

Side effects of desensitization for allergy—a general practice survey

D. A. RANDS, MB, MRCP

General Practitioner, Southampton

R. C. GODFREY, MD, FRCP

Consultant Physician, Western Hospital, Southampton

SUMMARY. Following the unexpected death from acute anaphylaxis of a patient receiving house dust mite desensitization, general practitioners throughout Hampshire were asked about their experience of desensitization and its side effects, by means of a questionnaire. From a total of 695 doctors, 452 (65 per cent) returned valid questionnaires. Sixty-three doctors (14 per cent) did not use desensitization at all, while 20 (4 per cent) used more than 20 courses per year, mainly for patients with hay fever. The majority of doctors were modest prescribers of five or less courses per year of any one preparation. Apart from the fatal case which stimulated this enquiry, one other death was reported.

Introduction

DESENSITIZATION for allergic conditions has been used for 70 years. The basic principle has always been to inject increasing quantities of allergen over a period of weeks or months in order to produce a state of unreactivity when further natural exposure occurs. Double-blind trials, which have been introduced only in the latter part of this long period of clinical use, have shown disappointing or equivocal results except in the case of grass pollen desensitization, where clinical benefit has been demonstrated in some 70 per cent of treated patients, compared with about 40 per cent who improve after placebo injections. This was shown by Frankland and Augustin¹ in the first ever double-blind trial. Neither immunological tolerance nor the production of blocking antibody have been shown to account satisfactorily for the occasional beneficial effects of desensitization.² Over the years, the trend has been towards slow release formulations of allergen to allow less numerous and less frequent injections, but the allergens themselves have remained relatively crude. Since the injection of foreign antigen always carries risk of adverse reaction, it is perhaps surprising that relatively few side effects have been reported from desensiti-

zation.³ Nevertheless, an unexpected and clinically unpredictable fatal anaphylaxis occurred after an injection of house dust mite⁴ and this fatality has led to the present enquiry.

Methods

All general practitioners on the Hampshire Family Practitioner Committee register were individually sent a questionnaire designed to discover the extent to which they employed desensitization and their experience of side effects. The questionnaire listed the six currently available desensitizing preparations, and asked doctors to indicate the approximate number of courses of each that they used per year. They were also asked to indicate side effects under headings of 'never observed', 'infrequently observed' (associated with less than 10 per cent of injections) or 'frequently observed' (associated with over 10 per cent of injections). Side effects listed for comments were: local immediate reactions, local delayed reactions, rhinitis, bronchospasm, anaphylaxis, and fatal reactions. The side effects were listed for each individual desensitizing preparation, and space was left for doctors to record side effects where the name of the responsible preparation could not be recalled. A space was also provided for the doctor to make any other comments about desensitization that he wished.

Results

Of 695 doctors, 455 returned completed questionnaires either singly or, in a few cases, jointly with other partners in a practice. Three questionnaires were invalid.

Sixty-three doctors (14 per cent) stated that they had either never used or had stopped using desensitization. Thirty-seven gave no reason for this decision. The reasons stated by the remaining 26 doctors are presented in Table 1.

The majority of doctors in this survey were modest users of desensitization; between 71 per cent and 91 per cent recorded prescriptions of less than five courses per year of various preparations, while only 1–4 per cent used more than 20 courses of any one preparation each year (with the exception of Allpyral—9 per cent). The relative popularities of various commercially available preparations are shown in Table 2.

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Tables 3 and 4 record side effects noted by general practitioners in this survey. Table 4 (serious side effects) includes data about side effects from preparations which could not be recalled by name, and it is in this group that the other death was recorded. It should be noted that bronchospasm was recorded as an infrequent side effect of specific desensitizing vaccines (SDV) by 38 doctors, a higher association than with any other preparation.

One hundred and forty-six doctors commented on desensitization. Of these, 55 comments were related to personal experience of side effects and 44 doctors commented on apparent ineffectiveness of the treatment. However, 12 doctors pointed out the benefits. 'Therapy tips' included recommendations on the period

of observation required after an injection, the prophylactic use of antihistamines, the need for adrenaline readily to hand in the surgery, and warnings about rejections in asthmatic patients.

Discussion

The response in this study of 65 per cent was not high enough to allow valid conclusions about the total prevalence of side effects from desensitization and, as with all retrospective studies, there must be some doubt about accuracy of recall. However, the findings underline the widely differing patterns of usage of desensitization among general practitioners. At one extreme, 14 per cent have decided not to use the treatment at all, while at the other about 4 per cent continue to use the treatment extensively. Considering the very large number of patients with hay fever who present to general practitioners each year, it is perhaps surprising that most practitioners make modest use of the treatment. It would be of interest to know how general practitioners select a small minority of patients for desensitization, and it may be that certain patients initiate the idea of desensitization to their doctor.

Table 1. Reasons given for not using desensitization (N = 26 doctors).

Personal observation of unwanted effects	12
Knowledge of dangerous adverse reactions	3
Poor clinical efficacy	13
Waste of time and/or too expensive	4

Table 2. Number of doctors using various commercial desensitizing preparations. (Percentages in parentheses.)

Preparation	Less than five courses per year	Five to 20 courses per year	Over 20 courses per year	Total
Alavac (alum precipitated)	158 (89)	16 (10)	2 (1)	176
Allpyral (alum precipitated)	133 (73)	36 (20)	12 (7)	181
Migen (tyrosine absorbed, house dust mite only)	131 (91)	11 (7)	2 (2)	144
Norisen (aluminium absorbed)	28 (84)	4 (13)	1 (3)	33
Pollinex (tyrosine absorbed, grass pollens only)	180 (71)	63 (25)	8 (4)	251
Specific desensitizing vaccines (aqueous)	204 (86)	33 (14)	0 (0)	237

Table 3. Doctors reporting minor reactions to desensitizing injections. (Percentages in parentheses.)

Preparation (and number of doctors prescribing)	Local immediate reaction		Local delayed reaction		Rhinitis	
	Infrequent*	Frequent**	Infrequent	Frequent	Infrequent	Frequent
Alavac (176)	64 (36)	4 (2)	21 (11)	0 (0)	13 (7)	0 (0)
Allpyral (181)	73 (40)	11 (6)	41 (22)	3 (1)	24 (13)	1 (1)
Migen (144)	35 (24)	5 (3)	19 (13)	2 (1)	5 (3)	2 (1)
Norisen (33)	4 (12)	1 (3)	3 (10)	1 (3)	3 (1)	0 (0)
Pollinex (251)	76 (30)	7 (3)	46 (18)	4 (1)	12 (4)	1 (1)
SDV (237)	85 (35)	18 (7)	55 (23)	4 (2)	20 (8)	1 (1)

*Infrequent = occurring after less than 10 per cent of injections.

**Frequent = occurring after more than 10 per cent of injections.

Table 4. Number of doctors reporting infrequent but serious unwanted effects from desensitizing injections.

Preparation (and number of doctors prescribing)	Bronchospasm	Anaphylaxis	Death
Alavac (176)	9 (5)	3 (1)	0
Allpyral (181)	18 (10)	3 (1)	0
Migen (144)	9 (6)	2 (1)	1 case
Norisen (33)	0 (0)	2 (6)	0
Pollinex (251)	8 (3)	1 (1)	0
SDV (237)	38 (16)	11 (5)	0
Unable to recall preparation	28	12	1 case

The study has also pointed to the large number of side effects noted by practitioners. Most of these are trivial, but the study indicates that a significant number of doctors have observed the serious unwanted effects of bronchospasm and anaphylaxis. SDV seemed particularly liable to cause bronchospasm, perhaps because these 'tailor-made' vaccines are more likely to be used in more severely affected patients. In addition to the death of a 19 year-old girl, which precipitated this enquiry, a further fatality was reported, although the practitioner concerned could not recall the desensitization preparation in use at the time. All these facts underline the need for extremely careful observation of patients after allergen injections, and at the minimum it is recommended that patients should be under close medical observation for 20 minutes. Adrenaline 1:1,000 should be to hand in the same room as the patient, and should be used intramuscularly at a dose of 0.5-1.01 ml if major anaphylaxis occurs, rather than subcutaneously as recommended by the manufacturer. It can be argued that desensitization should be a hospital procedure, and the large number of side effects reported in this study suggests that this might be a wise precaution.

In broader terms, the study leads us to question whether desensitization in its present form should be continued at all. The majority of clinical trials (reviewed by Price)² have shown doubtful clinical efficacy; the treatment is expensive, time-consuming, and not without risk. Following Rands' report⁴ of a fatal anaphylaxis, there was an exchange of views in the correspondence columns of the *British Medical Journal*; Pollard⁵ reported another fatal case, while Ewan⁶ argued that modern pharmaceutical preparations are both safer and more efficacious than desensitization. We strongly support this view.

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Address for correspondence

Dr D. A. Rands, 76 Whitworth Crescent, Southampton SO9 1NW.

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