

INVESTIGATIVE REPORT

Quality of Life Measurement and its Relationship to Disease Severity in Children with Atopic Dermatitis in General Practice

Rosalinda W.C. VAN VALBURG¹, Marjolein G. WILLEMSSEN¹, Pauline C. DIRVEN-MEIJER², Arnold P. ORANJE³, Johannes C. VAN DER WOUDE¹ and Heleen MOED¹

¹Department of General Practice, Erasmus MC-University Medical Center Rotterdam, ²General Practice, Renswoude, ³Department of Paediatrics (Paediatric Dermatology), Erasmus MC-University Medical Center Rotterdam and Sophia Children's Hospital, The Netherlands

Atopic dermatitis (AD) has a big impact on quality of life. The usefulness of health-related quality of life questionnaires for children with AD in general practice, and the relationship of quality of life to disease severity, as assessed by parents and by investigators, however, is not known. This study used the Infants' Dermatitis Quality of Life Index (IDQoL) to assess quality of life in children with AD selected from general practice. Severity of AD was determined by investigators and parents using the objective SCORAD (SCORing Atopic Dermatitis), the TIS (three-item severity scale), or by an additional question on the IDQoL. A total of 66 patients (41% boys, mean age 31 months) were included. Correlations between disease severity assessed by parents and by investigators were low (R_s 0.29–0.51). Correlations between IDQoL and severity assessed by investigators were also low (R_s 0.08–0.36). However, correlations between IDQoL and severity according to parents were high (R_s 0.67–0.73). In conclusion, disease severity and disease-related quality of life are different aspects of AD and must be taken into consideration when evaluating treatment or investigating new dermatological therapies in trials. *Key words:* atopic dermatitis; children; disease severity; quality of life; general practice.

(Accepted September 20, 2010.)

Acta Derm Venereol 2011; 91: 147–151.

Heleen Moed, Department of General Practice, Room GK1046, Erasmus MC-University Medical Center, Rotterdam, P O Box 2040, 3000 CA Rotterdam, The Netherlands. E-mail: h.moed@erasmusmc.nl

Atopic dermatitis (AD) is an inflammatory skin disease characterized by erythematous, papular or vesicular lesions in the acute form, and by lichenification in the chronic form. Patients experience itching, highly visible skin lesions, and psychological and social consequences (1).

The severity of AD is assessed with scoring systems such as the (objective) SCORAD (SCORing Atopic Dermatitis) and the 3-item severity scale (TIS) (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 effects and the 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 QoL in patients with 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 appears to be a reliable and easy-to-use questionnaire which is specifically suited to children aged ≤ 4 years with AD.

In many countries, including the Netherlands, general practitioners (GPs) are the 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.

This study therefore investigated whether the IDQoL is a reliable questionnaire to explore QoL in children with AD in general practice. Secondly, the severity of AD as determined by parents and by independent investigators, and the correlation between these two were examined. Finally, the correlation between QoL and severity of AD, as scored by patients and by investigators, was examined.

METHODS

Study population

Children (age range 0–6 years) with AD were included during a 5-month period (November 2007 to March 2008). Patients with a history of AD were selected from GP's 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 3 months, or having received a prescription for treatment of AD within the last 3 months and a diagnosis of AD according to Williams' criteria (13). Patients were excluded: (i) if there was a chronic disease other than AD, asthma, food intolerance or allergic rhinitis; (ii) in case of psychological problems that could influence follow-up; (iii) other skin conditions that precluded proper assessment of the severity of AD; and (iv) if parent or caregiver was unable adequately to read and write Dutch.

Parents of selected children received a written invitation sent by their general practitioner. All parents provided written informed consent. The prospective study was approved by the local medical ethics review board.

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) in the correct use of 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 TIS (3, 15). 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.

Infants' Dermatitis Quality of Life Index

The IDQoL questionnaire is a validated questionnaire that measures the impact of a child's dermatitis and was developed for use in children aged 0–4 years (5, 10). The present study examined the IDQoL in children aged 0–6 years.

The IDQoL includes 10 questions addressing symptoms and difficulties with mood, sleep (2 questions), play, family activities, mealtimes, treatments, dressing and bathing. The maximum score for each of the 10 questions is 3, resulting in 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 4-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 3-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 h later by the same parent (IDQoL₂) and was returned in a prepaid envelope. A 24-h 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 completed 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.

R_s and ICC results above 0.75 were classified 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, IL, USA).

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 from the database of 45 GPs. These selected patients were invited by post to participate. Of these, 89 had self-reported complaints of AD at the time of invitation and were willing to participate. A final total of 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% were male.

Infants' Dermatitis Quality of Life Index

IDQoL₁ was completed for all patients during the first home visit. For the 66 patients, 58 parents (88%) returned the IDQoL₂ after 24 h, 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 (standard deviation (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 I). 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 I).

Test-retest reliability of the Infants' Dermatitis Quality of Life Index

There was excellent agreement between scores for IDQoL₁ and IDQoL₂ ($R_s=0.89$, $p<0.001$). The ICC

Table I. Mean scores of separate questions of the Infants' Dermatitis Quality of Life Index (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 weeks Mean (SD) n=65
Question about the severity of atopic dermatitis	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)

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 II).

Severity of atopic dermatitis

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 h 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 atopic dermatitis 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 III).

Table II. Test-retest reliability with 24-h interval (Infants' Dermatitis Quality of Life Index (IDQoL₁ vs. IDQoL₂)): total IDQoL and separate items

	R _s *	ICC
Total IDQoL score	0.887	0.890
Question about the 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.

ICC: intraclass correlation coefficient; AD: atopic dermatitis.

Correlation between Infants' Dermatitis Quality of Life Index and severity of atopic dermatitis

Table III 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 National Institute for Health and Clinical Excellence (NICE) guidelines for management of atopic eczema in children recommend that, in addition to measurement of severity of AD, some form of assessment of QoL should also be performed (18). Most studies of 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 (15).

Table III. Correlation between Infants' Dermatitis Quality of Life Index (IDQoL) and severity of atopic dermatitis (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)

SCORAD: SCORing Atopic Dermatitis; TIS: three-item severity score.

The spectrum of severity of patients visiting the GP is different from patients who 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 al. (19) was performed in children visiting the GP, the second study was performed at a secondary care paediatric clinic (20). In the first study the median TIS score was 2.1, and 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 5 and 6 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 5 or 6 years of age and therefore the IDQoL is performed most of the time in children of the correct age category.

Similar to other studies (5, 6) the IDQoL showed good test-retest repeatability, implying that the parents completed 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 h.

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 AD (21) and criteria for diagnosing AD (13), 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 lead to problems with the physician-patient relationship or with 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 for determining QoL in children with AD presenting to the GP. However, there is a lack of correlation between the severity of the disease as assessed by parents and as assessed by observers. Moreover, QoL is not correlated with severity as established by the investigators. Since interpretation of the inconvenience of AD seems to differ between parents and physicians, clinical trials should not focus solely on investigator-based outcomes. An assessment of the symptoms and QoL of the study participants should be included when investigating new treatment options in clinical trials.

The authors declare no conflicts of interest

REFERENCES

1. Verboom P, Hakkaart-Van Roijen L, Sturkenboom M, De Zeeuw R, Menke H, Rutten F. The cost of atopic dermatitis in the Netherlands: an international comparison. *Br J Dermatol* 2002; 147: 716-724.
2. Charman C, Chambers C, Williams H. Measuring atopic dermatitis severity in randomized controlled clinical trials: what exactly are we measuring? *J Invest Dermatol* 2003; 120: 932-941.
3. Wolkerstorfer A, de Waard-van der Spek FB, Glazenburg EJ, Mulder PG, Oranje AP. Scoring the severity of atopic dermatitis: three item severity score as a rough system for daily practice and as a pre-screening tool for studies. *Acta Derm Venereol* 1999; 79: 458-465.
4. Oranje AP, Glazenburg EJ, Wolkerstorfer A, de Waard-van der Spek FB. Practical issues on interpretation of scoring atopic dermatitis: the SCORAD index, objective SCORAD and the three-item severity score. *Br J Dermatol* 2007; 157: 645-648.
5. Lewis-Jones MS, Finlay AY, Dykes PJ. The Infants' Dermatitis Quality of Life Index. *Br J Dermatol* 2001; 144: 104-110.
6. Lawson V, Lewis-Jones MS, Finlay AY, Reid P, Owens RG. The family impact of childhood atopic dermatitis: the Dermatitis Family Impact Questionnaire. *Br J Dermatol* 1998; 138: 107-113.
7. Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. *Br J Dermatol* 1995; 132: 942-949.
8. Whalley D, McKenna SP, Dewar AL, Erdman RA, Kohlmann T, Niero M, et al. A new instrument for assessing quality of life in atopic dermatitis: international development of the Quality of Life Index for Atopic Dermatitis (QoLIAD). *Br J Dermatol* 2004; 150: 274-283.
9. Chamlin SL, Lai JS, Cella D, Frieden IJ, Williams ML, Mancini AJ, et al. Childhood Atopic Dermatitis Impact

- Scale: reliability, discriminative and concurrent validity, and responsiveness. *Arch Dermatol* 2007; 143: 768–772.
10. Beattie PE, Lewis-Jones MS. An audit of the impact of a consultation with a paediatric dermatology team on quality of life in infants with atopic eczema and their families: further validation of the Infants' Dermatitis Quality of Life Index and Dermatitis Family Impact score. *Br J Dermatol* 2006; 155: 1249–1255.
 11. Lamberts H, Wood M. International classification of primary care. New York: Oxford University Press; 1987.
 12. World Health Organization (WHO). [2007 November] Available from: <http://www.whooc.no/atcddd>, ATC/DDD Index 2007, WHO Collaborating Centre for Drug Statistics Methodology.
 13. Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation. *Br J Dermatol* 1994; 131: 406–416.
 14. Kunz B, Oranje AP, Labreze L, Stalder JF, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. *Dermatology* 1997; 195: 10–19.
 15. Dirven-Meijer PC, Glazenburg EJ, Mulder PG, Oranje AP. Prevalence of atopic dermatitis in children younger than 4 years in a demarcated area in central Netherlands: the West Veluwe Study Group. *Br J Dermatol* 2008; 158: 846–847.
 16. Finlay AY, Lewis-Jones MS. Dutch version of the The Infant's Dermatitis Quality of Life Index questionnaire. [2007 November] Available from: <http://www.dermatology.org.uk/index.asp?portal/quality/idqol.html>.
 17. Fleiss JL. Statistical methods for rates and proportions. 2nd edn. New York: Wiley, 1981.
 18. National Institute for Health and Clinical Excellence (NICE). Atopic eczema in children, Management of atopic eczema in children from birth up to the age of 12 years. NICE clinical guideline 57. London: NICE; 2007.
 19. Willemsen MG, van Valburg RW, Dirven-Meijer PC, Oranje AP, van der Wouden JC, Moed H. Determining the severity of atopic dermatitis in children presenting in general practice: an easy and fast method. *Dermatol Res Pract* 2009 Nov 8.
 20. Cosickic A, Skokic F, Colic-Hadzic B, Jahic M. Clinical characteristics and estimation severity of the atopic dermatitis in children. *Med Arh* 2010; 64: 178–182.
 21. Cleveringa JP, Dirven-Meijer PC, Hartevelde-Faber G, Nonneman MMG, Weisscher P, Boukes FS. [Dutch College of General Practitioners' guideline on atopic dermatitis]. *Huisarts Wet* 2006; 49: 458–465 (in Dutch).
 22. Townshend AP, Chen CM, Williams HC. How prominent are patient-reported outcomes in clinical trials of dermatological treatments? *Br J Dermatol* 2008; 159: 1152–1159.