

Quality of Life Measurement and the Relation with Disease Severity in Children with Atopic Dermatitis in General Practice

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Running title: QoL in paediatric AD and disease severity

Abstract

Atopic dermatitis (AD) has a great impact on the quality of life (QoL). The usefulness of health-related QoL questionnaires for children with AD in general practice and the relation to disease severity as assessed by parents and by investigators has not yet been established. In this study, QoL was assessed using the IDQoL in children with AD, selected from general practice. Severity of AD was determined by investigators and parents using the objective SCORAD, the TIS or by an additional question of the IDQoL.

Sixty-six patients (41% boys, mean age 31 months) were included. Correlations between disease severity as assessed by parents and by investigators were low (R_s 0.29-0.51),

Correlations between IDQoL and severity assessed by investigators was low (R_s 0.08-0.36).

However, IDQoL and severity according to parents showed good correlations (R_s 0.67-0.73). In conclusion, both disease severity and disease-related QoL are two different aspects and are essential when evaluating treatment or when investigating new dermatological therapies in trials.

Key words: atopic dermatitis, children, disease severity, quality of life, general practice

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INTRODUCTION

Atopic dermatitis (AD) is an inflammatory skin disease characterized by erythematous, papular or vesicular lesions in the acute form of the disease, and by lichenification in the chronic form.

Patients suffer from itching, show highly visible skin lesions, and suffer from psychological and social consequences.¹

Severity of AD is assessed by making use of scoring systems like the (objective) SCORAD (scoring atopic dermatitis) and the TIS (three item severity scale).²⁻⁴ Whereas these systems are reliable measures to determine the extent and/or severity of AD, they fail to take into account the psychological suffering and impairment of quality of life (QoL).⁵ Although patient-based outcome measures are important when assessing improvement e.g. in clinical trials, the experience of patients is not often used as an outcome measure in such trials.

Several questionnaires are available to investigate the QoL in patients suffering from AD; these include the Dermatitis Family Impact (DFI),⁶ which measures the impact of the disease on the whole family; the Children's Dermatology Life Quality Index (CDLQI),⁷ demonstrating the impact of dermatological disorders in general on QoL; the Quality of Life in Atopic Dermatitis (QoLIAD),⁸ which can be used in adults; the Childhood Atopic Dermatitis Impact Scale (CADIS)⁹; and the Infants' Dermatitis Quality of Life Index (IDQoL).^{5,10}

Of these questionnaires, the IDQoL seems a reliable and easy to use questionnaire which is specifically suited for children aged ≤ 4 years who suffer from AD.

In many countries, including the Netherlands, general practitioners (GPs) are primary providers of care for patients with AD. However, the suitability of the IDQoL in general practice is not yet established, nor is the relationship between the IDQoL and disease severity, as determined by the patient and an objective observer.

Therefore, this study investigated whether the IDQoL is a reliable questionnaire to explore QoL in children with AD in general practice. Secondly, we determined the severity of AD as determined by parents and by independent investigators, and the correlation between these.

Finally, we examined the correlation between QoL and the severity of AD as scored by the patients and by the investigators.

METHODS

Study population

Children (aged 0-6 years) suffering from AD were included during a five-month period (November 2007 to March 2008). Patients with a history of AD were selected from GPs' computerized files either by diagnosis, which is coded according to the International Classification of Primary Care

(ICPC)¹¹ or by prescribed medication coded according to the Anatomical Therapeutic Chemical (ATC)¹² classification scheme. Patients were selected using the ICPC code S87 (Atopic Dermatitis), and/or ATC codes specific for topical treatment of AD (zinc products, soft paraffin and fat products, other emollients and protectives, tars, topical corticosteroids). Further inclusion criteria were age (0-6 years), having visited the GP for AD complaints during the last three months, or having received a prescription for treatment of AD within the last three months and a diagnosis of AD according to Williams' criteria¹³. Patients were excluded: a) if there was a chronic disease other than AD, asthma, food intolerance or allergic rhinitis; b) in case of psychological problems which could influence follow-up; c) other skin conditions that precluded proper assessment of the severity of AD; and d) if parent or caregiver was unable to adequately read and write Dutch.

Parents of selected children received a written invitation sent by their general practitioner. All parents provided written informed consent. The local Medical Ethical Review Board approved this prospective study.

Clinical scoring systems

To determine the clinical severity of AD the so-called objective SCORAD and the TIS score were used. Two investigators (MW and RvV) were trained by a paediatric dermatologist (APO) to correctly perform the objective SCORAD and the TIS.

The objective SCORAD, which was used as the gold standard, measures the extent and intensity (composed of six items; erythema, oedema/papules, effect of scratching, oozing/crust formation, lichenification and dryness) of the disease.^{4,14} The maximum score is 83 points; in case of disfiguring lesions or functional limiting lesions 10 bonus points are given.

The SCORAD items that represent acute symptoms are combined into the three-item severity score (TIS).³ In the TIS, the severity of AD is based on erythema, oedema and excoriations. The TIS is the sum of the three items, each scored on a scale from 0 to 3; therefore, the TIS score ranges from 0 to 9. Similar to the objective SCORAD, each item on TIS should be scored on the most representative lesion.

IDQoL

The IDQoL questionnaire is a validated questionnaire which measures the impact of a child's dermatitis and was developed for use in children aged 0-4 years.^{5,10} In the present study we examined the IDQoL in children aged 0-6 years.

The IDQoL has ten questions addressing symptoms and difficulties with mood, sleep (two questions), play, family activities, mealtimes, treatments, dressing and bathing. The maximum score for each of the ten questions is 3, resulting a possible maximum score of 30 (higher scores reflecting greater impairment). An additional question (which is scored separately) asks the parents to assess the current severity of AD on a four-point scale ranging from no AD (score 0) to extremely severe AD (score 4). The IDQoL assesses the AD problems during the preceding week. In the present study the validated Dutch version of the IDQoL questionnaire was used.¹⁶

Data collection

All patients were visited twice, with a three-week interval. At the first visit one of the parents was asked to complete the IDQoL (IDQoL₁). In order to determine test-retest reliability, a second IDQoL was completed 24 hours later by the same parent (IDQoL₂) and was returned in a prepaid envelope. A 24-hour period was chosen because this time is: i) long enough not to (precisely) remember the answers to the questions, and ii) the severity of eczema is still comparable to that at the time of the previous assessment. Two investigators independently examined the severity of AD in all children using the objective SCORAD and the TIS during the same visit, without knowing the score of the other observer. The mean of the scores of both investigators was calculated. During the second visit, a final IDQoL (IDQoL₃) was filled in by the same parent and the severity of AD (objective SCORAD and TIS) was again determined by two independent observers.

Statistical analyses

Spearman's rank correlation (R_s) and intraclass correlation coefficient (ICC) were used to analyse the test-retest reliability of the total IDQoL score and of each question separately (IDQoL₁ vs. IDQoL₂). R_s was also used to analyse the correlation between the severity of AD as observed by the parents (extra question of the IDQoL) and as evaluated by the investigators (TIS or SCORAD). Additionally, the R_s was used to determine the correlation between the total IDQoL scores and the severity of AD.

We classified R_s and ICC results above 0.75 as excellent agreement and below 0.40 as poor agreement; results between 0.4 and 0.75 were regarded as fair to good.¹⁷ Statistical analyses were carried out using SPSS version 15.0 (SPSS Inc. Chicago).

RESULTS

A total of 278 patients with an age below 7 years and with a history of AD (ICPC S87) or use of medical treatment for AD were selected in the database of 45 GPs. These selected patients were invited

by mail to participate. Of these, 89 had self-reported complaints of AD at the moment and were willing to participate. Finally 66 patients fulfilled the inclusion criteria and were included. The reasons for exclusion were: few or no complaints of AD at the moment of inclusion (n=12); response after completion of the inclusion period (n=8); and no informed consent (n=3). The mean age of the selected population was 31.3 months (range 0.5-83.5 months) and 41% was male.

IDQoL

IDQoL₁ was completed for all patients during the first home visit. Of the 66 patients, 58 parents (88%) returned IDQoL₂ after 24 hours, and for 65 of the 66 patients (98%) the IDQoL₃ was assessed during the second home visit. The mean score for IDQoL₁ was 6.64 (SD 4.32, range 1-20), for IDQoL₂ was 6.43 (SD 4.33, range 1-22), and the mean score for IDQoL₃ was 4.52 (SD 3.67, range 0-20) (Table 1). Regarding the separate questions, the highest score was found for itching and scratching (question 1: mean 1.28, SD 0.89). The lowest scores concerned family activities (question 6: mean 0.20, SD 0.47) and problems during mealtimes (question 7: mean 0.14, SD 0.35) (Table 1).

Test-retest reliability of the IDQoL

There was an excellent agreement between scores for IDQoL₁ and IDQoL₂ ($R_s=0.89$, $p<0.001$). The ICC for these assessments was also excellent (ICC=0.89). Individual items also showed a good or excellent agreement; however, questions 4 and 5 had a slightly lower correlation (Table 2).

Severity of AD

The mean score of disease severity as assessed by the parents was 1.89 (SD 1.0) at the first visit, 1.74 (SD 0.98) 24 hours later, and 1.43 (SD 0.95) after 3 weeks. The mean severity score as determined by the TIS by the two independent observers was 2.3 (SD 1.18) at the first visit and 2.0 (SD 1.06) at the second visit, and for the objective SCORAD it was 13.5 (SD 8.7) at the first visit and 11.9 (SD 7.8) at the second visit.

Correlation between severity of AD according to investigators and parents

The correlation between severity of AD as observed by the parents and as observed by the investigators (objective SCORAD and TIS) showed poor agreement for the first visit and fair agreement for the second visit (Table 3).

Correlation between IDQoL and severity of AD

Table 3 shows that the IDQoL had a good correlation with severity as observed by the parents (R_s for first visit=0.73, R_s for second visit=0.66). In contrast, QoL reported by the parents hardly correlated with severity as observed by the independent observers (R_s range 0.08-0.36).

DISCUSSION

In the present study the IDQoL was found to be a reliable questionnaire to determine QoL in children (aged 0-6 years) with AD in general practice.

Many studies have demonstrated the relevance of measuring QoL in AD.⁵⁻¹⁰ The NICE guidelines for management of atopic eczema in children recommend that next to measurement of severity of AD also some form of QoL assessment should be performed.¹⁸ Most studies about QoL have been performed in patients visiting the dermatologist. However, in many countries including the Netherlands, most patients with eczema are only treated by their general practitioner.

The spectrum of severity of patients visiting the GP is different from patients that are referred to a dermatologist. This difference in severity can be demonstrated by two different studies in which the TIS is used as a scale to measure severity. The first study of Willemsen et al¹⁹ was performed in children visiting the GP, the second study was done at a secondary care paediatric clinic.²⁰ In the first study the median TIS score was 2.1 in the second study the median TIS score was 4.4. As quality of life is an essential ingredient of studies in atopic dermatitis, it should also be included in studies in general practice.

Whereas the IDQoL was not developed for children of five and six years of age, we nevertheless decided to use the same instrument for these children, since the disease spectrum and activities of the children are comparable and questions are also applicable for these children. In this study only 9 out of 66 children (14%) were five or six years of age and therefore the IDQoL is performed most of the times in children of the right age category.

Similar to other studies^{5,6} the IDQoL showed good test-retest repeatability, implying that the parents filled in both questionnaires in a consistent way. A considerably lower correlation was found only for questions 4 (sleep disturbance) and 5 (problems with swimming and playing).

These questions may have been misunderstood by some parents or, as an alternative explanation, problems regarding these activities may have changed within 24 hours.

Similar to other studies,^{5,10} the IDQoL item with the highest score was itching and scratching. This is in accordance with the Dutch College of General Practitioners' guideline on AD²¹ and criteria for diagnosing AD¹³, where itch is considered to be the most prominent feature.

The severity of AD evaluated by the investigators showed low correlations with the severity according to the parents. This finding is important for the treatment of AD. Parents and physicians may interpret the severity of AD differently, which may lead to differences in expectations. For example, parents might expect additional treatment whereas the physician may consider it unnecessary; this may cause disturbance of the physician-patient relationship or treatment adherence. This discrepancy regarding disease severity warrants further investigation. It is also important when assessing parameters for AD in clinical trials. In most trials the primary outcome measure is severity of AD as determined by the investigators. The patient's assessment of severity and QoL is seldom investigated. However, since these are different aspects of the disease, both parameters should be included when studying the effects of treatments.²²

The correlations between the IDQoL and severity of AD determined by the observers (TIS scores and objective SCORAD scores) were rather low. This implies that, in our study population, the QoL in children with AD is not related to the severity of the AD as evaluated by the investigator. The severity of AD may not even influence the QoL. It is important that physicians are aware of this, because if the QoL is negatively affected it is more likely that a patient will seek a consultation. Because physicians also take the viewpoint of the patient into consideration, if the QoL is negatively affected the physician might treat these patients in a more intensive way. In conclusion, the IDQoL is a reliable questionnaire to determine QoL in children who visit the GP for their AD. However, there was a lack of correlation in the severity of the disease as assessed by parents and observers. Moreover, QoL is not correlated to severity as established by the investigators. Since interpretation of the inconvenience of AD seems to differ between parents and physician, clinical trials should not focus solely on investigator-based outcomes. Assessment of the symptoms or QoL of the study participants is an important and different aspect of AD that should be determined when investigating new treatment options in clinical trials.

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Table 1: Mean scores of separate questions of the IDQoL questionnaire assessed at different time points

| | IDQoL ₁ , t=0 Mean (SD) n=66 | IDQoL ₂ , t=24 h Mean (SD) n=58 | IDQoL ₃ , t=3 wks Mean (SD) n=65 |
|----------------------------------|---|--|--|
| Question (severity AD) | 1.89 (1.0) | 1.74 (0.98) | 1.43 (0.95) |
| 1. Itching and scratching | 1.28 (0.89) | 1.22 (0.77) | 0.97 (0.75) |
| 2. Mood | 0.53 (0.66) | 0.57 (0.68) | 0.40 (0.70) |
| 3. Time to get to sleep | 0.64 (0.76) | 0.69 (0.73) | 0.38 (0.55) |
| 4. Sleep disturbances | 0.51 (0.98) | 0.30 (0.79) | 0.21 (0.57) |
| 5. Disturbed playing or swimming | 0.30 (0.55) | 0.28 (0.48) | 0.17 (0.42) |
| 6. Disturbed family activities | 0.20 (0.47) | 0.17 (0.42) | 0.16 (0.41) |
| 7. Problems during mealtimes | 0.14 (0.35) | 0.14 (0.35) | 0.12 (0.33) |
| 8. Problems from treatment | 0.26 (0.48) | 0.31 (0.57) | 0.15 (0.40) |
| 9. Dressing problems | 0.40 (0.66) | 0.36 (0.67) | 0.18 (0.43) |
| 10. Problems at bath time | 0.49 (0.64) | 0.66 (0.83) | 0.34 (0.67) |
| Total score | 6.64 (4.32) | 6.43 (4.33) | 4.52 (3.67) |

Table 2: Test-retest reliability with 24 hrs interval (IDQoL₁ vs. IDQoL₂): total IDQoL and separate items

| | R _s | ICC |
|----------------------------------|----------------|-------|
| Total IDQoL score | 0.887* | 0.890 |
| Question (severity of AD) | 0.729* | 0.746 |
| 1. Itching and scratching | 0.711* | 0.708 |
| 2. Mood | 0.872* | 0.790 |
| 3. Time to get to sleep | 0.808* | 0.830 |
| 4. Sleep disturbances | 0.503* | 0.485 |
| 5. Disturbed playing or swimming | 0.523* | 0.589 |
| 6. Disturbed family activities | 0.604* | 0.615 |
| 7. Problems during mealtimes | 0.656* | 0.659 |
| 8. Problems from treatment | 0.693* | 0.655 |
| 9. Dressing problems | 0.888* | 0.941 |
| 10. Problems at bath time | 0.723* | 0.677 |

* p<0.001

Table 3 Correlation between IDQoL and severity of AD according to parents and investigators

| | R_s First visit, n=66 | R_s Second visit, n=65 |
|--|--|---|
| Severity parent vs. severity investigator (SCORAD) | 0.285 (p=0.02) | 0.451 (p<0.001) |
| Severity parent vs. severity investigator (TIS) | 0.303 (p=0.013) | 0.506 (p<0.001) |
| IDQoL vs. severity parent | 0.728 (p<0.001) | 0.662 (p<0.001) |
| IDQoL vs. severity investigator (SCORAD) | 0.080 (p=0.523) | 0.248 (p=0.047) |
| IDQoL vs. severity investigator (TIS) | 0.134 (p=0.284) | 0.356 (p=0.004) |