appears to be a worthwhile development in hyposensitization therapy,

reducing the number of injections to three, reducing the risk of patient default and reducing the work load on medical and nursing staff. It appears to be remarkably free from serious side effects and obtains a clinical result equal to that of the more prolonged courses of hyposensitization therapy.

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