PCR115

Qualitative assessment of the Idiopathic Hypersomnia Severity Scale: Suitability for use as a clinical trial endpoint as demonstrated in NCT NCT05156047

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Background

- Individuals with idiopathic hypersomnia (IH) can exhibit normative or even prolonged objectively measured sleep parameters (Arnulf et al. 2019)
- Objective sleepiness measures may not appropriately quantify key IH symptoms such as excessive daytime sleepiness (EDS), sleep inertia and cognitive difficulties; thus, their value in evaluating treatment effectiveness is uncertain (Arand and Bonnet 2019)
- Patient-reported outcome (PRO) measures such as the idiopathic hypersomnia severity scale (IHSS; Dauvilliers et al. 2019) which measures 3 key IH symptom domains and their functional consequences may be more appropriate for measuring treatment benefit than objective sleepiness measures
- Evidence is needed to further support the IHSS as a fit-for-purpose measure of patient-reported burden of IH symptoms

Objectives

- Explore the salient symptoms and their functional consequences in individuals living with IH
- Examine how the content of the IHSS maps to participants' descriptions of living with their IH condition

Methods

Qualitative interviews with a subset of participants (n=61) who were consecutively recruited at the completion of study NCT05156047

1:1 semi-structured interviews (≈ 60 mins) conducted at the end of the last study visit via video conference

Concept Elicitation
- Participants described their experience living with IH prior to enrolling in the study
- Interviewer probed further for details as appropriate

IHSS Relevancy
- Interviewer elicited qualitative feedback on the content of the IHSS from participants
- Participants rated the relevancy of IHSS content to their experience

- Interviews were recorded and professionally transcribed. Technical difficulties precluded one interview from being transcribed
- Transcripts (n=60) were analyzed following principles in line with applied thematic (content) analysis (Guest et al. 2012) to identify salient symptoms and functional consequences of IH using NVivo qualitative data analysis software
- Relevancy ratings were double-entered into a study database and summarized descriptively

Figure 1. Spontaneously Elicited Symptoms of IH and Functional Consequences

Sleepiness
Daytime sleepiness
Unrefreshing naps
Feeling sleepy*
Dozing off during activities*
Feeling like not enough sleep
Needing naps during the day

...I was falling asleep in my car on my way to work. I was falling asleep at work. I would have to take naps during the day...then I would fall asleep on my home from work.

Morning Awakening Problems
Difficulty waking up*
Need multiple alarms

…ended up having to get on of those alarm clocks with a bed shaker because I could not wake up in the morning…

Tiredness/Fatigue
Low energy*
Tired during the day*
Fatigue/exhaustion*

…I am so wiped out and so exhausted, I am not getting anything accomplished….you never have the energy to do what a normal person can do in a day.

Disturbances to Daily Life
Difficulty at work*
Interference with relationships*
Unable to enjoy activities*
Not productive at work or home*

…I can't do things I want to do…I can't work. My relationships are affected because people don't know how to deal with it

Sleep Inertia
Long time to feel functional
Clumsiness
Talking nonsense

"…when I get up…I bump into things and trip..they call it sleep drunkenness because it's like not having a balance and for some reason…everything is just really foggy…"

Poor Quality of Wakefulness
Problems thinking clearly*
Brain fog*
Problems focusing/concentrating*
Memory issues*
Not feeling motivated*
Negative mood*

"…overall like feeling of not being able to fully wake up or be alert….like it felt really heavy a lot in…my thinking, clouded…

Bold=reported by >50% of participants
*Symptom or functional consequence reported as most bothersome by at least one participant

Table 1. Participant Characteristics

Characteristic	Interviewed (n=60)	Not-interviewed (n=79)
Age (years), mean (SD)	38.5 (10.9)	41.1 (12.6)
Sex, n (%) female	48 (80.0)	62 (78.5)
Race, n (%) White/Caucasian	54 (90.0)	69 (87.3)
Baseline ESS Score[1], mean (SD)	16.3 (3.2)	16.7 (7.9)
Baseline IHSS Score[2], mean (SD)	34.1 (5.8)	33.1 (7.9)
Baseline PGI-S (EDS)[3], mean (SD)	3.9 (0.70)	3.8 (0.70)
Baseline CGI-S (IH)[3], mean (SD)	3.7 (0.60)	3.6 (0.60)

Abbreviations: CGI-S = Clinician Global Impression of Severity; EDS = excessive daytime sleepiness;
ESS = Epworth Sleepiness Scale; IHSS = Idiopathic Hypersomnia Severity Scale; PGI-S = Patient Global Impression of Severity

[1]Ranges from 0 to 24 with scores ≥ 16 indicating severe EDS

[2]Ranges from 0 to 50 with scores > 26 indicating severe symptoms

[3]5-point verbal rating scale ranging from 1 (none) to 5 (very severe)

Table 2: Conceptual Mapping of IHSS content

IHSS Item Content	Concept Elicited	Relevant[1] n (%)
1. Ideal duration of nighttime sleep	N	37 (61.6)
2. Feel like you have not had enough sleep	Y	51 (85.0)
3. Difficult/impossible to wake up without multiple alarms or help	Y	37 (61.6)
4. How long to feel operational after getting up	Y	42 (70.0)
5. Say things that are out of character or clumsiness in morning	N	27 (45,0)
6. Take nap during the day when circumstances allow	Y	46 (76.7)
7. Ideal length of naps	N	40 (67)
8. Feel after a nap	Y	46 (76.7)
9. Struggle to stay awake during not very stimulating activities	Y	53 (88.3)
10. Hypersomnia has an impact on general condition	Y	55 (91.6)
11. Hypersomnia interferes with your intellectual functioning	Y	47 (78.3)
12. Hypersomnia affects your mood	Y	42 (70.0)
13. Hypersomnia prevents performing your daily tasks properly	Y	55 (91/6)
14. Hypersomnia interferes with driving a car?	Y	37 (61.6)

Abbreviations: IHSS = Idiopathic Hypersomnia Severity Scale

[1]Number (percent) of participants rating as relevant or very relevant

Results

- The interviewed subsample of patients with IH was representative of the overall clinical study population; the sample experienced severe EDS with a high level of burden due to their IH condition (**Table 1**)
- Twenty-four symptoms and functional consequences of IH were spontaneously elicited across 6 domains (**Figure 1**)
- Almost all patients with IH described daytime sleepiness (98%) that disrupted their life; the majority reported poor quality of wakefulness (82%), morning awakening problems (74%), sleep inertia (70%) and tiredness/fatigue (67%)
- Most IHSS items (11 of 14) mapped to the spontaneously elicited symptoms and functional consequences (**Table 2)**
- Most patients with IH (93%) rated the overall content of the IHSS:
  - *"…almost every question relates to my experience."*
  - *"…it is pretty relevant. It asks relevant questions":*
  - *"there was a good mix of questions…kind of goes through day-today things"*
- Greater than 50% of participants rated all items except one as relevant or very relevant to their experience living with IH (**Table 2)**

Conclusions

- IHSS items map to participant descriptions of their experience living with IH
- Patients with IH rated the content of IHSS items as relevant to their condition
- The 3 items that did not map to elicited concepts were all rated as relevant or very relevant by a majority of participants

This evidence supports the utility of the IHSS as an endpoint measure for assessing IH symptoms and treatment efficacy in clinical trials among patients with IH

REFERENCES

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ACKNOWLEDGMENTS

The authors would like to thank the clinical trial participants without whom this work would not be possible. The authors would like to thank Viviana Hernandez and Robert Schroeder for their design contributions

DISCLOSURES

This study was funded by Harmony Biosciences.
EM is an employee of Fortrea and KJ was an employee of Fortrea when the study was conducted
SI, MM, KW and GN are employees of Harmony Biosciences

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