

Comparison of a generic and a rhinitis-specific quality of life instrument in patients with house dust mite allergy: Relationship between the SF-36 and the Rhinitis Quality of Life Questionnaire (RQLQ).

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Summary

Background: Generic and disease specific quality of life questionnaires are commonly used in subjects with allergic rhinitis. Allergic rhinitis, however, is closely associated with other disorders such as bronchial asthma and atopic dermatitis. These comorbid associations may have an effect on the interrelation of generic and disease specific quality of life outcomes and the behaviour of this interrelation in time.

Objective: To unravel the interrelationships between the outcome of a generic instrument (SF-36) and a disease specific instrument (RQLQ).

Material and Methods: In the framework of a randomised clinical trial to the efficacy of impermeable bedding covers in house dust mite allergy, SF-36 and RQLQ were administered to 224 adults with allergic rhinitis and/or allergic asthma and/or atopic dermatitis at baseline and after 12 months of intervention. Regression analysis and canonical correlation were used to estimate overlap.

Results: Overlap between SF-36 and RQLQ domains in terms of explained variance ranged from 6% to 56%. Canonical correlation yielded low coefficients (0.16-0.27). Moreover, both SF-36 and RQLQ did not change significantly during the intervention.

Conclusion: In patients with house dust mite allergy characterised by comorbid associations, SF-36 and RQLQ cover different aspects in quality of life. It is advocated to use both simultaneously in performing quality of life studies.

Key words Allergy , Canonical correlation, Redundancy analysis, Rhinitis, RQLQ, SF-36

Introduction

In the last decade interest in the impact of atopic disease on quality of life has grown. It is generally accepted that disease may hamper patients in their day-to-day functioning. As a consequence, instruments for measuring quality of life have been developed, both generic and disease specific.¹⁻⁵ In allergic rhinitis both types of questionnaires have been used to evaluate the burden of nasal symptoms.⁶⁻¹⁰ Previous research indicated that rhinitis-related quality of life is moderately associated with nasal symptoms and nasal hyperreactivity.¹¹

In day-to-day practice patients usually suffer from more than one atopic disorder. Rates of allergic rhinitis among asthmatics vary from 28% to 50% in studies published in the seventies and eighties.^{12, 13} Recently, in a population-based study the prevalence of rhinitis in patients with asthma was estimated at 78%.¹⁴ Edfors-Lubs showed that the prevalence of rhinitis in patients with dermatitis was 29%.¹² In a previous study we found that 92% of the asthmatic patients and 85% of the patients with atopic dermatitis had nasal symptoms.¹⁵ Despite all evidence for the high co-morbidity in atopic disease, in daily clinical care therapy focuses on the most predominant disease, i.e. asthma, atopic dermatitis or rhinitis.

Therefore, we recently evaluated the impact of different disorders (i.e. rhinitis, asthma and atopic dermatitis) and comorbidity on quality of life in general assessed by the SF-36 in adult patients with house dust mite allergy.¹⁶ This study was a part of a large multicentre clinical trial to investigate the effect of impermeable bedding covers on symptoms of allergic asthma, allergic rhinitis and atopic dermatitis.

Results indicated that these patients experienced impaired quality of life. The (co)-existence of asthma, expressed in terms of diagnostic criteria or symptom severity, or the presence of sleep disorders as a consequence of atopic dermatitis impaired quality of life even further. Due to the high prevalence of rhinitis, we could only evaluate the additional contribution of co-existing asthma and atopic dermatitis on generic quality of life. However, as both generic and disease specific quality of life have been assessed by questionnaires, this data-set enabled us to investigate the interrelationship between the generic SF-36 and the disease specific quality of life questionnaire for rhinoconjunctivitis (RQLQ) in a population characterised by rhinitis and concomitant allergic disorders. Moreover, the study design of the clinical trial permitted us to investigate the change of this overlap during one year of follow-up.

Study Design and Patients

Patients

Patients took part in a multicentre trial to study the effect of impermeable covers for bedding on complaints of atopic rhinitis, atopic asthma or atopic dermatitis or any combination of these conditions. 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 Committee of all three University Hospitals and all patients gave written informed consent. In- and exclusion criteria are described in Table 1.

After baseline measurements including nasal provocation and lung function tests, patients were diagnosed as having atopic rhinitis, atopic asthma or atopic dermatitis according to preset criteria, described extensively elsewhere.^{16, 17} Follow-up visits were scheduled 4 and 12 months after baseline measurements. All measurements were performed outside the pollen season to avoid interference.

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) and/or RAST ≥ 2 for the pet
2. Not pregnant or lactating	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. Clinical history of allergic rhinitis and a positive nasal provocation test with house dust mite	4. Daily use of cyclosporine
5. RAST $\geq 2^1$ and/or i.c. skin test index ² ≥ 0.7 for house dust mite	5. Regular use of antibiotics for upper or lower airway infection
6. ≥ 200 ng Der p1 or Der f1 in dust sample of mattress	6. Regular use of oral steroids for exacerbation of asthma

Randomisation and Blinding Procedures

The study was designed as a double-blind, placebo-controlled trial. The randomisation procedure for all centres was performed by the Julius Centre for Patient Oriented Research. Each patient was assigned a research number. Research number and bedding measures were sent 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 took the box home and opened it in the absence of research staff. Encasings for pillows, duvets and mattresses were applied after baseline measurements.

Clinical Measurements

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.¹⁸⁻²² SF-36 consists of 36 questions divided over 8 subscales, covering both physical and mental health. Physical health subscales are Physical functioning (PF), Role physical functioning (RP), Bodily pain (BP) and General health (GH); mental health subscales are Mental health (MH), Role emotional functioning (RE), Social functioning (SF) and Vitality (VT).

Questions are stated in either yes/no form or multiple choice. Sum score is calculated for each subscale and transformed to a percentage of the total possible score. High score indicates good quality of life, while low score indicates lower quality of life. 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.

The RQLQ (Rhinitis Quality of Life Questionnaire) developed by Juniper et al was used to estimate the severity of complaints caused by allergic rhinitis.¹ Patients had to score 28 items comprising the following domains: Nasal symptoms (NS, 4 items), Practical problems (PP, 3 items), Non nasal symptoms (NN, 7 items), Sleep(disorders) (SL, 3 items), (impairment of) Activities (Act, 3 items), Eye symptoms (ES, 4 items) and Emotions (EM, 4 items). They had to estimate their degree of impairment on a 7-point scale (0 = not bothered, 6 = extremely bothered). SF-36 and RQLQ were administered to the patient before tests were performed (e.g. the RQLQ was filled in prior to nasal provocation with house dust mite). 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. Since nasal complaints can be biased by use of medication, all nasal medication was stopped. Oral antihistaminics were stopped 17 days and nasal sprays four to six weeks before baseline and follow up visits to ensure a long enough wash out period. Patients were allowed to use acrivastine, 8 mg 1 to 3 times a day, but using rescue medication was discouraged.

Statistical analysis

Baseline variables for the impermeable cover group and non impermeable cover group were calculated with chi square test for categorical variables and ANOVA for continuous data. Analysis of the relationship between RQLQ and SF-36 was performed on the pooled data of the patients by means of canonical correlations for continuous data.²³⁻²⁵ A condition of proper use of canonical correlation is that the variables have multivariately a normal distribution. Secondly, linearity is assumed in canonical analysis. Finally, it is important that the variables within and across each set are not too highly intercorrelated. Squared multiple correlations (SMC) as a measure to identify multicollinearity and singularity were performed. Our data met the aforementioned criteria. BMDP Statistical Software was used for all analyses.

We wanted to investigate the relationship between SF-36 and RQLQ in terms of 'explained variance'. Explained variance is that part of the total variance of a variable that can be estimated or predicted by another variable. For example, if the explained variance of 'Nasal complaints' by 'Physical functioning' is 0.40 then 40% of the variance of 'Nasal complaints' can be predicted by 'Physical functioning'. Otherwise stated, the overlap between 'Nasal complaints' and 'Physical functioning' is 40%. Analysis was performed on the sumscores of the domains of both questionnaires.

Also, overlap between SF-36 and RQLQ was calculated by means of redundancy analysis. The redundancy is the average explained variance of the domains of one questionnaire multiplied by a factor called the canonical correlation squared.

RESULTS

General results

At baseline, 224 patients were included in the study; 183 patients completed the study. Data eligible for analysis were available for 160 patients. Loss to follow up was not significantly different between placebo (17) and intervention group (24) as were the reasons for leaving the study (data not shown). At baseline, biographic data, severity of atopic symptoms (assessed by VAS, SF-36, RQLQ) and sensitisation (assessed by RAST, skin tests, eosinophils) were not significantly different in placebo and intervention group (data not shown). After 12 months, SF-36 and RQLQ subscale scores were not significantly different in both groups as well (data not shown).

Redundancy analysis

Table 2a and 2b show the intercorrelation of SF-36 and RQLQ. At baseline Vitality and Non nasal symptoms show considerable overlap (-0.60). After 12 months Non nasal symptoms show a more or less similar overlap with Physical functioning, Role physical functioning, General health and Vitality. Vitality also has a moderate overlap with Emotions after 12 months. The results of the explained variance analysis (data not shown) showed that the domain of non-nasal complaints of the RQLQ had a moderate overlap of 44 percent with SF-36. After 12 months the overlap was 57 percent. At baseline the domain Vitality of the SF-36 had moderate overlap with RQLQ of 40 percent; after 12 months this percentage was 48 percent. The domain Role physical functioning of SF-36 had little overlap at baseline with RQLQ, but after 12 months explained variance was 41 percent. The overall redundancies for RQLQ and SF-36 subscales were 16 percent and 22 percent, respectively, at baseline. One year after the start of the study, these percentages were 25 for RQLQ and 27 for SF-36 (Table 3).

Table 2a. Intercorrelation matrix of RQLQ and SF-36 at baseline

	Act	SL	NN	PP	NS	ES	EM
PF	-0.15	-0.26	-0.36	-0.02	-0.13	-0.18	-0.19
RP	-0.23	-0.37	-0.49	-0.18	-0.28	-0.25	-0.34
GH	-0.10	-0.30	-0.46	-0.06	-0.19	-0.25	-0.38
BP	-0.23	-0.33	-0.38	-0.02	-0.11	-0.17	-0.35
SF	-0.16	-0.30	-0.46	-0.07	-0.13	-0.27	-0.37
VT	-0.20	-0.33	-0.60	-0.13	-0.25	-0.33	-0.46
MH	-0.07	-0.24	-0.36	-0.04	-0.15	-0.24	-0.39
RE	-0.02	-0.12	-0.30	0.02	-0.13	-0.13	-0.27

Table 2b. Intercorrelation matrix of RQLQ and SF-36 after 12 months

	Act	SL	NN	PP	NS	ES	EM
PF	-0.31	-0.37	-0.58	-0.27	-0.26	-0.29	-0.36
RP	-0.37	-0.41	-0.62	-0.25	-0.34	-0.32	-0.46
GH	-0.29	-0.30	-0.52	-0.28	-0.25	-0.37	-0.42
BP	-0.29	-0.35	-0.44	-0.19	-0.18	-0.21	-0.30
SF	-0.26	-0.38	-0.41	-0.28	-0.27	-0.28	-0.40
VT	-0.35	-0.47	-0.69	-0.34	-0.38	-0.36	-0.51
MH	-0.25	-0.24	-0.43	-0.22	-0.19	-0.27	-0.42
RE	-0.14	-0.17	-0.28	-0.11	-0.12	-0.08	-0.23

PF	Physical functioning	Act	(impairment of) Activities (Act, n = 3)
RP	Role physical functioning	SL	Sleep(disorders)
GH	General health	NN	Non nasal symptoms
BP	Bodily pain	PP	Practical problems
SF	Social functioning	NS	Nasal symptoms
VT	Vitality	ES	Eye symptoms
MH	Mental health	EM	emotions
RE	Role emotional functioning		

Table 3. Overall redundancy of RQLQ and SF-36 (pooled data)

Canonical variate	RQLQ	SF-36
Baseline		
1	0.16	0.22
2	0.01	0.01
12 months		
1	0.25	0.27
2	0.02	0.01

Redundancy coefficients: the percentage of variance extracted from its own set of variables multiplied by the canonical correlation squared for the pair. Only the first pair was of significance

Discussion

Quality of life questionnaires attempt to estimate the burden of disease. In allergic rhinitis both the generic SF-36 and the disease specific RQLQ have often been used.^{6-8, 26, 27 1, 11, 28, 29} It has been stated that generic instruments are more tailored to evaluate the burden of disease across different diseases, whereas specific instruments are more responsive for changes in clinical trials.³⁰ Although both instruments aim to evaluate quality of life, it is not known whether these instruments cover the similar domains rather than different domains in quality of life. It is possible that some domains are covered better by one instrument than by the other.

Recently, Juniper et al reported a moderate correlation between SF-36 and RQLQ.³¹ The subjects tested were not permitted to have other symptoms than rhinoconjunctivitis. By focussing on subjects with rhinitis only, this investigation gives clear insight in the interrelationship between the two instruments by studying a homogeneous patient population. It is, however, well known that rhinitis, asthma, and atopic dermatitis are closely associated. Atopy – the personal or familial tendency to produce IgE antibodies to low-dose antigens and to develop typical symptoms such as asthma, rhinoconjunctivitis and atopic dermatitis - forms the basis of the close connection between these disorders.³² Development of allergic sensitisation and diseases are partly under common genetic control. Evidence for linkage between candidate loci for allergic disease and total IgE concentrations is found in the same regions for which reasonable evidence for linkage to asthma has been reported.³³

The patient population of this study reflects the close association between allergic rhinitis, asthma, and atopic dermatitis as shown in a co-morbidity percentage of 53% (data not shown).

An exploration to the interrelation of SF-36 and RQLQ in this study group as opposed to the rhinoconjunctivitis group of Juniper was therefore a logical consequential step. The explained variance analysis showed overlap in the domains 'Non nasal complaints' of the RQLQ and 'Vitality' of the SF-36; in the intercorrelation matrix 'Non nasal complaints' also showed overlap with 'Vitality' at baseline and after 12 months. It is not surprising that these items of the RQLQ (i.e. being troubled by fatigue, thirst, reduced productivity, tiredness, poor concentration, headache and being worn out as a consequence of nose and eye symptoms) and the SF-36 "Vitality" domain (comprising questions as "Did you feel full of pep?", "Did you have a lot of energy?", "Did you feel worn out?" and "Did you feel tired?") can be explained by the other instrument. The same may hold true for the overlap of 'Non nasal complaints' after 12 months with 'Physical functioning', 'Role physical functioning' and 'General Health'. Other domains of the SF-36 apparently have little overlap with the domains of the RQLQ and vice versa. Overall redundancy coefficients were low, 0.16 and 0.21 for RQLQ and SF-36 respectively.

The overlap may be partly explained by our observation that associated non-nasal symptoms (i.e. asthma symptoms and sleep disorders) or disease (presence of asthma) influence generic quality of life.¹⁵ That the redundancy is moderate has partly to be attributed to the fact that the measurements are fallible. It had already been shown in the seventies of the last century by Andrew and Withey that a subjective quality of life judgement contains about 60% valid variance. The remaining variance comprises both the systematic and the random error variance.

In our analysis we used the pooled data of the patients under the assumption that a possible effect of the intervention would affect SF-36 and RQLQ equally. However, it is conceivable that the responsiveness of a disease specific instrument is better compared to a generic instrument. Since we could not demonstrate any effect of the covers on other clinical end points despite a significant reduction in exposure to allergen, we find it improbable that such a difference in responsiveness would have appeared.¹⁷

Results of questionnaires might be biased due to errors of the measurement instrument such as distortion by the format of questionnaire design or a patient's disposition to give socially desirable answers, to represent themselves as better than they actually feel (faking good) or the opposite (faking bad). A patient's frame of references can change considerably over time, as is known from oncology research, and this response shift has to be taken into account in all quality of life research ranging over time.^{34, 35} However, neither the overlap between both instruments changed substantially in 12 months, nor was a significant change in scores on SF36 and RQLQ subscales observed. These results are in line with our observation that the use of impermeable covers for bedding do not have a beneficial effect on allergic rhinitis, which excludes a differential effect of treatment on the outcome of both instruments.¹⁷ Although patients were monitored during 12 months, the findings do not suggest a response shift.

The limited overlap between RQLQ and SF-36 may have some consequences. The burden of rhinitis and the effect of a pharmacological intervention focused on rhinitis may be best evaluated by a disease

specific questionnaire as the RQLQ. Recognising the fact that allergic rhinitis forms a part of the atopic syndrome and comes with other atopic disorders, allergic rhinitis in the context of comorbid associations may be best evaluated by a generic instrument such as the SF-36. Therefore, the use of both types of instruments simultaneously may be advocated in the evaluation of the patient with allergic rhinitis. In conclusion, in patients with house dust mite allergy characterised by comorbid associations SF-36 and RQLQ cover different aspects in quality of life and should be used simultaneously in performing quality of life studies.

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