Title: Content validity and assessment of the psychometric properties and score interpretation of a pruritus numeric rating scale in atopic dermatitis

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Introduction

Pruritis is a key symptom of Atopic Dermatitis (AD); mitigating itch is an important outcome of treatment. The Pruritus Numeric Rating Scale (PNRS) is a single item that assesses worst itch severity over the past 24 hours using an 11-point NRS ranging from 0 (No itch) to 10 (Worst itch imaginable).

Objectives

This mixed-methods study aimed to gather evidence regarding the content validity and psychometric properties of the PNRS to determine whether it is fit-for-purpose for use in AD clinical trials.

Qualitative Methods

Concept elicitation and cognitive interviews with 21 patients (≥ 12 years) with moderate-to-severe AD were conducted to understand patients' experiences with AD and debrief the PNRS. Recruitment targets were developed to ensure diversity in age, sex, race/ethnicity, and educational background. Interview transcripts were analyzed thematically, and saturation was assessed to ensure data adequacy. Concepts extracted from interviews were categorized into a conceptual model of patient experience of itch in AD. Debriefing analysis assessed patients' understanding of the item and response choices. Patients' interpretations of meaningful change for the PNRS were compiled.

Quantitative Methods

Data collected daily from adults with moderate-to-severe AD enrolled in a phase 2b, randomized, double-blind, placebo-controlled study (NCT03443024) were used to assess the psychometric performance of the PNRS. This scale was summarized by a prorated weekly average for each visit (mean of the available assessments during the week preceding the visit). Test-retest reliability, construct validity, and ability to detect change (responsiveness) were assessed. Reliability was assessed by computing intraclass correlation coefficients [ICCs] between Week 12 and Week 16 in a subsample of patients who had no change in the Investigator Global Assessment [IGA] between the two timepoints of interest. Construct validity was assessed by computing polychoric correlation coefficients with clinician-reported outcomes (ClinROs) and patient-reported outcomes (PROs). Responsiveness was assessed by calculating effect-sizes (ES) in subgroups of patients defined by the Global Assessment of Change – AD

(GAC-AD) and change from baseline in IGA at Week 16. Anchor-based methods (using IGA and GAC-AD as anchors) were used to determine meaningful within-patient change (MWPC) in the PNRS.

Qualitative Results

15 adult and 6 adolescent patients aged 12-64 years were interviewed. All reported some itching within the last 24 hours; 12/21 rated their worst itching at 6 or 7 points on the 11-point PNRS. All patients confirmed that itch is a core concept in AD (n=20 reporting spontaneously, n=1 probed). Saturation was met for symptoms related to AD. 21 unique AD symptom concepts were organized into a conceptual model. Cognitive interview results indicated that the PNRS is relevant, appropriate, and interpreted as intended by adults and adolescents and that its recall period and response scale are acceptable and well-understood. Most patients stated that a 2-point (n=6) or 3-point (n=10) decrease in PNRS score indicated meaningful improvement. Patients described how improvement on the PNRS would be reflected in their day to day lives in a variety of ways, including itch being less noticeable and causing less interference in day-to-day activities (e.g., distraction from work or schoolwork, interference with sleep), not feeling compelled to scratch (in private, in public, or to an extent that causes skin damage), and not having to take regular steps to prevent or mitigate itching.

Quantitative Results

Patient characteristics are presented in Table 2. In stable patients defined with the IGA, ICC was 0.89 between Week 12 and Week 16. Lower correlations were observed with ClinROs than with PROs, as expected, and correlations were higher at Week 16 than at baseline. Large ES (> 0.80) were observed for improvement according to the change in IGA and according to the GAC-AD at Week 16; too few patients were in the worsened groups to draw solid conclusions. MWPC was defined as a 3-point improvement using the clinical trial data.

Conclusion

The PNRS provides a valid and reliable patient-reported measure of itching severity in patients with AD and can detect change. A 3-point improvement on the PNRS reflects MWPC according to qualitative and quantitative data. These findings provide evidence supporting the scale is fit-for-purpose for inclusion as an endpoint to evaluate the efficacy of AD treatments in moderate-to-severe AD patients.

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DISCLOSURES

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