Title: Content validity and assessment of the psychometric properties and score interpretation of a Sleep-Loss scale score in atopic dermatitis

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Introduction

Sleep interference associated with pruritus is a key impact of atopic dermatitis (AD) and can negatively affect quality of life; mitigating itch and its impact on sleep is thus an important outcome of AD treatment. However, no gold-standard patient-reported outcome (PRO) measure of sleep interference due to itch exists. A novel PRO measure, the Sleep-Loss Scale, is a single-item developed to assess itch interference with sleep during the previous night using a 5-point response scale ranging from 0 (“Not at all”) to 4 (“Unable to sleep at all”).

Objectives

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

Qualitative Methods

We conducted concept elicitation and cognitive interviews with moderate-to-severe AD patients to examine the impact of AD-related itch on sleep and debrief the Sleep-Loss Scale with both adults and adolescents. 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 sleep loss in AD. Debriefing analysis assessed patients’ understanding of the item and response choices. Patients’ interpretations of meaningful change for the scale 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 Sleep-Loss scale. 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 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 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 Sleep-Loss scale score.

Qualitative Results

15 adult and 6 adolescent patients aged 12-64 years were interviewed. 19/21 patients rated their previous night's sleep interference from 1 - "a little" to 3-"quite a bit" on the 5-point Sleep Loss Scale. Patients confirmed that sleep loss due to itch is an important impact of AD; all patients reported experiencing this impact over the course of disease. Saturation was met for symptoms and sleep-related impacts in AD. Twenty-one unique concepts related to AD symptoms were organized into a conceptual model. Cognitive interview results indicated that the Sleep-Loss Scale is relevant, appropriate, and interpreted as intended by adults and adolescents, i.e., respondents distinguished between itch-related sleep interference and other factors that cause sleep interference. The scale's recall period and response scale are acceptable and well-understood, and patients were able to distinguish among the five severity levels of the scale. 11/19 patients queried stated that a 1-point decrease in score indicated meaningful improvement. Patients stated that the daily life impact of an improved score would be reflected in improved rest/energy, functioning at work or school, and mood.

Quantitative Results

Table 2 presents patient characteristics. In stable patients defined by IGA, ICC was 0.81 between Week 12 and Week 16. Except for the Hospital Anxiety and Depression Scale (HADS) scores, lower correlations were observed with ClinROs than with PROs, as expected, and correlations were higher at Week 16 than at baseline. The highest correlation was with POEM sleep item (0.9 at Week 16). Medium to large ES (> 0.50) were observed for improvement according to the change in IGA and the GAC-AD at Week 16. MWPC was defined as a 1-point improvement using the clinical trial data.

Conclusion

The Sleep-Loss Scale is a valid and reliable tool that can detect change. A 1-point improvement on the scale reflects an MWPC according to qualitative and quantitative data. These findings provide evidence supporting the scale is fit-for-purpose for inclusion as an endpoint in moderate-to-severe AD.

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