

Reduction of house dust mite allergen levels in the home: use of the acaricide, pirimiphos methyl

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Summary

House dust mite sensitivity is very common in patients with bronchial asthma, yet dust mite avoidance frequently receives little attention in clinical management. It is likely that any reduction in allergen levels associated with routine cleaning is insufficient to allow clinical improvement. In the present study the acaricide pirimiphos methyl is shown to reduce the levels of *Dermatophagoides pteronyssinus*, antigen P₁ in homes. Following a single application the level of antigen P₁ in dust from carpets was reduced by up to 73% and by more than 50% in soft furnishings. Serial sampling showed a reduction for 6 weeks under conditions where carpets and chairs treated with solvent showed a progressive rise in allergen level. Furthermore the survival of mites in cultures or infested carpet segments was markedly inhibited, with antigen P₁ accumulation reduced by >90%. These results suggest major reductions in house dust mite allergen levels in the home can be achieved.

Introduction

The majority of young patients with bronchial asthma in the U.K. and many parts of the world are sensitive to the house dust mite, *Dermatophagoides pteronyssinus* [1,2]. House dust mite avoidance although often recommended is frequently not a high priority in patient management, perhaps because clinical trials using this approach have given confusing results [3–6]. However an improvement in the symptoms of asthma has been reported when dust allergic patients have been moved to Alpine sanatoria or 'allergen free' rooms [7,8], these rooms containing <2% of the mite

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allergen level present in patients houses [9]. Similar studies in the home environment require accurate quantification of house dust mite allergen levels throughout the house, with clinical benefit being assessed in terms of the total reduction achieved. It is likely that effective reduction will involve means other than routine cleaning. In this preliminary study, we report the effect of the acaricide pirimiphos methyl [10] on the survival of *D. pteronyssinus* and the accumulation of its major allergen antigen P₁ [11]. The acaricide was highly effective in killing mites in culture and preventing mite growth in carpet segments. Furthermore, a single application in homes was found to reduce antigen P₁ levels by up to 73% in carpets and 50% in soft furnishings.

Methods

Dermatophagoides pteronyssinus mites maintained in culture, were placed with a small quantity of food in 8 × 2 mm plastic Robinson chambers. The base of the well was formed with Whatman No. 1 filter paper previously treated with acaricide or solvent. Each well was sealed with a glass microscope slide and mites were observed and counted using an incident light stereo microscope (× 45 mag). Subsequently all wells were extracted with borate buffered saline with 0.1% TWEEN (BBS-TWEEN) as previously described and stored at -20°C [11].

Segments (4 cm²) cut from carpets previously treated with acaricide or solvent, were prepared with distilled water (0.5 ml) and 200 mg mite food (oxoid liver powder) and then placed in coded Petri dishes. Approximately 600 live mites were added to each carpet segment. After 24 h incubation at 75% relative humidity and 25°C, only a few mites (approximately twenty-five) were identifiable on the surface by microscopy. Separate carpet segments were examined and extracted at 7 and 14 days. Extraction involved immersion in 15 ml BBS-TWEEN with repeated squeezing over 24 h.

Ten homes were studied (six asthmatic subjects and four non-atopic subjects). Following base-line sampling, the houses were randomly allocated to two treatment groups: A, acaricide and B, solvent alone. After treatment dust samples were collected in each house from the total area of two carpets and soft furnishings using a handheld vacuum cleaner (Hoover model No. 2614C, Hoover Ltd, U.K.). Rooms sampled were comparable in each group, i.e. bedroom and living room in each house. While attempts were made to ensure that carpet types were similar, this had to be somewhat inaccurate. Samples were aliquoted and assayed for mite numbers and allergen levels as previously described [9]. To standardize conditions no routine vacuuming was performed throughout the study period.

The acaricide pirimiphos methyl (I.C.I. Plant Protection Division, Kent, U.K.) was supplied as a 98% stock solution and diluted in acetone for *in vitro* studies. Measured volumes (5 µl) were applied × 4 over 2 h to the filter paper in wells and allowed to dry over 7 h. For carpet treatment, the acaricide was supplied as a 25% solution in solvent, and following dilution in water applied at 2 g/m² using a Bissell (9000 S) carpet shampooer (Bissell Appliances Ltd, London). For curtains and soft furnishings a 5% aerosol, with a fixed discharge rate was used, again applying 2 g/m². Solvent alone was applied to both carpets and soft furnishings in a comparable manner. All extracted samples were assayed for the major *D. pteronyssinus* allergen, antigen P₁, using a double antibody inhibition radioimmunoassay [11].

Statistical analysis was performed using the Mann-Whitney *U* test. All procedures involving human subjects were passed by the Northwick Park Hospital Ethical Committee.

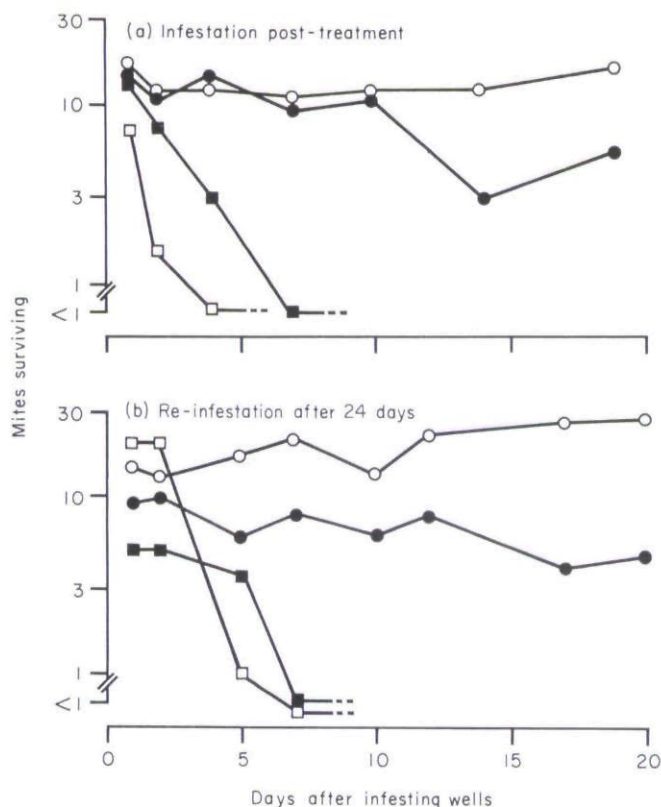


Fig. 1. Survival of mites in wells pretreated with pirimiphos methyl at: 44 g/m², □—□; 4.4 g/m², ■—■; 0.44 g/m², ●—●; or solvent only, ○—○. The number of mites surviving was assessed by counting moving mites and fully hydrated mites in duplicate wells (a). After 20 days, the wells were cleaned out and reinfested with fresh mites and food (b). At the end of the experiment, wells were extracted and assayed for antigen P₁ by radioimmunoassay (RIA) [11].

Results

Mite survival in culture

The survival of dust mites grown on filter paper treated with pirimiphos methyl at 44 and 4.4 g/m² was markedly reduced, while mites survived well on paper treated with 0.44 g/m² or diluent alone (Fig. 1a). These concentrations of acaricide also markedly reduced antigen P₁ accumulation; thus after 10 days antigen P₁/chamber was 297 ng, 267 ng, 26 ng and 14 ng in chambers treated with diluent, 0.44 g, 4.4 g and 44 g/m² of pirimiphos methyl, respectively. Furthermore, when mites and their debris were removed after 24 days and the cultures reinfested, the treated paper was still highly effective at preventing mite growth and antigen P₁ accumulation (Fig. 1b and data not shown). When similar experiments were carried out with carpet segments that had been treated with 2 g/m² of pirimiphos methyl, we found that infestation was dramatically reduced when mites were added 3 weeks post-treatment, but that the chemical had little effect on allergen accumulation if mites were added to the carpet 6 weeks after treatment (Table 1).

Table 1. Pirimiphos methyl reduces antigen P₁ accumulation in carpet segments

Carpets	Duration between treatment and mite addition (weeks)	Antigen P ₁ (ng) content post-mite addition*	
		(7 days)	(14 days)
Treated	3	690	410
Untreated	3	2190	5380
Treated	6	2090	3900
Untreated	6	2602	7100

* Values are ng antigen P₁ measured by RIA [11]. The quantity of extractable antigen P₁ added with the live mites was 400 ng approx.

Pirimiphos methyl: assessment of potential irritancy

Before using pirimiphos methyl in homes, we carried out studies in hospital to see whether the chemical or the solvent had any effect on lung function in normal individuals or asthmatic patients. Within 12 h of the application of pirimiphos methyl (2 g/m²) to a carpet (12 × 6'), specially laid in a 20 × 12' hospital room, four asthmatic and four normal subjects spent 3 h in the room. Peak expiratory flow rate (PEFR) was measured four times, while forced vital capacity (FVC) and forced expiratory volume 1 sec (FEV₁) were measured at the beginning and the end of 3 h. The mean fall in PEFR

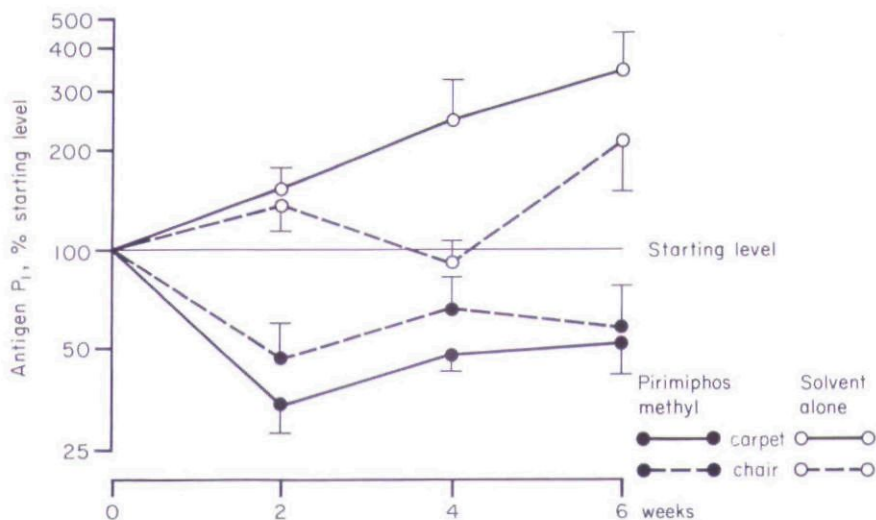


Fig. 2. Two carpets in each of ten houses (six of asthmatic patients, four of normal controls) were treated with pirimiphos methyl or solvent alone using a Bissell (9000S) carpet shampooer (Bissell Appliances Ltd, London). Statistical analysis was performed using the Mann-Whitney *U* test. The differences in the antigen P₁ levels in samples from the total area of each carpet at the beginning and at 2, 4 and 6 weeks for chemical treated and placebo treated carpets was $P < 0.002$ at each sampling point. A piece of soft furnishing treated with chemical or placebo via an aerosol was also sampled.

was < 1% for asthmatic subjects and 2% for normal subjects. No significant changes in FEV₁ or FVC occurred, and despite the obvious smell of solvent, no symptoms of discomfort were reported.

Antigen P₁ levels in homes

Ten houses were randomly allocated for treatment with 2 g/m² pirimiphos methyl or solvent alone. Carpets and upholstered furniture were sampled before and three times following this treatment. Within 2 weeks, a significant reduction in allergen level was apparent in dust from treated carpets. Eight out of ten treated carpets showed a greater than 50% reduction while only one of the untreated carpets showed such a reduction ($t = P < 0.002$). The quantity of antigen P₁ ranged from 950–35 000 ng/g of dust and the % decrease was not related to the starting level. The only treated carpet which showed an increased level of allergen after 2 weeks had been treated with a water repellent shortly before our study. Over 6 weeks, the treated carpets remained well below pretreatment levels of allergen (mean 48% reduction at 6 weeks) while the untreated carpets showed progressive increase in antigen P₁ content (Fig. 2). Similar but less marked effects were seen in chairs treated with a hand held aerosol (Fig. 2).

Discussion

Pirimiphos methyl is a very effective acaricide. Dust mite survival and allergen accumulation in laboratory cultures was markedly reduced either on filter paper or in carpet segments. Furthermore, this effect persists for at least 3 weeks after application. In homes, a single application of the chemical produced > 66% reduction in allergen in carpets and > 50% reduction in chairs. The concentration used was determined both from the laboratory studies and preliminary studies on houses. In the present study, a progressive increase in allergen level was seen in untreated carpets. This, presumably, reflects the lack of regular vacuum cleaning requested to standardize conditions in each house. These results suggest that regular cleaning plus pirimiphos methyl treatment every 6 weeks should produce progressive falls in mite allergen levels. There is plenty of evidence from previous studies and from our own longitudinal results that regular vacuuming of carpets alone is not an effective method of reducing mite numbers or allergen concentrations [9].

Pirimiphos methyl is an organophosphorous insecticide that is registered and widely applied in the U.K. and many countries for agricultural stored product protection and public health uses. Approval has been granted by the Health and Safety Executive in the U.K. to conduct trials with pirimiphos methyl on house dust mite control. The insecticide has low mammalian toxicity and is classified as 'slightly hazardous' in the WHO Classification of Pesticides by Hazard [12]. It does not produce significant skin or eye irritation and is not a strong skin sensitizer. Pirimiphos methyl is not teratogenic and has not been shown to have any mutagenic or carcinogenic effects. The agent is a cholinesterase inhibitor but no effects were observed in seven subjects given an oral dose of 0.25 mg/kg daily for 56 days. Neurotoxicological studies indicated that even in the most susceptible species pirimiphos methyl caused no neurotoxic effects. The FAO/WHO [13] Joint Expert Committee on pesticide residues have recommended 0.01 mg/kg daily as an acceptable daily intake for man. As with all chemicals routine precautions are advised with its use, e.g. wearing of gloves and avoidance of contact with eyes, skin, or mouth. Also food, drink, cigarettes, or flame should not be exposed to the acaricide.

The place of house dust mite avoidance in the management of allergic disease in sensitive patients is at present unproven. Studies on the effects of cleaning houses have often been restricted to bedrooms although dust mite infestation is usually demonstrable throughout the house [9]. The two studies which have reported the best clinical results have involved very vigorous intervention in the bedrooms [3,6], while two of the studies that reported no benefit documented that the cleaning regime used did not significantly reduce mite numbers or allergen levels [4,5]. Clearly, clinical trials are still necessary to answer whether generalized reduction of dust mite antigen has a clinical benefit in asthma, atopic dermatitis [14], or perennial rhinitis. If improvement can be demonstrated, then the place of this acaricide in the overall strategy of disease management would have to be considered. The role of acaricide will depend on an assessment of its potential side effects, the effectiveness of other approaches to dust allergen avoidance, and the likelihood of patients or family members applying the agent throughout the house at 4–6-week intervals. This approach may be particularly appropriate for those interested in self help and in cases of poor compliance with drug therapy.

In conclusion, pirimiphos methyl is highly effective at reducing house dust mite levels, has low mammalian toxicity, and appears to be non-irritant to asthmatic lungs. A controlled clinical trial assessing its role in the management of bronchial asthma is underway.

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