

Development of the Hygiene Extension Limb position Pain (HELP) Tool to monitor waning of clinical efficacy in patients with spasticity or cervical dystonia treated with botulinum toxins

Atul Patel,¹ Stefan Wietek,² Edward Dabrowski³

¹Kansas City Bone and Joint Clinic, Overland Park, KS, United States; ²Ipsen, Cambridge, MA, United States; ³Oakland University School of Medicine and Beaumont Hospital, Grosse Pointe, MI, United States

BACKGROUND

- Spasticity, a stretch reflex disorder that manifests as a velocity-dependent increase in muscle tone, is commonly caused by upper motor neuron damage.¹
- Cervical dystonia (CD) is a chronic neurological movement disorder characterized by excessive involuntary muscle contractions leading to abnormal head movements and neck pain.²
- Intramuscular injections of botulinum neurotoxin into the affected muscles is an approved first-line treatment for upper and lower limb spasticity³ and CD symptoms.⁴
- The waning of treatment effect over time is common and is estimated to impact 80% patients regularly treated with botulinum neurotoxin A (BoNT-A).⁵
- The development of the HELP Tool, a patient-reported outcome (PRO) instrument, is needed in order to provide greater discernment of waning clinical efficacy after BoNT-A injections prior to the next scheduled treatment.
- The HELP Tool is under development for utilization by adult or pediatric patients with upper and/or lower limb spasticity, adults with cervical dystonia (CD), and parents and caregivers.
- The impact of spasticity or CD symptom recurrence on patients will be more easily gauged with the HELP Tool, which will aid in determining appropriate treatment optimization.

OBJECTIVE

- The objective of this study is to present the progress of the development of HELP Tool, a PRO instrument. The key design goals for the HELP Tool include:
 - Reportable by either patient or caregiver
 - Takes 5-10 minutes to complete
 - Self-administered
 - Easy to score
 - Usable in various settings (office/home) and media (paper/electronic)

METHODS

- Working with a consultant experienced in the development and psychometric validation of PRO instruments, a panel of 9 subject-matter experts developed preliminary ~20-item questionnaires for potential use with patients with spasticity and CD and their parents/caregivers.
- Content validity will be assessed qualitatively (via patient feedback) and the questionnaire will be modified to provide a clinically useful screening tool to identify when treatment is waning prior to the next scheduled BoNT-A treatment.
- Psychometric properties of the new tool will be assessed quantitatively.
- Patient satisfaction with treatment relevant to symptoms will also be evaluated.
- After the first 11 interviews of adult spasticity and CD patients for concept elicitation (CE), a virtual advisory board with subject matter experts was conducted to develop and refine a relevant and meaningful HELP Tool and ensure content validity.
- A second round of testing the questionnaires via interviews in a larger patient and parent/caregiver cohort is underway, with subsequent HELP Tool finalization.

RESULTS

Patient Interviews

- CE interviews were conducted with 11 patients and caregivers in the US and Canada (3 patients with CD, 4 with spasticity due to stroke, and 4 with spasticity due to cerebral palsy; **Table 1**) to review the draft questions and discuss the following feedback from within the last year:
 - Experience with spasticity
 - Perceived changes related to botulinum toxin injections
 - Description of experiences and changes from one injection to the next injection

Table 1. Interviews conducted to elicit user feedback

	Condition					TOTAL
	Cervical dystonia	Cerebral palsy	Spinal cord injury	Stroke	Traumatic brain injury	
Muscle Area						
Upper limb	–	1 (torso)	–	2	–	3
Lower limb	–	4	–	2	–	6
Neck	3	–	–	–	–	3
CE Interviews (round 1)	3	4*	0	4*	0	11
CE + CD Interviews (round 2)	4-5	3-4	7-8	3-4	7-8	27
TOTAL	7-8	7-8	7-8	7-8	7-8	38

*Included 1 caregiver (parent) of adult child. CE, concept elicitation; CD, cognitive debriefing.

The Waning of Effect

- For many patients, the waning started around 8 to 10 weeks, even though most were on a 12-week reinjection schedule. Because it takes approximately a week after an injection to achieve the full effect, patients are undertreated for 3-5 weeks of every cycle.
- Patient discussions of waning of indications are summarized in **Tables 2 and 3**. Across both disease states feelings of being less relaxed and more mentally and physically fatigued were indications of treatment waning, as were symptoms of uncontrolled movement, spasms/tremors, stiffness, pain, and functional difficulties with walking smoothly.

Table 2. Changes reported at treatment waning in patients with cervical dystonia

Patients with CD, n=3	
Feelings	n
Less control	3
Less relaxed	2
More self-conscious; more embarrassed; more fatigue; 1 response each	
Symptoms	n
Uncontrolled movement	3
Spasms or tremors	2
Muscle stiffness/tightening; pain; 1 response each	
Function Difficulties	n
Driving	3
Using computer, working at a desk, completing a form	2
Getting comfortable in bed for sleep (e.g., change sleeping position)	2
Holding head straight; walking smoothly (with a normal gait); playing golf; 1 response each	

Table 3. Changes reported at treatment waning in patients with spasticity

Patients with spasticity, n=8	
Feelings	n
Relaxed	6
Fatigue	3
Depression	2
Increased strength	2
Risk of injury	2
Independence; embarrassment; self-conscious; control; 1 response each	
Symptoms	n
Muscle stiffness/tightening	6
Spasms or tremors	5
Pain	4
Uncontrolled movement	3
Function Difficulties	n
Put on jacket, pants (buttoning and zipping)	4
Walk fast (have to walk slower)	4
Stand for long periods of time	4
"Harder to do things"	3
Put shoes on	3
Walk smoothly (with a normal gait)	3
Stand up straight	3
Get comfortable in bed for sleep (have to change sleeping position)	2
Getting in/out of bath/shower	2
Toileting (make it to the bathroom; getting up/off toilet)	2
Carry things	2
Coordination	2
Keep good balance	2
Straighten arms	2
Stand from sitting position	2
Straighten out fingers; drive; working at a desk or writing (use hands); bend over; use stairs; straighten legs; 1 response each	

- Data suggest measuring 4 symptoms between injections: uncontrolled large movements, spasm/tremor, stiffness/tightening, and pain.
- Patient interviews identified several concepts that may be incorporated into future versions:
 - Driving, working at a computer or desk, and filling out forms will be added as functions.
 - Additional details for certain functions that include complex operations may be improved and will be probed during the next phase of cognitive debriefing interviews (eg, getting dressed/undressed may also include putting on shoes, tying shoes, or using buttons).
 - Feelings are not explicitly incorporated in the HELP Tool but may be captured by the functional questions.

Advisory Board Discussion

- The current draft of the HELP Tool (**Figure 1**) was reviewed with consultants during a virtual advisory board meeting. The following was concluded:
 - No concepts were missing from the current HELP Tool.
 - There is an agreement on the basic need for individualized goal setting and the value of the tool.
 - Advisors for CD noted pain as a particularly important symptom.
 - CD may need a separate tool from spasticity.
 - In pediatric spasticity, goals often change as the child grows.
- Limitations: small initial population; and testing in larger cohorts is still ongoing.

Figure 1. Current draft of the HELP Tool concepts

		Very relevant or Somewhat relevant, n
Hygiene	<input type="checkbox"/> Brushing hair or teeth	4
	<input type="checkbox"/> Bathing or showering	4
	<input type="checkbox"/> Using the toilet (stand from a seated position)	3
Activities of Daily Life	<input type="checkbox"/> Getting dressed or undressed	5
	<input type="checkbox"/> Eating	4
	<input type="checkbox"/> Using a computer	4
	<input type="checkbox"/> Drinking	4
	<input type="checkbox"/> Sleeping	4
	<input type="checkbox"/> Preparing food or meals	4
	<input type="checkbox"/> Leisure activities or hobbies	4
	<input type="checkbox"/> Taking care of others, such as children or elderly parents	4
	<input type="checkbox"/> Household chores, such as cleaning and doing laundry	3
	<input type="checkbox"/> Shopping for groceries or other necessary household items	3
Mobility and Physical Function	<input type="checkbox"/> Yardwork/outdoor chores, such as mowing the lawn, gardening	2
	<input type="checkbox"/> Driving	2
	<input type="checkbox"/> Sitting upright (with good posture)	6
	<input type="checkbox"/> Getting in or out of bed	5
	<input type="checkbox"/> Getting in or out of a chair (or wheelchair)	5
	<input type="checkbox"/> Getting in or out of a vehicle, such as a car or van	5
	<input type="checkbox"/> Getting in or out of a bus or train	5
	<input type="checkbox"/> Standing upright (with good posture)	4
	<input type="checkbox"/> Walking outside	4
	<input type="checkbox"/> Walking or moving smoothly	4
	<input type="checkbox"/> Moving around or walking inside	4
	<input type="checkbox"/> Exercising or participating in other physical activities	4
	<input type="checkbox"/> Walking or moving quickly	3
Social Function and Relationships	<input type="checkbox"/> Working outside the home (paid or volunteer)	2
	<input type="checkbox"/> Sexual activity	4
	<input type="checkbox"/> Socializing with friends or family	3
	<input type="checkbox"/> Being in public places (around other people)	3
	<input type="checkbox"/> Dating or developing intimate relationships	3
	<input type="checkbox"/> Being physically touched	2

CONCLUSIONS

- Development and a second round of cognitive debriefing interviews with patients to finalize the HELP Tool are ongoing. Results from the patient CE interviews and advisory board discussions have been presented.
- Based on the first round of patient interviews and the discussion with subject matter experts, the following topics are being considered in the next iteration of the HELP Tool:
 - Balance and ambulatory aids (cane, 4-point cane, walker)
 - Orthotic use (donning, doffing, comfort for long-term wear)
 - Restriction/tight out forms
 - Working at a computer or desk; filling out forms
 - Driving
 - Range of motion, posturing
- The HELP Tool data will be used in the development of a user friendly PRO instrument to assist in detecting the waning of treatment effectiveness for use by patients with CD or spasticity and their caregivers.

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