Development of a Pediatric Version of the Study Medication Withdrawal Questionnaire

Andrew Palsgrove,[1] Dorothee Oberdhan,[1] Mark J. Atkinson,[1] Jason C. Cole,[2] Caroline L. Ward,[1] Manit Srisurapanont[3]

[1]Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, USA; [2]P3 Research Consulting, Inc., Torrance, CA, USA; [3]Chiang Mai University, Chiang Mai, Thailand

Introduction

- Discontinuation of common medications used to treat attention-deficit/hyperactivity disorder (ADHD) may be associated with withdrawal symptoms[1]
- As withdrawal symptoms can negatively impact patients, it is important to assess these symptoms in clinical trials of ADHD medications
- The Study Medication Withdrawal Questionnaire (SMWQ) assesses withdrawal symptoms in adults,[2] but it has been suggested that different questions may be needed for assessment in pediatrics; no pediatric-specific adaptation exists

Objective

- To develop a new pediatric questionnaire based on the SMWQ for assessing medication withdrawal symptoms in children with ADHD

Methods

Inclusion Criteria

- Parent/guardian participants with a child aged 4–7 years with ADHD and children aged 8–17 years with a parent-reported diagnosis of ADHD were eligible if the child was:
  - Taking or had taken ADHD medication for ≥3 months, was fluent in English, and was willing to participate in one 60-minute audio-recorded interview
- Efforts were made to recruit participants taking a "drug holiday," defined as deliberately not taking ADHD medication for ≥2 consecutive days

Exclusion Criteria

- Participants with visual, auditory, cognitive, or linguistic impairments that could prevent the understanding and answering of questions were excluded

Development of Initial Questionnaires

- Literature searches were conducted for concepts related to medication withdrawal in children and adolescents (defined as aged 4–12 and 13–17 years, respectively)
- Initial draft questionnaires suitable for various age groups were developed according to ISPOR[3] and FDA[4] guidances, based on literature-derived concepts and consultation with expert clinicians
- After development of draft questionnaires, recruited participants provided feedback in concept confirmation and debriefing interviews

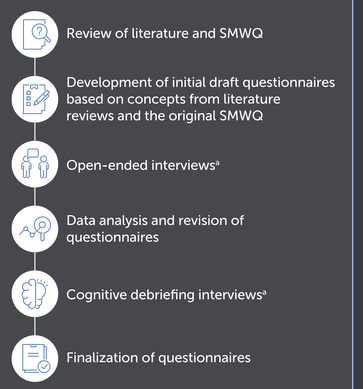
Participant Interviews

- Interviews with parents or guardians of children aged 4–7 years and with children aged 8–17 years with ADHD were conducted in 2 parts
  - Open-ended questions designed to understand participants' experiences with ADHD medications and symptoms of withdrawal
  - Cognitive debriefing to assess participants' understanding of the items and response options
    - Interviewers asked specific follow-up questions to gain additional clarity

Data Analysis

- Interviews were recorded, and anonymized transcripts were created
- A coding guide document linked to the study objectives was developed and debriefed with the coding team
- Transcripts were analyzed thematically through detailed line-by-line open and inductive coding using ATLAS.ti software (ATLAS.ti Scientific Software Development GmbH)
- After review of the codes and associated quotes from the first 2 transcripts, Modus Outcomes researchers revised a common codebook to reach coder agreement; this was revised further as new concepts emerged in the remaining transcripts
- Further revisions were made after analysis of interview data from the first 7 parents and 9 children; revised versions were debriefed with the remaining participants
- Interim data from an ongoing clinical trial was used to evaluate the questionnaires

Figure 1. Overview of Study Methods



[a]Includes interviews with parents/guardians of children aged 4–7 years with ADHD, and with children aged 8–17 years with ADHD.
ADHD, attention-deficit/hyperactivity disorder; SMWQ, Study Medication Withdrawal Questionnaire.

Results

Table 1. Participant Demographics and Characteristics

Parameter	Parents of Children With ADHD Aged 4–7 Years[a] (n=11)	Children With ADHD Aged 8–17 Years (n=15)
Age, mean (range), years	6 (4–7)	11 (8–16)
ADHD subtype, n (%)		
Predominantly inattentive	1 (9)	3 (20)
Predominantly hyperactive	1 (9)	1 (7)
Combined	8 (73)	11 (73)
Other	1 (9)	0
Gender identity, n (%)		
Male	4 (36)	12 (80)
Female	7 (64)	2 (13)
Trans-male/nonbinary	0	1 (7)
Ethnicity, n (%)		
Non-Hispanic/ non-Latino	1 (9)	11 (73)
Hispanic/Latino	10 (91)	3 (20)
Preferred not to answer	0	1 (7)
Race, n (%)		
White	9 (82)	14 (93)
Biracial	0	1 (7)
Asian	2 (18)	0
Current education level, n (%)		
Preschool	1 (9)	0
Grades K-5	10 (91)	8 (53)
Grades 6-8	0	4 (27)
Grades 9-12	0	3 (20)
Living situation, n (%)		
Both parents	8 (73)	10 (67)
One parent	2 (18)	2 (13)
Both parents, 2 households	0	1 (7)
Other family member or guardian	1 (9)	2 (13)

[a]Characteristics of children aged 4–7 provided by parent(s) or guardian(s).
ADHD, attention-deficit/hyperactivity disorder; K, kindergarten.

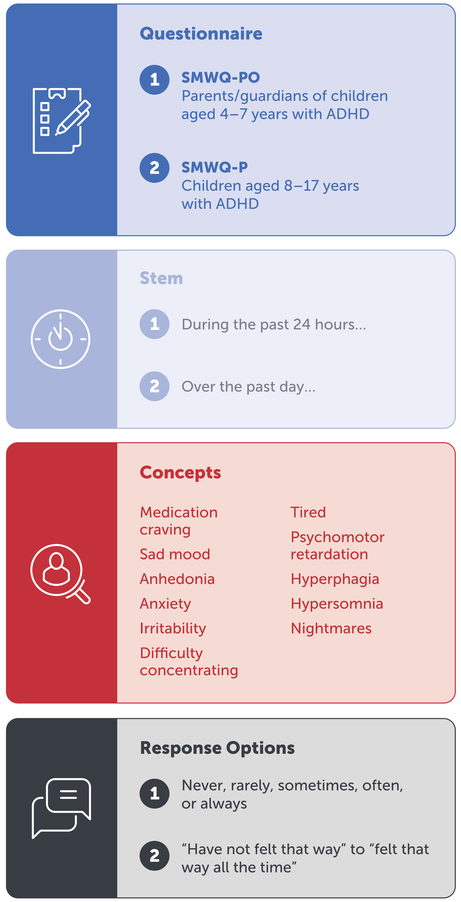
Concept Elicitation

- Concepts elicited regarding drug holiday experiences included difficulty staying focused, feeling agitated or cranky, wanting to eat more, being forgetful, feeling hyperactive (and related behavioral impacts), feeling overwhelmed, losing track of time, having a headache, legs feeling tired, and having a stomachache
- Exploration of the understanding of the word "craving" revealed that 4 of 15 participants (aged 8, 8, 9, and 11 years) did not know the meaning of the word

Questionnaire Finalization

- After iterative rounds of edits and review, two 11-item questionnaires were finalized
  - The SMWQ–Pediatric Observer (SMWQ-PO) questionnaire for parents or guardians of children aged 4–7 years with ADHD
  - The SMWQ–Pediatric Self-Report (SMWQ-P) questionnaire for children aged 8–17 years with ADHD

Figure 2. Structure of the SMWQ-PO and SMWQ-P



ADHD, attention-deficit/hyperactivity disorder; SMWQ-PO, Study Medication Withdrawal Questionnaire (SWMQ)–Pediatric Observer; SMWQ-P, SMWQ–Pediatric Self-Report.

Questionnaire Psychometrics

- The SMWQ-PO and the SMWQ-P have been operationalized in 2 ongoing phase 3 studies in pediatric ADHD
- Data from 218 participants on the SMWQ-P in these ongoing clinical trials achieved an internal consistency of $\alpha = 0.76$, which was slightly below the target of $\alpha = 0.80$
  - Exploration of item-level reliability revealed that item 1 (medication craving) was poorly related to every other item (corrected item total correlation = −0.04)
  - Removing item 1 resulted in an internal consistency of $\alpha = 0.79$ and 0.80 for standardized items
- Confirmatory factor analysis was conducted to confirm the validity of using items 2 through 11 as a total score, with item 1 scored separately
  - The model obtained strong fit (comparative fit index = 0.95; Tucker-Lewis index = 0.93; root mean squared error of approximation = 0.053; standardized root mean square residual = 0.047)
- SMWQ-PO results are similar and will be confirmed via additional data

Limitations

- The study is limited by a small sample size for each age group
- Participants were not currently in a withdrawal state during the interviews
- Although drug holiday was used as a proxy for withdrawal, there may be concepts that were not elicited
- Further research is necessary for psychometric validation and scoring development

Conclusions

- The new SMWQ-PO and SMWQ-P are fit-for-purpose questionnaires with appropriate content validity designed to assess symptoms of withdrawal in pediatric ADHD
- Based on the current results, the SMWQ-P has 2 scores: a summary score (items 2–11) and a medication craving score (item 1)
  - Additional analyses are planned to further validate this instrument
- Evaluation of the psychometric properties of the SMWQ-PO is ongoing

References

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Disclosures

Andrew Palsgrove, Dorothee Oberdhan, Mark Atkinson, and Caroline Ward are employees of Otsuka Pharmaceutical Development & Commercialization, Inc.
Jason C. Cole serves as a consultant for Otsuka.
Manit Srisurapanont developed the SMWQ (Adult Version) and serves as a consultant for Otsuka.

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