

Treatment of patients allergic to house dust mites

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I. INTRODUCTION

In the treatment of patients allergic to house dust mites two different principles can be applied; symptomatic or specific treatment. The symptomatic treatment includes medicament treatment and the elimination of non-specific irritants, while specific treatment includes elimination of allergens and immunotherapy. These are supplementary approaches, as nearly all patients need some kind of symptomatic treatment and elimination of allergens should always be carried out as far as possible. In the following, symptomatic, medicament treatment and immunotherapy will be reviewed.

II. SYMPTOMATIC, MEDICAMENTAL TREATMENT

II. a. Bronchial asthma

The purpose of therapy is to keep patients free of symptoms and provide normal lung functioning. It is important neither to undertreat nor overtreat and this means variable and individual pharmacotherapy. A recommendable step-wise approach to therapy will be summarized in the following (3, 11).

1. INTERMITTENT ASTHMA

Inhaled β -2-agonists p.n. Inhaled β -2-agonists taken e.g. 4 times daily may be recommendable in elderly persons not able to administer intermittent inhalant therapy.

2. DAILY MODERATE ASTHMA SYMPTOMS

Low dosage inhaled steroids such as cromolyn sodium may be preferable for children. The

next step could be oral theophylline or β -2-agonists alone or in combination as slow-release preparation.

3. SEVERE ASTHMA

Inhaled steroids should be given in the recommended maximum dosage. Oral steroids are indicated as a short course for exacerbations of asthma, and if needed continually at the lowest possible dosage to control symptoms, because of the risk of side effects in long-term treatment.

With the growing evidence of asthma as an inflammatory disease, it seems well indicated to start treatment with inhaled steroids even in high dosages if further therapy than intermittent use of inhaled β -2-agonists is needed (3, 18).

Cromolyn sodium is an antiallergic drug. It is indicated in moderate asthma, and because of the lack of side effects is preferred in childhood asthma, but also children with severe symptoms should be treated with inhaled steroids, even with high doses, as cromolyn is ineffective in this group of patients (37).

II. b. Rhinitis

In rhinitis and conjunctivitis a treatment strategy as discussed below may be used (7, 30, 31):

Antihistamines are indicated alone if symptoms are few, and a non-sedative antihistamine is preferred; those drugs also have an effect on conjunctival symptoms. In perennial rhinitis the use of topical nasal steroids is often necessary. As in asthma some will prefer cromo-

lyn for children, but the drug is not as effective as nasal steroids (7, 30).

Conjunctival symptoms are treated with cromolyn or antihistamine-vasoconstrictor eye-drops. If needed, the use of topical steroids in the eyes should be carried out only under the control of an ophthalmologist.

III. IMMUNOTHERAPY

III.a. Introduction

Immunotherapy in general has been reviewed in position papers by working groups under the Danish Society of Allergology and the European Academy of Allergology and Clinical Immunology (17, 22). Here we will concentrate on our current knowledge of immunotherapy in house dust mite allergy.

Since about 1920 house dust has been known to elicit attacks of asthma and rhinitis, and in 1964, house dust mites were recognized as a major source of allergens (Voorhorst et al. (39)).

Since then many studies have been published concerning the effect of immunotherapy with extracts of house dust and house dust mites. Differences in selection of patients, the quality of extracts, the regimens and duration of immunotherapy as well as the diagnostic and evaluation methods have made it difficult to compare the studies. In this review only studies meeting criteria as proposed by Aas (1) have been included, using reproducible diagnostic and evaluating methods, preferably by placebo control (28).

III.b. Extracts

The quality of the extracts used for immunotherapy is of crucial importance and has a great impact on the clinical efficacy of the treatment and side effects.

Extracts should be standardized (21) as follows:

1. Biological potency determined by e.g. RAST-inhibition, histamine release or quantitative skin prick testing.

2. Determination of the single antigens, as an extract used for immunotherapy should include all relevant antigenic components, reflecting the possible combinations of serum-specific IgE in the allergic people to be treated. This can be done by e.g. crossed immunoelectrophoresis (CIE), or crossed radioimmunoelectrophoresis (CRIE). It is important that extracts of the same compound be used for specific diagnosis and immunotherapy.

III.c. Clinical efficacy

The studies on which the evaluation of the clinical efficacy of immunotherapy is based are summarized in Tables 1 and 2.

III.c.1. House dust

Previously, studies have been conducted examining the effect of immunotherapy in asthmatics with extracts of house dust or "mite-fortified" house dust without demonstrating any effect of the treatment (24, 8), whereas a study of longer duration has shown increased tolerance in bronchial challenge with house dust (2). As house dust has been shown to contain a mixture of allergens from house dust mites, animal danders and moulds and with the documentation of better results of immunotherapy with extracts of house dust mites as compared with house dust (26), the latter treatment is now considered obsolete.

III.c.2. House dust mites

A. Bronchial asthma

Thirteen international publications published from 1971 to 1989 have been reviewed. In 8 of these, the authors have found a significant effect of immunotherapy in asthmatics (5, 12, 25, 26, 36, 38, 40, 41), while in 5 publications a non-significant effect was found (16, 27, 29, 32, 34) (Table 1).

B. Rhinitis

Two recent papers have reported a positive effect on nasal symptoms (9, 14), whereas in two

Table 1
Clinical effect of immunotherapy in asthma

Authors and year of publication	Diagnostic methods*	Duration of treatment	Maximum tolerated dosage	Evaluation of effect*	Number of patients		Effect Yes/No	Level of significance
					Controls	Treated		
McAllen 1961 (24)	A + BPT	< 12 weeks	no	A + BPT	20	20	no	?
Br. Tub. Ass. 1968 (7)	Sc. + PEF	15 weeks	no	Sc. + PEF	37	33	no	NS
Aas 1971 (2)	A + SPT + BPT	2-3 years	yes	A + BPT	28	52	yes	$P < 0.01$
Maunsell 1971 (26)	A + SPT + Sc	6-9 months	no	A + Sc.	16	18	yes	$P < 0.05$
Smith 1971 (36)	A + SPT	16 weeks	no	A + Sc. + PEF	9	11	yes	$P < 0.005$
D'Souza 1973 (12)	A + Sc. + SPT + RAST + NPT	12 weeks	no	A + Sc. + SPT + RAST + NPT	46	45	yes	$P < 0.02$
Taylor 1973 (38)	A + SPT	10 weeks	no	Gowth + PEF	21	21	yes	$P < 0.025$
Gaddie 1976 (16)	A + SPT + NPT	12 months	no	Sc. + SPT + NPT	29	26	no	NS
Marques 1978 (25)	SPT	6 weeks 8 months	no no	Sc.	5 7	7 9	yes yes	?
Newton 1978 (32)	BPT + A + SPT + NPT	15 months	no	Sc. + PEF + SPT BPT	7	7	no yes	$P < 0.05$
Warner 1978 (41)	A + SPT + BPT	12 + 12 months	no	Sc. + BPT	24	27	yes	$P < 0.05$
Br. Thor. Ass. 1979 (27)	A + SPT + NPT	4-18 months	no	Sc. + SPT	17	29	no	?
Pauli 1984 (34)	A + SPT + RAST + NPT + BPT	12 months	no	Sc. + PEF	9	9	no	NS
Bousquet 1985 (5)	SPT + RAST + BPT	7 weeks	yes	SPT + BPT	10	20	yes	$P < 0.01$
Wahn 1988 (40)	SPT + RAST + BPT	24 months	yes	SPT + BPT		24	yes	$P < 0.01$
Mosbech 1989 (29)	SPT + RAST + BPT + NPT + CPT	24 months	yes	SPT + RAST + BPT + NPT + CPT + Sc.	15	31	no	NS

A = anamnesis; Sc. = symptom and/or medicine score; SPT = skin prick test; PEF = peak expiratory flow; BPT = bronchial provocation test; NPT = nasal provocation test; CPR = conjunctival provocation test.

Clinical effect of immunotherapy in rhinitis

Authors and year of publication	Diagnostic methods*	Duration of treatment	Maximum tolerated dosage	Evaluation of effect*	Number of patients		Effect Yes/No	Level of significance
					Controls	Treated		
Gabriel 1977 (15)	NPT + SPT + RAST	12 months	no	SPT + NPT + Sc.	35	37	no	NS
Blainey 1984 (4)	A + SPT + NPT	6 weeks	no	NPT	18	17	yes	$P < 0.01$
Ewan 1988 (14)	A + SPT + NPT + RAST	12 months	yes	Sc. + NPT	9	14	?	$P < 0.05$
Corrado 1989 (9)	A + SPT + NPT + Sc.	3 months	yes	SPT + NPT	20?	16?	yes	$P < 0.05$
		15 months	yes	A + NPT + Sc.	29	22	yes	$P < 0.001$

A = anamnesis; Sc. = symptom and/or medicine score; SPT = skin prick test; PEF = peak expiratory flow; BPT = bronchial provocation test; NPT = nasal provocation test; CPR = conjunctival provocation test.

other studies a positive effect has been shown, but only in some of the parameters examined (4, 15).

III.c.3. Storage mites

Concerning the effect of immunotherapy with extracts of storage mites, no controlled studies have been carried out, but in a pilot study by Cuthberth et al. (10), amelioration of symptoms was seen in 8 of 9 patients.

To summarize, a majority of studies have demonstrated a significant effect of immunotherapy in house dust mite allergy, and therefore the following conclusions can be drawn:

III.d. Selection of patients

In the majority of studies, only a small number of patients with mild or moderate asthma have been included. In the few studies also examining the effect of immunotherapy in patients with a need of systemic steroids, these patients have had significantly less benefit from the treatment than patients without need of systemic steroids (27). Accordingly, among the patients in the study by Warner et al. (41), no significant improvement was found in the children with severe asthma and an effect of immunotherapy could not be demonstrated in the children with very mild asthma. On the other hand, Bousquet et al. (6) found immunotherapy with house dust mite extracts more effective in children than in adults. It is important to make clear to oneself and to the patients that the treatment is not equally effective in all, even when a selection as indicated above has been done. No parameters have been found to predict the efficacy of immunotherapy in a single patient.

III.e. Specificity

Immunotherapy with house dust mite extracts seems to be an efficient, specific treatment. This is illustrated by the studies in which specific bronchial challenge with extracts of house dust

mites has been used for evaluation. Only one of these studies (29), have given a negative result, while other studies have demonstrated effect in either immediate (5, 40), or late bronchial reactions (41). In the study by Newton (32) a significant effect was found by bronchial challenge, but not in the patients' symptom scores.

III.f. Dosage and duration of treatment

Apart from one study (29), as is illustrated in Tables 1 and 2, a significant effect of immunotherapy has been found in all studies, where maximum tolerated doses were given, which suggests a dose-response relationship. Further, it has been possible to obtain a significant effect even on a 7-week course of rush immunotherapy (5). On the other hand, a longer-lasting effect requires a longer duration of treatment, as shown in a follow-up of the study by Warner et al. (35), where asthmatic children given immunotherapy for 12 months had relapse of their symptoms when given placebo injections during the following 12 months, whereas a significant effect was found in children who continued active immunotherapy. Further studies are needed to examine the duration of the effect of immunotherapy after discontinuation of treatment.

III.g. Side effects

The side effects seen during immunotherapy with extracts of house dust mite are not different from side effects seen with other extracts, which are either local swelling at the site of injections or systemic side effects such as urticaria, angioedema, rhinoconjunctivitis, asthma and anaphylaxis.

Serious systemic side effects have been especially ascribed to immunotherapy with house dust mite extracts (23). This could be explained by the potency of the extracts, and by the fact that immunotherapy with such extracts is widely used in the treatment of asthmatics, and that the risk of side effects seems more pronounced in asthmatics

as compared with patients suffering from rhinitis (33). Serious side effects were reported in only 2 of the studies referred to in the present paper and in both cases a very aggressive dosage regimen was used (5, 14). In a recent retrospective survey from the United States (19), covering the period from 1945 until 1984, complete information of 24 deaths in connection with immunotherapy was reported, but in none of these studies was pure mite extract given. It is estimated that 7-10 million allergen "shots" are given each year in the United States.

III.g. Indications for immunotherapy with house dust mite

In principle they are not different from immunotherapy with other extracts and the following general recommendations can be applied (17):

1. Allergen elimination should be considered, and the degree of exposure to mite allergens in the patient's environment should be assessed.
2. The specific diagnosis must be ascertained by history, skin prick test and RAST (13), and in asthmatics, bronchial challenge is recommendable, as it offers a quantitative and reproducible reflection of the specific reactivity in the shock organ.
3. Contraindications should be considered. These are immunological systemic diseases, malignancies, poor compliance, serious cardiovascular diseases and ongoing treatment with beta-blockers. Pregnancy is a relative contraindication.
4. Finally, it is individual how intensive symptomatic treatment should be carried out, or how severe the patient's symptoms should be before immunotherapy should be started.

III.i. Conclusion

If the above-mentioned indications are followed, immunotherapy is an efficient part of the treat-

ment in some patients with allergy to house dust mites.

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