The effect of encasings on quality of life in adult house dust mite allergic patients with rhinitis, asthma and/or atopic dermatitis

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Summary

Background: Environmental control has been put forward as an integral part of the management of house dust mite allergy in sensitised patients. To validate this statement allergic disorders involved in house dust mite allergy - allergic asthma, rhinitis and AEDS (atopic eczema/dermatitis syndrome) - should be taken together and studied in terms of the efficacy of environmental control. Because a generic quality of life questionnaire exceeds the borders of disease, this may be used as major outcome parameter.

Research objective: to study the effects of bedding encasings in house dust mite allergic patients with asthma, rhinitis and AEDS.

Material and Methods: 224 adult house dust mite allergic patients with rhinitis and/or asthma and/or dermatitis were randomly allocated impermeable or non impermeable encasings for mattress, pillow and duvet. SF-36 (Short Form 36) was filled in at baseline and after 12 months.

Results: Lower Physical ($p = 0.01$) and Emotional ($p < 0.001$) sumscores were seen in females. Also, the presence of asthma resulted in lower Physical sumscore ($p = 0.01$). However, no effect was seen of encasings on either sumscore.

Conclusion: Bedding encasings do not improve quality of life in a mixed population of subjects with combinations with rhinitis, asthma and atopic dermatitis and sensitised to house dust mites.

Key Words SF-36, allergic rhinitis, allergic asthma, AEDS, house dust mite, encasings, random regression

Introduction

Environmental control has been put forward as an integral part of management of house dust mite allergy in sensitised patients.[1,2] Analysing the various methods in a randomised controlled clinical trial (RCT) has been proven difficult. So far, only application of chemical substances and physical barriers has been appropriately tested in a RCT. The results of studies to the efficacy of encasings on both symptoms of asthma and AEDS (atopic eczema/dermatitis syndrome) have been conflicting; in rhinitis only one randomised trial has been performed with negative results.[3-10] Comparison of effects in different diseases will be hampered by differences in clinical presentation and outcome measures. However, when studying the effects of an intervention in patients with atopic disease, one may easily encounter subjects with multiple atopic disorders.[11] To test the hypothesis that the use of encasings is effective in rhinitis, asthma and AEDS, ideally a common outcome measure should be used, capturing all the different aspects of these diseases.

The growing interest in quality of life research in the last decades has provided us with new tools for the evaluation of disease. The availability of generic quality of life questionnaires enables us to address the question whether encasings are effective in patients with house dust mite allergy, irrespective of their affected organ whereas disease specific questionnaires only inform us about one selected organ. The use of a generic quality of life questionnaire, a common outcome for different diseases, may be particularly appropriate for these patients with more than one atopic disorder. In particular, the generic SF-36 (short form-36) serves our purpose as this instrument has been used in the evaluation of allergic rhinitis, asthma and atopic dermatitis.[12,13] [14,15] [16,17] We studied the effect of encasings in house dust mite allergic patients with one or more atopic disorder. Our goal was to evaluate the effects of encasings on allergic complaints of asthma, rhinitis and AEDS by means of SF-36.

Material and Methods

Patients

Patients took part in a double blind, placebo controlled, multicentre trial to study the effect of bedding encasings on complaints of allergic rhinitis and/or asthma and/or AEDS. Participating centres were the Allergology departments of the University Hospitals of Groningen and Rotterdam and the Dermatology department of the University Hospital Utrecht. The study was approved by the Medical Ethics Committees of all three University Hospitals and all patients gave written informed consent.

Participants were adult house dust mite allergic patients suffering from atopic rhinitis, atopic asthma and/or AEDS in varying degrees of severity. House dust mite allergy was assessed by skin test and/or RAST.[18,19] In- and exclusion criteria are described in Table 1. Patients were diagnosed as having rhinitis, asthma or AEDS according to pre-set criteria described elsewhere.[20] Follow up consisted of baseline visits and visits after 12 months. Before each visit nasal medication, both antihistaminics and nasal sprays, was stopped and replaced by acrivastine; acrivastine was stopped 3 days before

baseline and follow up visits. Class 3 and 4 topical corticosteroids for the skin were replaced by class 1 and 2 corticosteroids. Asthma medication was continued but all relevant medication was stopped before lung function tests. The mean PC20 showed room for improvement at baseline measurements (Z. Tempels, personal communication). Exacerbations were treated by the general practitioner or the specialist of the patient. After these visits a trained student visited the patient at home to obtain dust samples of the mattress, bedroom floor and living room floor. All measurements took place in autumn (September until November 1997, 1998 and 1999) since this is the house dust mite season in the Netherlands; also we avoided interference by pollen because pollen disappear at the beginning of September.

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Age 8 –50 years	1. Pets at home and positive skin test (index ≥ 0.7)[18,19] and/or RAST* ≥ 2 for the pet
2. Not pregnant or breastfeeding	2. Daily use of inhalation steroids ≥ 1600 mcg/day (adults) or ≥ 800 mcg/day (children)
3. No encasings or willing to remove them for the period of the study	3. Daily use of oral steroids
4. Allergic rhinitis and/or asthma and/or atopic eczema/dermatitis syndrome	4. Daily use of cyclosporine
5. RAST class ≥ 2 and/or intracutaneous skin test index ≥ 0.7 house dust mite	5. Regular use of antibiotics for upper or lower airway infection
6. ≥ 200 ng Der P1 of F1 in dust sample of mattress	6. Regular use of oral steroids for exacerbation of asthma

* RAST radioallergosorbent technique

Endpoints of the study

Generic quality of life was measured by means of the SF-36. We used the translation of Aaronson of the MOS SF-36, originally developed by Ware and co-workers.[21-25] SF-36 consists of 36 questions divided over 8 subscales, covering both physical and mental health. Physical health subscales are Physical functioning, Role physical functioning, Bodily pain and General health; mental health subscales are Mental health, Role mental functioning, Social functioning and Vitality. Questions are stated in both yes/no form and multiple choice. Sum score was calculated for each subscale and transformed to a percentage of the total possible score. After transforming subscale scores average score was taken for physical subscales (Physical sumscore) and for emotional subscales (Emotional sumscore). The reliability in two general population samples as reported by Aaronson using Cronbach's α varied from 0.76 to 0.92 while the item discriminant validities varied from 0.09 to 0.64. SF-36 was administered to the patient before tests were performed. Trained personnel instructed the patient according to the guidelines, defined by the designers of the questionnaires. All patients filled in their questionnaires in a private room without the presence of other persons.

Blinding and randomisation procedures

If a patient was considered eligible, he or she was taken into the randomisation procedure: initials, date of birth and the measures of all pillows, duvets and mattress(es) were faxed to the Julius Centre for Patient Oriented Research. Each patient was assigned a research number. Research number and measures were sent by the Julius Centre to the manufacturer of the encasings, HAL, Haarlem, the Netherlands. A carton box, containing all encasings, was sent to the research centre, with the research number written on the outside of the box. Patients were instructed to take the box home and apply the encasings after baseline visits in absence of the research staff. We did not check if the encasings were in use since that would have compromised the blinding.

Statistical analysis

Categorical variables were analysed with chi-square test. ANOVA was used to compare continuous variables. Data were analysed using Statistical Analysis Systems (SAS) statistical programme. The levels and the dispersion of the data were represented by means and standard deviations, respectively. To analyse longitudinal data Random Regression Modelling (RRM) for continuous data was applied. RRM is a highly flexible and proper approach for repeated measurements. RRM enables to model change across time and at both group and individual level. The qualities of RRM above and beyond to multivariate analysis of variance for repeated measurements is that RRM is not restricted to modelling time as fixed effect; on the contrary, in RRM both the number of measurements across time and the moments of measurement may vary. Time-constant and time-varying variables can be entered in RRM. The structural form of the within subject covariance matrix of MANOVA for repeated measurements is assumed to meet the criteria of 'compound symmetry', that is to say that the variances and covariances are assumed to be constant across time. RRM, however, is utmost flexible in that variances and covariances across time may assume other kinds of error structure. In this study it is assumed to be unstructured (fully parameterised). In addition, RRM can handle missing data if the missing data can be assumed to be missing at random.[26] This implies that patients who were missing at a given measurement moment, were not excluded from analysis. RRM estimates the trend (of any kind) across time for every patient on the basis of individual data, augmented by time trend being for all patients together and the effects of all covariables in the model, including centre as a confounding variable. The analysis strategy was as follows:

Model 1 comprised fixed terms such as linear time trend and treatment condition without any interaction; only the intercept was considered to vary randomly. Model 2 was identical to model 1 but different in that in this model the quadratic time trend was added. In model 3 linear time trend was added as random term to model 1. Model 4 equals model 2 including linear time trend as random term. Model 5 is different from model 4 only in that in the first mentioned model quadratic time trend was added as random term. Models 6 to 10 were similar to models 1 to 5 consecutively;

however the interaction of linear time trend and treatment was entered. Models 11 to 15 corresponded to models 6 to 10, only now the interaction of quadratic time trend and treatment was included. All 15 models were applied on both the sumscore of all physical subscales of the SF-36 (FF) and on the sumscore of all emotional subscales of the SF-36 (EF). Since the distributions of the sumscore of both FF and EF were skewed to the right, logvalue was calculated of FF and EF after transformation being Log (101 – FF) or Log(101 – EF), respectively. The models were fitted by maximising the likelihood function for the data. The likelihood function (L) measures the likelihood of the parameters given the data and is defined by the density function of the observations. Akaike's information criterion (AIC) makes allowance for the number of parameters fitted; AIC enables to make comparisons between models fitting the same fixed effects.[27] In addition, Schwarz's information criterion (SIC) takes into account the number of fixed effects, the number of covariance parameters and the number of observations.[28] Models with larger values of AIC and SIC indicate better fits. To statistically test for fixed effects of the models the difference of –2 restricted loglikelihood ratios for the respective models is estimated along with the corresponding degrees of freedom. Testing for random effect runs as follows: the p-values of the models with degrees of freedom belonging to the respective models were averaged.

Results

General results

At baseline 224 patients entered the study. All baseline parameters were equally distributed between both groups (Table 2a). Loss to follow up is described in Figure 1; no significant differences were found between the impermeable and non impermeable encasing group. Mean baseline scores on SF-36 physical and emotional subscales were not significantly different in both groups, neither were both sumscores; in comparison to the general Dutch population, the scores on the subscales were significantly lower on almost every subscale (Table 2b). Most patients suffered from rhinitis (85), rhinitis and asthma (62) or rhinitis, asthma and AEDS (31); 20 patients had rhinitis and AEDS, 5 had asthma and AEDS, 13 suffered from only asthma and 8 patients had only AEDS.

Random regression modelling

We applied all 15 models described above on the Physical sumscore (FF) and the Emotional sumscore (EF). For the Physical sumscore model 1 was by far the best fitting model (data not shown); Model 3 was the best model for Emotional sumscore (data not shown). When considering the results of both models in detail, a few aspects strike the eye immediately (Table 3). Treatment – the use of encasings on mattress, pillow and duvet - has no effect in this analysis. Less surprising was the finding that females indicated to have a lower Physical and Emotional sumscore (scores were logtransformed after subtraction of the sumscore as described in the statistical paragraph) which is in line with earlier results of this study.[20]

The negative effect of asthma – presence of asthma resulted in lower Physical sumscores - is also in line with earlier findings.[20] The linear time trend is significant in Physical sumscore but the effect (estimate –0.01) is negligible.

Figure 1. Patients enrolled, randomized and withdrawn from trial

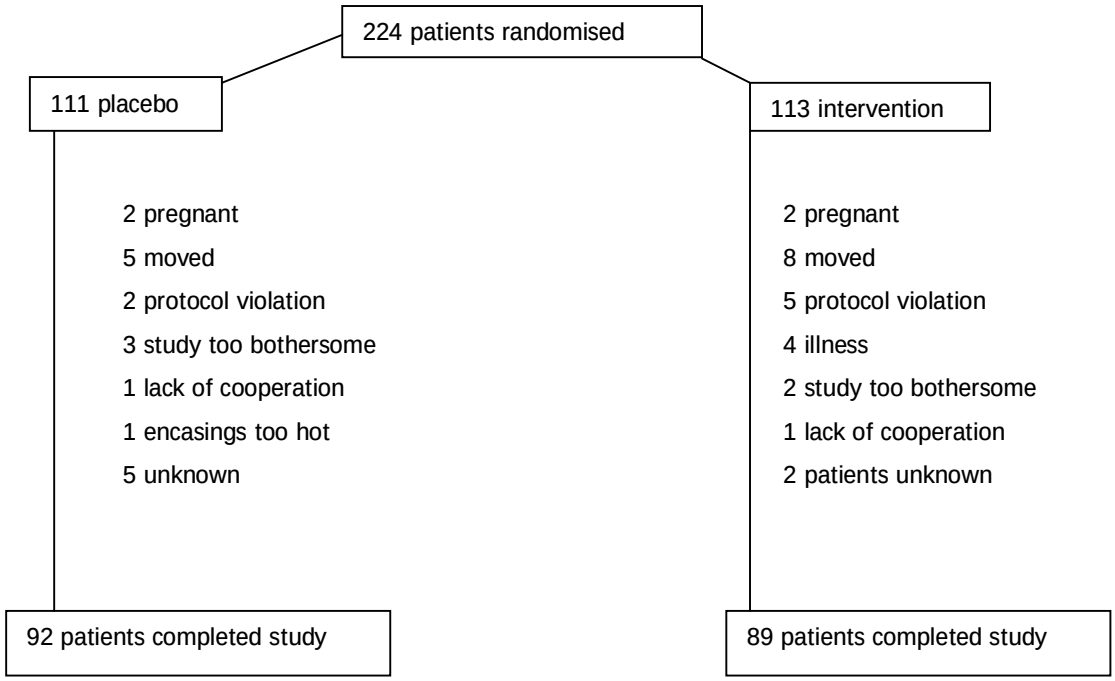

Table 2a. Baseline parameters

	Impermeable encasing group N = 113	Non impermeable encasing group N = 111
Age (1)	31.5 (SD 8.1)	33.4 (SD 8.2)
Male (2)	41 (18.3%)	39 (17.4%)
Smokers (2)	23 (10.3%)	17 (7.6%)
Rhinitis (2)	100 (44.6%)	98 (43.8%)
Asthma (2)	53 (23.7%)	58 (25.9%)
AEDS (2)	31 (13.8%)	33 (14.7%)
VAS rhinitis	48.4 (SD 29.7)	50.3 (SD 29.6)
ICT	1.2 (SD 0.35)	1.3 (SD 0.37)
Blood eosinophils 10^6/L	293 (SD 220)	286 (SD 195)

(1) Mean, SD

(2) Number of patients, percentage

ICT intracutaneous skin test; a ratio (allergen wheal diameter divided by histamine wheal diameter)≥ 0.7 is positive

VAS: visual analogue scale 0 – 100 mm, zero representing no complaints, 100 very severe complaints

Table 2b. General score on SF-36 subscales

	National Study N=1742	This study N=224	p value	AR n=85	AR + AA n=62	AR + AA + AEDS n=31
	m (sd)	m (sd)		m (sd)	m (sd)	m (sd)
PF	93.1 (11.8)	85.2 (15.8)	<0.01	86.9 (16.6)	84.0 (14.3)	81.6 (15.2)
RP	86.4 (27.6)	78.0 (33.2)	<0.01	81.5 (31.4)	74.6 (37.2)	75.8 (33.8)
BP	80.9 (19.4)	80.5 (20.3)	>0.05	79.9 (21)	82.0 (20.0)	76.6 (20)
GH	78.2 (17.3)	63.8 (21.3)	<0.01	67.2 (22)*	61.5 (20.1)	54.2 (19.6)*
VT	70.7 (16.4)	64.8 (19.3)	<0.01	65.9 (20.6)	64.9 (16.8)	60.5 (22.6)
SF	87.8 (19.1)	84.9 (20.1)	<0.01	86.0 (20.6)	85.9 (21.3)	84.3 (14.4)
RE	85.4 (30.0)	86.6 (29.1)	>0.05	86.3 (29.2)	83.9 (31.8)	88.2 (28)
MH	78.7 (15.2)	79.1 (14.7)	>0.05	79.2 (14.7)	79.4 (15.5)	80.4 (15)

* only GH was significantly different between AR and AR+AA+AEDS (p=0.004)

PF	Physical functioning	MH	Mental health
RP	Role physical functioning	RE	Role emotional functioning
BP	Bodily pain	SF	Social functioning
GH	General health	VT	Vitality

Table 3. Results of best fitting model for Physical and Emotional sumscore of SF-36

	Estimate[1]	**SE[2]**	**t[3]**	**p[4]**	**95% CI[5]**
Physical sumscore					
Intercept	0.99	0.15	6.79	< 0.001	0.70 to 1.27
Linear time trend	-0.01	0.00	-3.13	0.002	-0.01 to 0.00
Treatment	0.03	0.05	0.65	0.51	-0.07 to 0.13
Sex	0.14	0.05	2.53	0.01	0.03 to 0.24
Age	0.00	0.00	0.99	0.32	0.00 to 0.01
AEDS	0.05	0.06	0.88	0.38	-0.06 to 0.17
Asthma	0.13	0.05	2.56	0.01	0.03 to 0.23
Rhinitis	-0.03	0.08	-0.32	0.75	-0.19 to 0.14
Emotional sumscore					
Intercept	1.28	0.11	11.8	<0.001	1.07 to 1.50
Linear time trend	0.00	0.00	-1.67	0.10	-0.01 to 0.00
Treatment	0.04	0.04	0.95	0.34	-0.04 to 0.11
Sex	0.10	0.04	2.55	0.01	0.02 to 0.18
Age	0.00	0.00	0.39	0.70	0.00 to 0.01
AEDS	0.04	0.04	0.85	0.39	-0.04 to 0.12
Asthma	-0.03	0.04	-0.86	0.39	-0.10 to 0.04
Rhinitis	-0.08	0.06	-1.29	0.20	-0.20 to 0.04

1) estimate: unstandardised regression coefficient adjusted for centre

2) SE: standard error of the estimate

3) t: statistic t-value

4) p: p-value

5) 95% CI: 95% confidence interval

Discussion

The goal of this study was to evaluate the effect of encasings in house dust mite allergic patients by means of a general quality of life questionnaire, the SF-36. In an earlier study encasings had no effect on clinical outcome measures like visual analogue scale or daily symptom score in spite of a significant reduction on allergen exposure.[10] In this study we could not demonstrate any effect of encasings on quality of life scores assessed by SF-36; we did find a negative impact of asthma and sex. This was also in line with the result of an earlier study.[20] Before accepting these results, potential limitations of this study have to be addressed. First, lack of effect could be due to inefficacy of the encasings. However, as reported elsewhere the results of the dust samples at baseline and after 12 months clearly showed a significant 3-fold reduction in favour of the impermeable encasing group.[6,10] Secondly, allergens from other sources may modulate the effects of intervention in multi-sensitised subjects. Interference by other relevant allergens has been avoided by evaluation of patients outside the pollen season and by not allowing pets in case of sensitisation to pets. Allergy to moulds or cockroach was not investigated since this is not an important problem in the Netherlands.[29] In contrast, neither dust mite exposure from other sources in the house, nor exposure to other allergens outside the house was controlled in this study. Perhaps the use of encasings as a mono intervention does not sufficiently reduce allergen exposure to ameliorate symptoms. It is also possible that the house dust mite is not responsible for eliciting symptoms although all patients had a positive skin test. The relation between atopic eczema and house dust mite allergy is still a matter of controversy although Tupker could induce skin responses in patients with AEDS after bronchial provocation with house dust mite.[30] Bronchial provocation with house dust mite can induce a response in asthma patients, but since we only performed challenge tests with methacholine and adenosine, it is possible that in some of our asthma patients house dust mite does not elicite a bronchial response. However, we assume that we included subjects with asthma due to house dust mite exposure, knowing that the degree of allergic sensitisation and the degree of bronchial hyperreactivity may predict the bronchial response to allergens.[31] The diagnosis of rhinitis could only be obtained if a suggestive history was followed by a positive nasal challenge test with house dust mite allergen; so, in this patient group we are certain that allergen exposure was responsible for nasal complaints.

Finally, one could speculate that the instrument used, the SF-36, might have been a less adequate choice in terms of responsiveness to change and that a disease specific questionnaire might have been a better option. Although generic instruments are less sensitive in detecting treatment effects, our results are backed up by separate analyses using medical outcome measures in children and adults with AEDS and in rhinitis.[32] [10,20] [6]

As discussed earlier, the choice of outcome measure was linked to and warranted by the aims of this study. We chose to evaluate the intervention in this mixed population instead of focussing on a distinct group of subjects with rhinitis, asthma or atopic dermatitis for a the following reasons.

Not only would the latter approach lower the number of eligible patients, but more importantly, we considered these patients with combined atopic disorders as representative of the allergic subjects seen and treated in daily practice. In addition, according to position papers environmental control has been advocated to subjects allergic to house dust mites in general.

The commonly accepted statement that environmental control is an integral part of the management in patients sensitised to house dust mites has been based on early observations that children with asthma and allergy to house dust mites recover at HDM free high altitudes.[33] Moreover, it appeared that a long-term stay in hospital induced a decrease in bronchial hyperreactivity in asthmatic subjects allergic to house dust mites.[34] It may be possible, however, that the beneficial effects of an allergen free environment can not be obtained by house dust mite reducing measures in our daily environment.[34] Our study corresponds with both a recent meta-analysis of 29 trials in 939 asthmatic patients, showing that neither physical methods (15 trials), chemical methods (9 trials) nor a combination of methods (5 trials) resulted in improvement of asthma, and a recent study by Woodcock.[35,36] The observation that women had a lower Physical and Emotional sumscore is in line with other studies.[21] The linear time trend was significant but the actual effect is negligible. The finding that the presence of asthma negatively influences quality of life is an extension and confirmation of an analysis on the baseline data of this set.[20] We therefore conclude that further studies are warranted to evaluate the effects of environmental control in house dust mite allergic patients.

Conclusion: The application of encasings does not have a beneficial effect on asthma, rhinitis or AEDS in subjects allergic to house dust mite as measured with the generic SF-36 questionnaire.

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