Dermatological Applications of Needs-Based Quality of Life Instruments

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ABSTRACT

Needs-based instruments have been developed for a wide range of diseases. Recently, they have been applied widely in dermatology. This paper describes these applications and shows how they have proved of value.

Keywords: clinical meaningfulness, PIQoL-AD, PSORIQoL, QoLIAD, RGHQoL.

Atopic Dermatitis

PIQoL-AD

Clinical trials. The Parents’ Index of Quality of Life in Atopic Dermatitis (PIQoL-AD) has been employed as an outcome measure in several clinical trials [1]. It was included in two 26-week pediatric atopic dermatitis (AD) trials with identical designs conducted in the US [2]. These were designed to evaluate the efficacy and safety of pimecrolimus (Elidel®, SDZ ASM 981; Novartis Pharmaceuticals, East Hanover, NJ, USA) cream 1%. A secondary aim of both trials was to evaluate the QoL impact of pimecrolimus compared with its vehicle. Patients were randomized to receive either pimecrolimus or vehicle for 6 weeks after which all participants received the active treatment for a further 20 weeks.

PIQoL-AD scores were available for 241 cases at baseline (158-pimecrolimus, 83-vehicle), 193 at 6 weeks (132 pimecrolimus, 61 vehicle), and 161 at 6 months (113-pimecrolimus, 48-vehicle). Improvement in parents’ QoL was seen for both groups between baseline and 6 weeks (P < 0.001 pimecrolimus, P < 0.05 vehicle) and 6 months (P < 0.001 both groups). Analysis of covariance conducted on PIQoL-AD scores at 6 weeks showed statistically significant superiority of pimecrolimus compared with vehicle (P < 0.05). These trials indicated that the PIQoL-AD is sensitive to changes in QoL in the parents of children being treated for AD and its expediency for use in clinical trials was confirmed.

PIQoL-AD data are also available from two 12-month international clinical trials evaluating the efficacy and safety of pimecrolimus in the long term treatment of pediatric AD [3,4]. Both trials were randomized and double-blinded and compared two treatment strategies, one involving the use of emollients, pimecrolimus, and topical corticosteroids, the other “usual care,” emollients plus topical corticosteroids, with a vehicle cream to maintain study blinding. Trial A involved infants aged between 3 months and 2 years, while trial B included children aged 2 to 17 years. QoL assessments were conducted at baseline, 6 weeks, 6 months, and 12 months.

PIQoL-AD scores were available for 154 cases in trial A (126 pimecrolimus, 28 usual care) and 231 cases in trial B (157 pimecrolimus, 74 usual care). Generalized linear modelling of PIQoL-AD scores at each postbaseline visit showed a greater impact on QoL for pimecrolimus compared with control at all time points in both trials, confirming findings from the earlier shorter term trials.

Clinical meaning of PIQoL-AD scores. Data from clinical trials in which the PIQoL-AD was employed were analyzed to examine the clinical meaning of PIQoL-AD scores [5]. These secondary analyses were aimed at gaining a clearer understanding of the underlying meaning of PIQoL-AD absolute and change scores.

An anchor-based method of determining clinical significance was employed. PIQoL-AD scores were anchored to four AD severity indicators (the Eczema Area Severity Index (EASI [6]); the Investigator’s Global Assessment (IGA), Pruritus Severity (PRU), and Subject’s Assessment of how well the
AD is controlled (SA)). Data (from at least 3 time-points) were evaluated from the 4 clinical trials of pimecrolimus cream 1% involving 1393 children with AD. Low levels of correlation (0.38–0.44) were observed between PIQoL-AD scores and the severity indicators, confirming previous findings in dermatological studies [7–9].

Data for all time-points in all trials were combined and PIQoL-AD mean, median, standard deviation, and 95% confidence interval scores were calculated for each of the severity levels in the anchor measures. The results showed a clear progression in mean PIQoL-AD scores with increasing severity of AD according to the IGA, PRU, SA, and EASI measures. There was an absence of overlap of the 95% confidence levels in most cases. Statistical tests indicated that PIQoL-AD scores varied by levels on all four anchor measures at \( P < 0.001 \).

The analyses give an indication of what the PIQoL-AD absolute and change scores mean in terms of the severity indicators. For example, the parent of a child rated as IGA category 3 (moderate disease) would be expected to score between 8.4 and 9.4 on the PIQoL-AD. The largest mean PIQoL-AD change score between any two consecutive severity levels for any of the 4 clinical measures is 3.1, which represents a reduction in pruritus from 3 (severe) to 2 (moderate).

The results also suggested that the relations between disease severity and QoL are not necessarily linear. For example, improving the severity of pruritus from 3 to 2 would produce a greater improvement in QoL than an improvement in pruritus from 1 to 0 (Fig. 1).

Discriminative ability. The application of the PIQoL-AD to parents of children with AD showed that the QoL of the parent is related to the location of AD lesions [1]. Parents whose children had AD on their hands or face had worse QoL than those whose children did not. Although the observed differences reached statistical significance \((P < 0.05)\) in the UK and Germany only, the number of children who were not affected on their hands or face was relatively small in most countries (see Fig. 2).

The PIQoL-AD was also able to show differences at the 99% significance level between severity groups (mild, moderate, quite/very severe) in all countries, with scores deteriorating with increased severity of the child’s AD.

**QoLIAD**

Application of the QoLIAD. The international application of the Quality of Life Index for Atopic Dermatitis (QoLIAD [10]) designed for use with adults also found that QoL was dependent on the location of AD lesions. Higher QoLIAD scores, indicating worse QoL, were observed for those whose face or hands were affected (Fig. 3) with these differences reaching statistical significance in the UK, France, and Germany. In contrast, the Psychological General Well-Being Scale [11] failed to show differences associated with location of lesions in this or the PIQoL-AD validation study reported above.
To date the QoLIAD has only been used in a trial in Germany [12]. The study involved 192 patients with mild-to-severe AD who were randomized to receive either pimecrolimus cream 1% or vehicle cream for 24 weeks. Statistically, a significantly greater improvement ($P = 0.002$) was observed for patients in the pimecrolimus group than for those in the control group. In the two groups, the QoLIAD scores improved by 25.6% and 7.4%, respectively.

Psoriasis

**PSORIQoL and PSAQoL**

*Application of PSORIQoL and PSAQoL.* As with the PIQoL-AD and QoLIAD, scores on the UK and US versions of the Psoriasis Index of Quality of Life (PSORIQoL [13]) were also related to whether or not patients had lesions on their face and/or hands. In contrast, Psoriatic Arthritis Quality of Life (PsAQoL [14]) scores were unrelated to whether or not facial skin was affected. However, patients whose hands were affected by psoriasis scored significantly worse than those whose hands were not affected ($P < 0.001$).

It is significant that it was consistently found that the visibility of dermatological disease is important in determining the QoL of the affected patient. Severity indicators such as the EASI and PASI scores do not take this factor into account, possibly reducing the level of association between severity and QoL measures.

The recently developed PSORIQoL has only been employed in a small-scale trial with patients. The measure is currently being adapted for use in a number of European languages and French- and English-Canadian versions are also being developed.

**Recurrent Genital Herpes**

**RGHQoL**

*Application of RGHQoL.* In a study by Patel and colleagues [15], the Recurrent Genital Herpes Quality of Life instrument (RGHQoL [16]) was employed to assess the impact of suppressive antiviral therapy on the QoL of 1349 patients with recurrent genital herpes (RGH). Mean RGHQoL change scores were significantly ($P < 0.05$) greater from baseline to 3, 6, and 12 months in the treatment groups (valaciclovir and acyclovir) than in the placebo group. Retrospective analysis also indicated that, at baseline, patients who had experienced more than 10 RGH outbreaks in a year had much poorer QoL than patients who experienced fewer outbreaks. The study confirmed the sensitivity of the RGHQoL to changes in QoL associated with active treatment.

In a later study [17], the RGHQoL was used together with the SF-36 to gauge perceptions of 298 patients about the burden of RGH. The RGHQoL was able to discriminate between patients who varied according to the frequency of RGH outbreaks, with those experiencing fewer outbreaks obtaining significantly ($P < 0.002$) better RGHQoL scores. In contrast, SF-36 scores did not vary with outbreak frequency.

*Other research with the RGHQoL.* It has been shown that both relative and absolute utility values can be elicited from RGH patients’ preferences for situations derived from RGHQoL items [18]. This represents the first work undertaken to derive utility values from a disease-specific QoL instrument. Using conjoint analysis for the derivation of relative utility and time trade-off and ranking exercises for absolute utility derivation, it was shown that utility values could be elicited suitable for use in QALY-type analyses.

**Summary**

This paper has outlined instances of the application of needs-based QoL instruments in dermatology.
Use of measures specific to atopic dermatitis (pediatric and adult), psoriasis, psoriatic arthritis, and recurrent genital herpes have been described. The measures have been applied in both clinical trials and nonclinical investigative studies. It is hoped that studies of the clinical meaning of QoL instruments (such as that of the PIQoL-AD) which helps relate QoL to measures of disease severity will encourage greater use of QoL instruments in dermatological research.

References


