

Treatment of Spasticity with Botulinum Toxin: The Stroke Patient's Perspective

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Abstract

Objective: To explore self-reported reasons why individuals continue to receive botulinum toxin for treatment of their tone related impairment (spasticity).

Methods: Qualitative cross-sectional study, using semi-structured interviews, exploring patient reports of expectations, outcomes, experiences and perceptions of botulinum toxin injections. Interviews were digitally audio recorded and transcribed verbatim. Inductive content analysis was used to identify themes. Analysis began after the first interview was completed and continued in parallel with data collection until saturation of themes was reached.

Results: Content analysis of the interview transcripts identified the following thematic categories: 1) Themes with Functional Implication, including a) Impact on Mobility, b) Impact on Activities of Daily Living Performance, and c) Regional Pain Control, as well as 2) Themes with Psychosocial Implications, including a) Limb Appearance and b) the Physician-Patient Relationship. Participants had realistic treatment goals and expectations and the decision to continue receiving botulinum toxin was based on these goals, as well as, in part, influenced by strong positive relationships with their physicians.

Conclusions: This study provides insight into why patients choose to continue receiving treatment for their spasticity. These findings can help physicians to better set individual goals, expectations and treatment plans for patients and improve outcomes.

Keywords: Qualitative; Patient interviews; Botulinum toxin; Spasticity; Stroke

Introduction

Among individuals with stroke, the rate of spasticity has been reported to be as high as 46% after one year [1], with 28-41% of individuals identifying spasticity as severe enough to significantly hinder their daily life [2-4]. Botulinum toxin type A is commonly used in the treatment of focal spasticity by acting on the presynaptic nerve at the neuromuscular junction, causing temporary inhibition of acetylcholine release thereby effectively paralyzing neurologic activity [5]. Spasticity, in the target muscle, returns over a period of 3 to 6 months post injection; as a result, individuals require repeat injections.

While Botulinum toxin type A has been shown to be effective in reducing post stroke tone-related impairment and spasticity, using outcome measures such as the Ashworth scale and modified Ashworth scale [6,7], studies attempting to measure active functional improvement have reported unclear benefit [8]. Despite the lack of objectively demonstrable functional gains, individuals receiving Botulinum toxin type A return for these injections regularly (e.g., every 3-4 months) [9] and may continue for several years. Mahoney et al. [10] have suggested that spasticity has the potential to affect seven domains of an individual's life including physical, activity, emotional,

economic, interpersonal, cognitive, and self-management. Therefore, it is possible that patients return for reasons other than improvements in function [11].

Why patients choose to receive Botulinum toxin type A has rarely been studied in the neurological population and is currently unknown among patients with stroke [12,13]. Understanding why patients continue to receive Botulinum toxin type A injections despite a lack of direct improvements in function is important from a medical perspective, and despite intuitive clinical reasons for continued use, it has not been directly studied nor documented in the scientific literature. Therefore, this paper will explore patient-perceived reasons for continuing to receive Botulinum toxin type A for post-stroke spasticity.

Methods

An ethnographic study using qualitative content analysis of semi-structured interviews that probed stroke survivor and caregiver reasons for ongoing botulinum toxin treatment for spasticity. Ethical approval was obtained from the Research Ethics Board of Western University, London, Ontario, Canada (#106931). The ethics start date of the study was October 15, 2015 and the end date was October 15, 2018. The study was funded by an unrestricted free education grant by Allergan Inc.

Participants were recruited from four tertiary outpatient spasticity clinics in London, Ontario. Clinic appointments are made by physician referral. Patients attending the clinic are typically assessed by a physician using a standardized spasticity assessment form. Based on the patient's clinical presentation and the physician's clinical judgment, treatments are provided and referrals for additional services are made (e.g., physiotherapy, occupational therapy, splinting, etc.), as appropriate. One of the key treatment modalities offered in these outpatient clinics is chemodenervation *via* Botulinum toxin type A injections.

Potential participants were identified by the treating physician and briefly informed of the study. For those who expressed interest, a research assistant explained the purpose of the study in greater detail. Those who were interested were assessed for eligibility according to the following inclusion criteria: 1) ≥ 18 years of age; 2) history of stroke; and 3) currently receiving Botulinum toxin type A injections in the upper and/or lower extremity for spasticity. Recruitment was conducted at the outpatient clinics between July 1, 2015 and June 30, 2016. Caregivers were invited to participate in the interview process if: 1) the participant expressed that they were more comfortable with the caregiver present, and/or 2) the participant was unable to communicate independently (e.g., expressive aphasia) and required a proxy. All patients, or their proxies, provided written informed consent.

Prior to recruitment, an interview guide was developed collaboratively with the outpatient physicians and researchers. The guide contained the study protocol, as well as semi-structured interview questions and prompts (Table 1). Interviews were conducted by a research assistant and questions were phrased in an open-ended

format to enable participants' freedom of expression when sharing their experience. The prompts were used to initiate conversation, progress it if it had stalled, and/or to further explore emerging topics or themes. The primary role of the interviewer was to allow the participant to share their experience, in their own words, and follow the ideas and opinions expressed by the participant. The interviews focused on patients' understanding of spasticity and Botulinum toxin type A, as well as their perception of the treatment procedure, and the overall effectiveness of the treatment. The interviewer also documented non-verbal expressions and behaviour in a reflective journal. The interviews were conducted in a private room in the clinic, lasted approximately 60 minutes in duration and were digitally audio-recorded.

All recordings were transcribed verbatim and de-identified. Two researchers reviewed the transcripts (RV, SJ) in their entirety to familiarize themselves with the content. The transcripts were then analysed using inductive content analysis, a process by which a set of codes are created from the data and then organized into patterns and themes [14]. Any discrepancy in the identification of themes was resolved through discussion with the other authors. Analysis of the transcripts commenced after the completion of the first interview and continued in parallel with data collection until thematic saturation was reached. Thematic saturation was the point at which major themes had been identified and no new information was being added to the list of themes or the detail of existing themes. To ensure thematic saturation, two other treating researchers (MP, KS) reviewed the theme and coding structure and the original transcripts. If other themes came to light, interviews were continued. Interview prompts were modified to allow for further exploration of emerging themes.

Questions	Prompts
When did you have your stroke?	
What was the diagnosis that led to you being referred to this clinic?	
Can you tell me about why you were referred to this clinic?	Do you know what you are treating when you come to this clinic? What does spasticity mean to you? What other symptoms do you have from this diagnosis? How long have you been coming to this clinic? Number of injections, location, etc.
Over the years do you feel like the injections have helped? If so, how?	What types of changes do you see before and after the injections?
How long does it take before you see improvements?	How long do these benefits last?
Do you notice any changes to your function after an injection? If so, how?	Activities of Daily Living (Try to get detail as to how performing the tasks is different before and after treatment) Walking (gait aid, speed, balance, confidence) Dressing (independent or help, devices, how long)
	Eating Hygiene Bathing (easier to move, position) Meal prep, household tasks, etc. Use of assistive devices Confidence Effort Safety Appearance Participation Endurance, strength, etc. Pain
Have you tried any other therapies or treatments, and if so, did they help?	

Is there anything that botulinum toxin does not do that you wish it could?	
Do the injections cost you money or are they covered? If they are not covered, do you think they are worth the cost?	
Do the injections cost you money or are they covered? If they are not covered, do you think they are worth the cost?	
How much longer to you see yourself receiving these injections?	
What would have to happen for you to stop getting these injections?	
Are there any other reasons you keep coming back to the clinic?	

Table 1: Interview Questions and Prompts.

Results

Thematic saturation was achieved after 19 interviews; all participants remained in the study until completion. Participants had a mean age of 58.3 ± 13.9 years (range 38-80). All but three individuals were between 1 and 9 years post stroke (4.9 ± 2.9 years); three individuals were 12, 18, and 34 years post stroke, respectively. The mean treatment duration with Botulinum toxin type A was 3.6 ± 2.2 years (range 1-9). All participants had their treatment paid for by a single payer public health funding system.

Content analysis of the interview transcripts identified two thematic categories. The first being Themes with Functional Implication, including a) Impact on Mobility, b) Impact on Activities of Daily Living Performance, and c) Regional Pain Control. The second was Themes with Psychosocial Implications, including a) Limb Appearance and b) the Physician-Patient Relationship (Table 2).

Functional Implications

Impact on mobility

The impact on mobility was identified as a key reason for returning for injections and was described by study participants as increased confidence, improved balance, and improved range of motion. Participants initially generically reported improved walking but when probed, the concept of confidence came to light rather than increased speed or quality of walking.

"[...] I feel like I am not going to trip over my left foot so just as far as fear, [...] I have more confidence"(Participant 10),

"[the patient] knows the [Botulinum toxin type A] is in there so she has a little bit of confidence, like you know they got it in there so maybe it will feel better"(Caregiver 13).

Participants described improved balance as a sense of being cantered, these comments would often co-occur with reports of increased confidence and how they were associated with a reduced fear of falling.

"A little bit in the balance but not the speed. I mean I am pretty slow now and I am really careful about not falling"(Participant 6).

"Yeah, we are not increasing her speed in any way, it is mainly the balance"(Caregiver 11).

Improved range of motion was initially described in terms of alignment, including descriptors like the foot and ankle appeared

straighter. With further probing regarding alignment, responses were changed as they described improved freedom of movement across the joint, or a sense of having a greater degree of available range in the foot and ankle.

"[...] I am much stiffer and that is what the [Botulinum toxin type A] does for me. In my terms, it loosens me up and allows me to move more freely"(Participant 7).

Impact on activities of daily living performance

Another category of function discussed is the impact on activities of daily living, which was described again as a positive increase in confidence as well as improved passive performance. Regarding activities of daily living confidence, participants and caregivers shared that the participants could do more, or participate to a greater extent, in activities of daily living tasks. When probed for detail it became clear that the actual quality of task performance or ability to perform a task had not improved, rather the participant was more willing to participate because they had increased confidence. One caregiver described a particularly difficult situation where a participant was having severe issues with activities of daily living prior to receiving Botulinum toxin type A:

"As far as dressing she had a hard time with that as she couldn't get her arm up. Activities? No, there wasn't anything there, eating, same thing, no ambition to eat. I would pretty much have to come home and try and get her to eat. She was crying all the time, she couldn't sleep. She had a hard time getting out of bed. She was up and down, up and down all night. There was so much pain"(Caregiver 13).

After the caregiver was asked how Botulinum toxin type A helped, the individual responded,

"[...] after the injections, like, holy. It is like night and day here, I think her confidence is built up when [the doctor] comes in and does that for her."

In this particular case, the injections had a significant positive impact on the participant's confidence with activities of daily living.

For the purpose of this study, passive performance was defined as care provided to an individual that required little or no active participation on their part. Improved passive participation in activities of daily living tasks was reported as important by both participants and caregivers. In general, participants and caregivers shared that Botulinum toxin type A made moving or positioning the limb easier or less of a struggle.

"It is a little easier because I can actually pull this arm out to wash under my armpits and like, you know, otherwise it is always in the way"(Participant 6)

"Yeah, like even washing my hand, like I can open it enough to get up in there where before I would have to fight just to try to get a washcloth"(Participant 8).

"[...] after it kicks in, your hand is much more flexible and instead of [the hand] being a fist, [the participant] can at least open it up" (Caregiver 19).

Regional pain control

The last item regarding functional impact was regional pain control. Several participants described the benefit achieved from Botulinum toxin type A was improvement in pain of the spastic limb or specific joint affected by tone. The reduction in pain was described as quite significant and, in some cases, reportedly led to increased ability to participate in activities, improvement in mobility, and better quality of life.

"[...] helped immensely with pain"(Participant 4)

"you know it definitely is, it is helping, it is getting rid of the pain. She has been a lot better since we have been doing this. If it wasn't for this stuff I don't think I would know what to do with her. She would be at home just crying because of so much pain."(Caregiver 13)

"[...] I really have tried to start walking again for exercise and I find without the [Botulinum toxin type A] my left leg gets really fatigued so my knee snaps back. [The physician] is helping my foot land and my knee so those two things alone help with the pain and the fatigue." (Participant 10)

For some individuals the pain was relieved completely:

"It is improved, yeah, because [the participant] used to have a lot of shoulder pain and now he doesn't have any, like [the participant] got rid of the pain in the shoulder"(Caregiver 14),

"I have had no pain since I have been getting the injections; it has taken the pain away. It has made my life more comfortable, so it has been a great thing"(Participant 17).

Psychosocial Implications

Limb appearance

Appearance of the limb was not reported as important by all participants but for those who did identify appearance as a motivator, it was significantly influential in encouraging those to return for injections. Participants spoke about how others perceive their posturing and their discomfort with the attention paid to them.

"Yeah, when it is curled up people stare at you, [...] it is embarrassing. When you are walking, you are walking home with your arm all crammed up, people do stare at you."(Participant 8)

Some individuals described the role of Botulinum toxin type A in improving one's physical appearance by reducing tone and softening or reducing the contracture. These aesthetic changes helped hands, arms, and feet to *"look a bit more normal"*(Participant 2), or *"to look better and [...] relaxed"*(Participant 9). Interestingly, one participant (19) reported that Botulinum toxin type A was used *"more as an aesthetic thing than a physical thing."*

Physician-patient relationship

The physician-patient relationship was discussed frequently among participants with specific reference to how they deferred their choice to receive Botulinum toxin type A injections to physician judgement.

"[...] we believe very much in the doctor, they are the professionals, they treat the patients."(Participant 15)

"we are leaving [the decision for treatment] up to [physician], whatever he feels that enough is enough, because he keeps trying difference places [...]."(Participant 17)

Some participants even described giving full responsibility for the decision stating;

"I guess whatever they suggest"(Caregiver 6)

"Whatever it takes we are in for it"(Participant 17).

Furthermore, participants appreciated how the physicians were accessible to them;

"It's nice to know that [the physician] is there, [...] anytime you need it just call and [the physician] will get you in just like that" (Participant 9).

Physicians were reported to fully explain participants' conditions and the treatments available to promote rehabilitation and recovery.

"[Physician] is very detailed and he explains stuff, probably puts more in than he really needs too but that is just who he is, and he takes the time to listen and is really patient [...]."(Caregiver 4)

Main Theme Categories	Sub-Themes
	<ul style="list-style-type: none"> • Impact on Mobility <ul style="list-style-type: none"> o Confidence o Balance o Range of Motion • Impact on Activities of Daily Living Performance <ul style="list-style-type: none"> o Confidence o Passive Performance • Regional Pain Control
Themes with Functional Implications	
Themes with Psychosocial Implications	<ul style="list-style-type: none"> • Limb Appearance • Physician-Patient Relationship

Table 2: Theme Categories and Subthemes.

Discussion

This study explored the patient-perceived reasons for continuing to receive Botulinum toxin type A for post-stroke spasticity; a content analysis revealed both functional and psychosocial influences for ongoing treatment.

Interestingly, participants in this study have identified an impact on mobility as a major motivator for return to treatment. These participants reported improved control or alignment and improved sense of balance as major contributors to improved confidence and safety with walking. The report of change in balance and range of motion is consistent with the current literature's report of improved spatio-temporal parameters. The literature evaluating the impact of Botulinum toxin type A on gait, specifically spatio-temporal gait parameters, has clearly demonstrated statistically significant changes in gait speed, stride-length, cadence, stride-time, step width as well as single and double limb support [8,15]. However, the use of functional

scales such as the Berg Balance Scale and the Rivermead Mobility Index consistently find no change with the intervention [15]. Interpretations of these findings have been divided. Proponents of treatment would often explain the lack of change as a shortcoming of these outcome measures, specifically that they lack the sensitivity to detect change. Others state that the lack of functional change is evidence that the changes detected may be statistically significant but carry little clinical benefit. Improved confidence and subsequent reduction in fear of falling are typically not assessed in the available literature in this population and their impact would be missed in the current functional scales used. Ultimately, these improvements may translate into increased activity participation and improvements in quality of life.

In terms of active function, studies examining changes as a result of Botulinum toxin type A have used outcome measures focused primarily on active participation in activities of daily living. They have failed to find improvement using these measures. In our study, while participants did not report an improvement in active function, they did specify an improvement in activities of daily living participation as a significant motivator for ongoing treatment. The difference is that participants and their caregivers value the improvement in ease of receiving or providing care and express a sense of reduced burden of care for this participant and caregiver population, which has a positive impact on activity participation.

The role of Botulinum toxin Type A in pain management is not fully understood. While it is likely multifactorial, the two main proposed mechanisms of action are: 1) tone reduction which leads to improved muscle movement and joint range of motion, including the central effects on the gamma afferent efferent loop, thereby reducing pain; and 2) reduction through inhibition of the release of pro-inflammatory cytokines (substance P and calcitonin gene-related peptide) leading to a reduction in local chemical irritation of soft-tissue afferents and sensory neurons [16]. A reduction in pain from Botulinum toxin type A explained by something other than a decrease in tone has also been postulated in many pain states such as migraine [17], neuropathic pain [18] and myofascial pain [19]. Given that patients with stroke in this study reported pain control as a major motivator for continued treatment, it should be a continued area of exploration in future Botulinum toxin type A trials.

In addition to functional improvements, psychosocial factors were highlighted as a reason for continued treatment in this study. Botulinum toxin type A for aesthetic or cosmetic use is well represented in the literature and has been studied in cerebral palsy patients post chemodeneration [20]. At the time of this study, the issue of limb appearance had not been explored as a motivation or goal of management in patients with stroke despite that hemiplegia and hemiparesis post stroke can lead to contracture and flexor synergy posturing in the upper extremity and extension synergy posturing in the lower extremity (e.g., equinovarus or wrist flexion with clenched fist). This is an important area for future study.

The physician-patient relationship, or therapeutic relationship, is central to providing effective, collaborative health care [21]. It is encouraging to receive feedback that participants viewed their physicians favourably. However, participants' decision to defer treatment decisions completely to the physician warrants attention. Studies suggest that a patient-centered model of care, with open communication and shared decision making, positively influences choice to follow treatment [22,23]. In this study, the physician-patient relationship was often described as excellent by the participants and

this may have influenced their report of effect and continuation with treatment. As it is likely common practice in other outpatient clinics, in these clinics, participants and families are educated on the limitations of Botulinum toxin type A and to set realistic goals and expectations. At every encounter, the goals of treatment are reviewed and there is a discussion around the decision to continue or stop injections. Physicians must recognize participants' underlying desire to proceed with the treatment. They must explain the importance of shared decision making, ensure that the decision to continue treatment is based on identifiable findings, and that it is in the participant's best interest. This diligence may reduce physician recommendations for inefficacious treatments [24]. While strong physician-patient relationships can reduce nonadherence, it is important that following physician recommendation does not lead to adverse clinical effect through under- or over-treatment, or where cost outweighs the benefit [24]. This is particularly important with Botulinum toxin type A injections since there are some risks, albeit minor, associated with the procedure (e.g., injection site infection, systemic effects). Additionally, when treatment is not covered by a public health insurance system, there is a significant cost to the individual being treated.

This study was of patients with stroke with limitations of a chronic nature and represents those who continue to receive toxin years after their initial neurologic deficit. The findings are contained to a single centre thereby limiting findings to those with characteristics in this region. While participants may not be representative of the entire population of stroke survivors receiving Botulinum toxin type A for spasticity, they were recruited from four different clinics each drawing referrals from a mix of urban and rural settings with a total catchment of approximately 1 million people. In the current study appropriate measures were taken to ensure that saturation of themes was achieved before interviews were discontinued. While it was not the intent of this study to analyse or include objective information with validated outcome measures regarding change in spasticity (e.g., Modified Ashworth Scale), pain (e.g., Visual Analogue Scale), gait, or personal goals (e.g., Goal Attainment Scale), this information could have served as an objective measure to compare or contrast to the statements made by participants. The decision not to collect this data was deliberate as the objective of the study was to understand individuals' motivations to continue with treatment, no matter what their outcome may or may not have been; however, it offers a potentially interesting avenue for future study.

Conclusion

This preliminary qualitative study highlights why patient's follow up for Botulinum toxin type A treatment. The psychosocial relationship between patient and physician is complex. Understanding the myriad reasons for patient follow up for Botulinum toxin type A treatment may elucidate the factors that influence why patients follow up for treatment of other conditions as well. This will ultimately help us to better set individual goals, expectations and treatment plans for our patients and improve outcomes.

Clinical Message

1. Patients continue to receive botulinum toxin injections for treatment of spasticity because of a positive impact on mobility, activities of daily living performance, and regional pain control, as well as an improvement in limb appearance.

2. Patients have realistic treatment goals and expectations; their decision to continue receiving treatment is in part, influenced by strong positive relationships with their physicians.

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