Which factors impact on quality of life for adults with blepharospasm and hemifacial spasm?

Sadie Lawes-Wickwar[ab], Hayley McBain[a*], Shashivadan P. Hirani[a], Catherine S. Hurt[a], Nicola Dunlop[b], Dianne Solly[b], Bridget Crampton[b], Stanton P. Newman[a] and Daniel G. Ezra[b]

[a]*Centre for Health Services Research, City, University of London, London, UK;* [b]*Moorfields Eye Hospital NHS Foundation Trust, London, UK*

Dr Hayley McBain, School of Health Sciences, City, University of London, 10 Northampton Square, London, EC1V 0HB, United Kingdom, Hayley.mcbain.1@city.ac.uk

Which factors impact on quality of life for adults with blepharospasm and hemifacial spasm?

Purpose: Benign essential blepharospasm (BEB) and hemifacial spasm (HFS) are debilitating conditions causing spasms to the eyes and/or face and can significantly impact on quality of life (QoL). Initial research has highlighted potential factors impacting on QoL in BEB, but there remains a wealth of demographic, clinical and psychosocial factors that may contribute to QoL but have not received attention.

Methods: Cross-sectional baseline data were collected before a single-masked randomised controlled trial from 130 adults with BEB and HFS recruited from botulinum toxin clinics at Moorfields Eye Hospital, London. QoL was measured using the 24-item Craniocervical Dystonia Questionnaire (CDQ24), which provides a total score and five subscale scores relating to *Stigma*, *Emotional state*, *Pain*, *Activities of daily living (ADL)*, and *Social/ family life*. Treating clinicians provided clinical data. Hierarchical multiple regressions were performed on this baseline data to identify significant predictors of QoL.

Results: *ADL* and *Stigma* were the areas most impacted upon whilst patients experienced better adjustment in relation to *Pain*, *Social/family life* and *Emotional state*. *CDQ24 Total* scores were explained by the model (80% variance) and were significantly associated with appearance concerns, emotional representations, perceived negative consequences of the condition, mood, and dose of botulinum toxin.

Conclusions: Patients with BEB and HFS report a detrimental impact on ADL and perceived stigma in relation to their condition. Predominantly, individual perceptions and mood are associated with QoL in this population, rather than demographic and clinical factors, signifying areas to target in the design of future healthcare services or interventions.

Keywords: benign essential blepharospasm, hemifacial spasm, facial dystonia, quality of life, psychosocial impact

Introduction

Benign essential blepharospasm (BEB) and hemifacial spasm (HFS) are types of movement disorders characterised by excessive involuntary contractions in the eyes and face.[1;2] BEB (persistent closure of both eyes) affects between 16 and 133 per million,[3] HFS (spasms affecting one side of the face) is estimated to affect up to 100 per million,[2] and both conditions are more common in adults aged 40 and over.[4] Although the pathophysiology of these two conditions is different, the illness and treatment experiences of patients share many similarities. For instance, both conditions impact on the ability to carry on with normal daily activities, such as working or reading.[5;2] BEB, and many instances of HFS, are currently without a definitive cure. Repeated injections of botulinum toxin are the most effective treatment.[6] The effects of botulinum toxin injections, however, do not last, resulting in periods of relief being followed by a return of symptoms.[7.] This is reflected in a recent study where the chronic, cyclical, and unpredictable nature of the conditions were identified along with patients' understanding of the conditions.[8]

A growing body of research has found both conditions to have a detrimental impact on psychosocial outcomes, including mood,[5;9] and quality of life. [4;10;11] As many as 37% of patients with BEB have been found to high levels of self-reported depression,[11] and 17% of patients with HFS meet the criteria for a clinical diagnosis of major depressive disorder.[12] A recent systematic review found several determinants of poorer quality of life in BEB including patients with lower disease duration, female patients, those with cognitive impairments, and psychiatric problems including depression and obsessive-compulsive disorder[13]. Few studies were found to investigate quality of life in HFS[13].

However, while for some patients the impact of the condition is extreme, others are only mildly affected. This heterogeneity in adjustment is a common finding across chronic

conditions,[14] including other chronic eye conditions.[15;16] It is useful to determine which factors may be contributing to adjustment so that health services can be directed to these determinants. Little previous research has investigated the specific factors associated with quality of life in BEB and HFS. A number of studies have found evidence for significant relationships between quality of life and depression,[9; 11; 17] and quality of life and anxiety,[18] (in BEB) and significant relationships between demographic, clinical factors and depressed mood,[12] and quality of life,[17; 19] in HFS. There remain, however, a wealth of individual patient perceptions that have not been previously investigated in BEB or HFS and may determine psychosocial outcomes.

There is evidence from a larger body of research in Parkinson's Disease (PD), also characterised by a movement disorder, that individual beliefs and coping styles can determine psychosocial outcomes, including mood,[20;21] and quality of life.[21; 22] It is important to understand the range of individual perceptions patients with chronic conditions hold so that healthcare and psychological services can be designed to target the most important factors contributing to quality of life. With the limited previous research in BEB or HFS, this study aimed to investigate the predictive value of demographic, clinical and individual beliefs for quality of life in BEB and HFS.

Materials and Methods

Ethics

Ethical approval was obtained from National Research Ethics Service (NRES) London – Queen Square (REC reference 15/LO/0439) in April 2015. Botulinum toxin is part of the usual treatment at Moorfields Eye Hospital, London (MEH) and the study adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Study design

This article presents a cross sectional study of the baseline data collected for a single-masked randomised controlled trial (RCT) to assess the effectiveness of a patient-initiated treatment service compared to standard care.[23]

Participants

Participants were recruited between August 2015 and February 2017 from the nurse-led botulinum toxin clinics at MEH, London, for the RCT. Patients were aged 18 years or over with a diagnosis of BEB or HFS, were stable on botulinum toxin defined as having received two previous cycles at stable doses and free from complications, and had mental capacity to provide informed consent as judged by the research nurse. Patients attending the nurse-led botulinum toxin clinic were identified as eligible by the research nurse and invited to take part in the study prior to their next clinic appointment. Patients were approached by their treating clinician and those expressing an interest in taking part were recruited by a research psychologist. Patients were excluded from the study if they were identified by their treating clinician as not having a comprehensive understanding of written or spoken English to

complete study measures, or were suffering from psychiatric or co-morbid health conditions that rendered them too ill or distressed to take part.

Measures

Demographics

Participants' age, gender, marital status, ethnicity, employment status, level of education, and accommodation and living situation were collected in a questionnaire given to participants on the day they were recruited.

Clinical variables

Data collected from patients' medical notes included diagnosis, duration of botulinum toxin treatment, number of previous cycles, frequency of previous cycles, last dose of botulinum toxin, and any existing comorbidities. Participants also provided the period of experienced benefit of botulinum toxin in days, weeks, or months.

Disease severity. For patients with BEB, disease severity and frequency of symptoms were assessed using the Jankovic Rating Scale (JRS),[24] a clinician-completed measure consisting of two items, each with a score of 0 (no symptoms) to 4 (severe symptoms). Patients with HFS were rated on the JRS and received an additional rating scale for severity and frequency of cheek involvement based on two items recommended by Wabbels and Roggenkämper.[2] The severity and frequency scores were added to create a sum score, giving participants a score between 0 and 8 for the severity and frequency of eye spasms, and participants with HFS a score of between 0 and 8 for severity and frequency of check spasms. Higher scores indicate more severe and frequent spasms.

Disease disability. All participants completed the Blepharospasm Disability Index (BSDI)©,[25] a patient-reported measure that asks about impairment in six areas: driving, reading, watching TV, shopping, walking and doing everyday activities. Each item is rated on a scale from 0 (no impairment) to 4 (no longer possible due to illness), with higher scores indicating greater disability as a result of the condition. A "not applicable" option is available for each item and the total score is a mean item score, calculated by dividing the sum score by the number of applicable items. Thus, any participants answering "not applicable" in all areas did not receive a score on the BSDI. The measure is also recommended for use in hemifacial spasm.[2]

Treatment side effects. The occurrence of adverse events from the last treatment including ptosis, double or blurred vision, tearing, hematoma and foreign body sensation were also recorded by the treating clinician at the point of recruitment.

Psychosocial variables

Participants were asked to complete a range of questionnaires included in the pack given to them on the day of recruitment.

Mood. The Hospital Anxiety & Depression scale (HADS) was used to screen for depression and anxiety, with higher total subscale scores indicating greater levels of anxious or depressed mood.[26] Cut-off scores were also applied to identify non-cases (0 to 7), doubtful cases (8 to 10), and cases of possible clinical anxiety or depression (scores of 11 and over). The HADS has demonstrated excellent internal consistency (Cronbach's alpha: anxiety 0.68-0.93; depression 0.67-0.90) and high test-retest reliability (r=0.86-0.89).[26]

Appearance concerns. The Derriford Appearance Scale (DAS24) was used to measure the impact of appearance-related social anxiety and avoidance, with higher scores indicating

greater levels of appearance-related social anxiety and avoidance.[27] This measure has demonstrated high internal consistency (α = .92) and good test-retest reliability (r=0.82).[27]

Illness beliefs. Beliefs about illness were measured using the revised illness perceptions questionnaire (IPQ-R).[28] The IPQ-R is divided into two sections, with the identity subscale presented first as a list of 14 commonly experienced symptoms and respondents judge whether each symptom is related to their condition. As recommended by the authors of the scale for the purpose of this study, four blepharospasm and hemifacial spasm symptoms were added to this scale (i) frequent blinking, (ii) irritation of the eye, (iii) uncontrollable eye closure and, (iv) muscle twitching around the face and/or eye; bringing the maximum score up to 18.

The second section of the scale measures all other subscales other than causes. Responses are rated on a 5-point Likert scale, from 1 (strongly disagree) to 5 (strongly disagree). To increase the validity of the IPQ-R scale, these items were subject to a principle components analysis (PCA) to identify the factor structure of the measure specifically in BEB and HFS, the methods are described in a recent article[8]. After one item was removed from the original IPQ-R, the measure was found to include ten separate factors: *timeline acute*, *timeline chronic*, *timeline cyclical*, *illness uncertainty*, *consequences, emotional representations, treatment control*, *negative personal control*, *positive personal control*, and *coherence*. The new IPQ-R structure was found to possess good internal reliability, with Cronbach's alphas ranging from 0.67 to 0.89, and good construct validity demonstrated by relationships with similar variables (Spearman's rhos ranging from 0.2 to 0.7). High scores on the *timeline acute*, *timeline chronic*, *timeline cyclical*, *illness uncertainty*, *consequences*, and *emotional representations* subscales represent strongly held beliefs about the incurable, chronic, and cyclical nature of the condition, the unpredictability of the condition, and the negative

consequences and emotional response associated with the condition, respectively. High scores on the negative and positive personal, treatment control and coherence dimensions represent positive beliefs about the controllability of the condition and its treatment and a personal understanding of the condition.

Illness cause is assessed in the last 18 items of the IPQ-R, which were also subjected to PCA in the present BEB and HFS population, and found to be structured into four subscales: *psychological attributions*, *risk factors*, *lifestyle* and *chance*, which were also found to possess good internal reliability, with Cronbach's alphas ranging from 0.50 to 0.86[8].

Treatment beliefs. Beliefs about treatment were measured using the Treatment Representations Inventory (TRI).[29] This 27 item measure was also subject to PCA in a BEB and HFS population and was found to be structured by four factors representing *treatment value*, *treatment concerns*, *decision satisfaction* and *cure*, with higher scores representing stronger beliefs about the benefits of treatment in controlling the condition, more anxiety about treatment, satisfaction with and suitability of treatment, and the ability of the treatment to remove the condition.[8] After one item was removed, the subscales demonstrated good internal reliability (Cronbach's alpha: 0.79, 0.84, 0.86 & 0.67 respectively) and has demonstrated good construct validity.[8; 29]

Quality of life. Quality of life was measured using the Craniocervical dystonia questionnaire (CDQ-24),[30] which has been used with success in patients with blepharospasm and hemifacial spasm.[31] The 24 item CDQ assesses quality of life across five domains: stigma, emotional well-being, pain, activities of daily living and social/family life. Each item relates to issues experienced in the past two weeks, with a scale ranging from 0 (never) to 4 (always). To obtain comparable scores for the individual subscales, the raw subscores (sum

of the individual item score) were linearly transformed to a 0-100 scale, with higher scores indicating poorer quality of life.

Statistical analyses

All analyses were undertaken using IBM SPSS Statistics Version 22.0. Levels of missing data were identified and analysed using Little's Missing Completely at Random (MCAR) test, which if found not to be significant suggests data were missing completely at random. Missing data were then dealt with in two stages: first, using mean imputation methods to limit the impact of missing data and secondly, multiple imputations were performed where less than 50% of data for any variable were missing. If a single case was found to have >50% total data missing their data were removed from the analysis. Missing data were not imputed for the JRS and BSDI scales, as this would have led to errors in scoring.

Hierarchical multiple regressions were used to assess which demographic, clinical, and psychosocial factors were most strongly associated with quality of life in BEB and HFS. Variables entered into each regression model were chosen based on their significant associations with each dependent variable (CDQ subscales) in prior univariate regression analyses ($p<0.05$). Subscales within the following categories were entered into the regression model in the following order: demographic variables (block 1), clinical variables (block 2), appearance concerns (block 3), illness and treatment beliefs (block 4) and mood (block 5). Entry methods were used for the hierarchical regressions. Multicollinearity was assessed using tolerance and VIF statistics provided in SPSS output and any variables scoring VIF statistic over 10 were removed and the regression re-run, to avoid multicollinearity between variables. The same approach was used with the same variables to test their ability to explain the variance in each subscale of the CDQ, since each subscale deals with a different aspect of quality of life (i.e. stigma, emotional state, pain, activities of daily life, and social/family life).

Results

Participants

During the recruitment period, 247 patients screened by the research nurse were identified as eligible and invited to take part in the trial. Five eligible patients did not attend a clinic appointment during the recruitment period and 87 declined to participate when approached in their clinic visit. A total of 155 patients provided written consent and 130 participants returned a baseline questionnaire and were randomised into the trial. After removing one participant who missed over 50% of the responses in the questionnaire, all analyses included the data for 129 participants. Participant characteristics shown in Table 1.

[Table 1 near here]

Missing data

Little's Missing Completely at Random (MCAR) test was found not to be significant (χ^2 = 2172.83, *df* = 2223, *p* = 0.773), thus data were MCAR. A total of 11.9% of the data were missing. Ten imputations were therefore generated, and the analysis was conducted on all 10 datasets and the results pooled. One participant had over 50% of their total data missing and were removed from the analyses.

Psychosocial factors

Participants' scores on the psychosocial outcome variables are shown in Table 2.

[Insert Table 2 near here]

CDQ Total

Gender, age, relationship status, housing, experienced benefits of botulinum toxin, diagnosis, disability, timing of treatment, last dose, severity of eye spasms, appearance concerns, anxiety and depression, illness identity, emotional representations, illness coherence, cyclical timeline, consequences, psychological causes, risk factor causes and lifestyle causes, and all four treatment beliefs, were found to significantly correlate ($p<0.05$) with CDQ Total scores after univariate regressions.

The total variance explained by the model as a whole was 79.7% ($F_{26,89} = 13.46$, $p<0.001$). In the final model, the variables found to make a unique statistically significant contribution, in order of importance (high to low Beta values) were appearance concerns, depression, anxiety, emotional representations of the illness, perceived negative consequences associated with the condition, and last dose (Table 3).

[Insert Table 3 near here]

CDQ Stigma

Gender, age, relationship status, housing, experienced benefits of botulinum toxin, disability, timing of treatment, last dose, appearance concerns, illness identity, emotional representations, coherence, consequences, uncertainty, psychological causes, risk factor cause, treatment concerns, treatment value, and mood, were all found to significantly correlate with CDQ Stigma scores after univariate regressions.

The total variance in CDQ Stigma scores explained by the model as a whole was 64% ($F_{20,100} = 8.91$, $p<0.001$). In the final model appearance concerns and depression were found to make a unique statistically significant contribution.

CDQ Emotional state

Gender, age, relationship status, housing, living situation, experienced benefits of botulinum toxin, disability, timing of treatment, last dose, diagnosis, laterality, number of previous cycles, appearance concerns, illness identity, emotional representations, cyclical timeline, coherence, consequences, uncertainty, all four causal beliefs, treatment concerns, decision satisfaction, treatment value, and mood, were all found to significantly correlate with CDQ Emotional State scores after univariate regressions.

Preliminary analyses indicated that diagnosis, laterality and appearance concerns revealed VIF scores above 10, suggesting multicollinearity. After removing laterality from the hierarchical regression model, because this was already indicated by whether the condition was BEB (both eyes) or HFS (one side of the face), all VIF scores were below 10.

[Insert Table 4 near here]

The total variance in CDQ Emotional State scores explained by the model as a whole was 76% ($F_{27, 93} = 10.69$, $p<0.001$). In the final model, the variables found to make a unique statistically significant contribution, in order of importance (high to low Beta values) were anxiety, appearance concerns, emotional representations of the illness and perceived negative consequences associated with the condition (Table 4).

CDQ Pain

Age, housing, experienced benefits of botulinum toxin, disability, timing of treatment, severity of eyelid spasms, severity of cheek spasms, appearance concerns, illness identity, emotional representations, coherence, consequences, uncertainty, psychological causes, risk factor causes, lifestyle causes, treatment concerns, treatment value, and mood, were all found to significantly correlate with CDQ Pain scores after univariate regressions.

The total variance in CDQ Pain scores explained by the model as a whole was 39% ($F_{20, 95}$ = 3.05, p<0.001). No statistically significant unique predictors for CDQ Pain scores were found.

CDQ ADL

Gender, experienced benefits of botulinum toxin, disability, timing of treatment, last dose, diagnosis, laterality, having a comorbid condition, severity of eyelid spasms, appearance concerns, illness identity, emotional representations, coherence, consequences, uncertainty, timeline chronic, psychological causes, risk factor causes, treatment decision satisfaction, treatment cure, and mood, were all found to significantly correlate with CDQ ADL scores after univariate regressions.

The total variance in CDQ ADL scores explained by the model as a whole was 72.2% ($F_{23, 92}$ = 10.40, p<0.001). In the final model, the variables found to make a unique statistically significant contribution, in order of importance (high to low Beta values) were disability, perceptions of symptoms related to the condition (illness identity) and emotional representations of the illness (Table 4).

CDQ Social/family life

Gender, relationship status, housing, living situation, disability, timing of treatment, last dose, diagnosis, laterality, appearance concerns, illness identity, emotional representations, cyclical timeline, coherence, consequences, uncertainty, lifestyle, risk and psychological causes, treatment concerns, treatment value, and mood, were all found to significantly correlate with CDQ Social/family life scores after univariate regressions.

The total variance in CDQ Social/family life scores explained by the model as a whole was 59.4% ($F_{22, 98}$ = 6.53, p<0.001). In the final model, the variables found to make a unique

statistically significant contribution, in order of importance (high to low Beta values) were emotional representations and last dose (Table 4).

Discussion

Participants' essential activities of daily life and experiences with feeling stigmatised were the areas most impacted upon. These subscale scores, along with social/family life, and overall quality of life, were comparable to other BEB populations.[30] However the pain subscale scores in this sample was notably lower than other studies suggesting the participants in our study were generally not as affected by pain and it is possible that they were not representative of the wider BEB population. After initiating treatment with botulinum toxin, future regular treatment would normally lead to a reduction in severity over time, this having been found in patients with CD,[32] which is characterised by involuntary movements of the head and neck. Thus maximum severity was unlikely to be observed in this study of patients undergoing regular botulinum toxin injections.

This study also examined the factors associated with quality of life in BEB and HFS where there were variations in adjustment. Specifically, better *overall quality of life* was associated with a lower previous toxin dose, less appearance-related distress, less negative emotional beliefs about the condition, fewer negative consequences associated with having the condition, and better mood. Perceived *stigma* was associated with greater appearance-related distress, and higher levels of depressed mood. Poorer *emotional state* was associated with greater appearance-related distress, more negative emotional beliefs, more negative perceived consequences and more anxious mood. As can be expected, greater difficulty in *ADL* was associated with more disease disability, more symptoms, and more negative emotions. Poorer *social and family life* was associated with higher levels of disability, higher previous dose of toxin, and more negative emotions. This study indicates that rather than clinical and demographic variables, it was the beliefs patients held about their appearance, illness and

treatment, which contributed more strongly and consistently to adjustment. Suggesting that these factors are suitable targets for improving psychological adjustment in BEB and HFS.

The finding that neither participants' demographic factors, nor clinical factors associated with the condition, were associated with quality of life in this study contradicts previous findings.[12] Notably, the diagnosis of either HFS or BEB was not a determinant of difference in quality of life measures. This indicates that although the pathophysiology of these conditions is different, they share much in their clinical phenotype in terms of facial involvement and exposure to very similar treatment modalities, as well as their illness beliefs. The finding that mood was associated with all areas of quality of life is in common with previous studies in BEB,[9;11;17;18] and one study in HFS.[17] However this study has expanded on previous evidence, also finding that greater appearance-related distress, more negative emotional beliefs, negative consequences associated with the condition, greater disability in everyday life, and perceived illness identity, are important factors determining poorer quality of life in these patient groups.

This study found that more negative illness beliefs were associated with poorer quality of life in BEB and HFS, in particular the negative emotions, perceived consequences of having the condition, and the number of symptoms patients associate with their condition. These are factors also identified as important in the adjustment of patients with other conditions such as coronary artery disease,[33] and Parkinson's disease.[22] Moreover, the perceptions found to be the strongest predictors of psychological outcomes in a recent meta-analysis across a range of long-term health conditions imply that beliefs intervene to improve conditions and are therefore important considerations in healthcare practice.[34]

The treatment beliefs of patients with BEB and HFS were also examined in this study and demonstrated that both groups of patients value their botulinum toxin treatment, are satisfied

with the decisions made about using this treatment, believe their injections cure their condition, and generally do not have concerns about botulinum toxin. Given that there is currently no cure for BEB and HFS and botulinum toxin is the standard treatment, these are encouraging findings.

There are a number of limitations to this study including the cross-sectional design, which does not establish causal direction in the associations identified between variables. In addition, as participants were recruited from one centre in the UK, this may limit the generalisability of the findings to other locations across the UK and overseas.

Conclusions

Patients with BEB and HFS report a detrimental impact deriving from their condition, particularly in terms of *ADL* and perceived *stigma*. Predominantly individual perceptions and mood were found to be associated with quality of life, rather than demographic and clinical factors in this population, which is a finding common across chronic conditions. Such psychosocial factors may be amenable to change in future healthcare interventions that target them.

Acknowledgements

The authors would like to acknowledge the valuable contribution made by the patients who took part in the research and for giving up their time. This project received funding from Merz Pharma Ltd and Moorfields Eye Charity. DGE received partial funding from the Department of Health's NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye Hospital and UCL Institute of Ophthalmology.

Disclosure of interest

The authors have no financial interest or other conflict of interest to report.

References

1. Jankovic J, Kenney C, Grafe S, Goertelmeyer R, Comes G. Relationship between various clinical outcome assessments in patients with blepharospasm. Mov Disord 2009; 24(3):407-413.

2. Wabbels B, Roggenkämper P. Botulinum toxin in hemifacial spasm: the challenge to assess the effect of treatment. J Neural Transm 2012; 119(8):963-980

3. Defazio, G, Livrea, P. Epidemiology of primary blepharospasm. Mov Disord 2002, 17(1), 7-12.

4. Reimer J, Gilg K, Karow A, Esser J, Franke GH. Health-related quality of life in blepharospasm or hemifacial spasm. Acta Neurol Scand 2005; 111(1):64-70

5. Tucha O, Naumann M, Berg D, Alders GL, Lange KW. Quality of life in patients with blepharospasm. Acta Neurol Scand 2001;103(1):49-52.

6. Kraft SP, Lang AE. Cranial dystonia, blepharospasm and hemifacial spasm: clinical features and treatment, including the use of botulinum toxin. CMAJ 1988; 139(9):837

7. Colosimo C, Tiple D, Berardelli A. Efficacy and safety of long-term botulinum toxin treatment in craniocervical dystonia: a systematic review. Neurotox Res 2012; 22(4):265-273

8. Lawes-Wickwar S, McBain H, Hirani SP, et al. (*Submitted*). What beliefs do adults with periocular facial dystonias hold about their condition and its treatment? *Psychology & Health.*

9. Pekmezovic T, Svetel M, Ivanovic N, et al. Quality of life in patients with focal dystonia. Clin Neurol Neurosurg. 2009; 1;111(2):161-4.

10. Hall TA, McGwin G, Searcey K, et al. Health-related quality of life and psychosocial characteristics of patients with benign essential blepharospasm. Arch Ophtalmol. 2006;1;124(1):116-9.

11. Müller J, Kemmler G, Wissel J, et al. The impact of blepharospasm and cervical dystonia on health-related quality of life and depression. J Neurol 2002; 249(7):842-846.

12. Tan EK, Lum SY, Fook-Chong S, Chan LL, Gabriel C, Lim L. Behind the facial twitch: depressive symptoms in hemifacial spasm. Parkinsonism Relat. Disord. 2005; 1;11(4):241-5.

13. Girach A, Aragon AV, Zis P. Quality of life in idiopathic dystonia: a systematic review. Journal of neurology. 2019 Dec 1:1-0.

14. Stanton AL, Revenson TA, Tennen H. Health psychology: psychological adjustment to chronic disease. Annu. Rev. Psychol. 2007, 58, 565-592.

15. McBain H, MacKenzie K, Au CK, et al. Factors associated with quality of life and mood in adults with strabismus. Br J Ophthalmol 2014, 98(4), pp. 550-555

16. Wickwar S, McBain HB, Ezra DG, Hirani SP, Rose GE, Newman SP. Which factors are associated with quality of life in patients with Graves' orbitopathy presenting for orbital decompression surgery? Eye. 2015;29(7):951.

17. Setthawatcharawanich S, Sathirapanya P, Limapichat K, Phabphal K. Factors associated with quality of life in hemifacial spasm and blepharospasm during long-term treatment with botulinum toxin. Qual Life Res 2011;1;20(9):1519-23.

18. Gürsoy AE, Ugurad I, Babacan-Yıldız G, Kolukısa M, Çelebi A. Effects of botulinum toxin type a on quality of life assessed with the WHOQOL-BREF in hemifacial spasm and blepharospasm. Neurol Psychiatry Brain Res. 2013; 1;19(1):12-8.

19. Tan EK, Hameed S, Fook-Chong S, Hussein K, Lum SY, Chan LL. Treatment outcome correlates with knowledge of disease in hemifacial spasm. Clin Neurol Neurosurg 2008, 110(8), 813-817.

20. Evans D, Norman P. Illness representations, coping and psychological adjustment to Parkinson's disease. Psychol Health 2009, 24(10), 1181-1196.

21. Simpson J, Lekwuwa G, Crawford T. Illness beliefs and psychological outcome in people with Parkinson's disease. Chronic Illness 2013, 9(2), 165-176.

22. Hurt CS, Burn DJ, Hindle J, Samuel M, Wilson K, Brown RG. Thinking positively about chronic illness: An exploration of optimism, illness perceptions and well-being in patients with Parkinson's disease. Br J Health Psychol 2014;19(2):363-79.

23. Wickwar S, McBain H, Newman SP, et al. Effectiveness and cost-effectiveness of a patient-initiated botulinum toxin treatment model for blepharospasm and hemifacial spasm compared to standard care: study protocol for a randomised controlled trial. Trials. 2016;17(1):129.

24. Jankovic J, Orman J. Botulinum A toxin for cranial-cervical dystonia A double-blind, placebo-controlled study. Neurol 1987; 37(4):616

25. Goertelmeyer S, Brinkmann G, Comes A, Delcker A. The Blepharospasm Disability Index (BSDI) for the assessment of functional health in focal dystonia. Clin Neurophysiol 2002; 113(Suppl 1):S77-S78

26. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67(6):361-370.

27. Carr T, Moss TP, Harris DL. The DAS24: a short form of the Derriford Appearance Scale

DAS59 to measure individual responses to living with problems of appearance. Br J Health Psychol 2005, 10, 285-298

28. Moss-Morris R, Weinman J, Petrie K, Horne R, Cameron L, Buick D. The revised illness perception questionnaire (IPQ-R). Psychol Health 2002; 17(1):1-16

29. Hirani SP, Patterson DL, Newman SP. What do coronary artery disease patients think about their treatments? An assessment of patients' treatment representations. J Health Psychol 2008; 13(3):311-322.

30. Müller J, Wissel J, Kemmler G, et al. Craniocervical dystonia questionnaire (CDQ-24): development and validation of a disease-specific quality of life instrument. J Neurol Neurosurg Psychiatry 2004; 75(5):749-753.

31. Malhotra R, Then SY, Richards A, Cheek E. The effect of Bangerter occlusion foils on blepharospasm and hemifacial spasm in occlusion-positive and occlusion-negative patients. The open ophthalmology journal 2010; 4:1

32. Kessler KR, Skutta M, Benecke R, German Dystonia Study Group. Long-term treatment of cervical dystonia with botulinum toxin A: efficacy, safety, and antibody frequency. J Neurol 1999: 1;246(4):265-74.

33. Stafford L, Berk M, Jackson HJ. Are illness perceptions about coronary artery disease predictive of depression and quality of life outcomes? J Psychosom Res 2009, 66(3), 211-220.

34. Dempster M, Howell D, McCorry NK. Illness perceptions and coping in physical health conditions: A meta-analysis. J Psychosom Res 2015, 79(6), 506-513

Table 1. Participants' demographic and clinical characteristics

Variable	Number (%)	Range	Mean ± SD
Age (years)		37 - 88	63.84 ± 10.8
Gender			
Male	37 (29%)		
Female	92 (71%)		
Ethnicity			
White British/Irish/Other	89 (69%)		
Black African/Caribbean/Asian/Other	40 (31%)		
Diagnosis			
BEB	76 (59%)		
HFS	53 (41%)		
Relationship Status			
Married/Living with partner	80 (62%)		
Single/Other	49 (38%)		
Employment status			
Paid employment	43 (33%)		
Retired/Unemployed/Other	87 (67%)		
Qualifications			
Received GCSEs/A Levels/Degree/Other	102 (79%)		
No qualifications	27 (21%)		
Living situation			
Living alone (with/without children)	37 (29%)		
Living with others	92 (71%)		
Housing situation			
Owner occupied	98 (76%)		
Rented/Other	31 (24%)		
Duration of botulinum toxin (months)		4 - 336	81.4± 71.8
Number of previous cycles		2-121	21.5± 21.1
Last dose of botulinum toxin (units)		1.25 - 280	33.9 ± 41.0
Usual time between treatments (months)		1 - 9	3.19 ± 1.2
Side effects from previous treatment			
Ptosis	27 (21%)		
Diplopia	15 (12%)		
Tearing	13 (10%)		
Hematoma	9 (7%)		
Foreign body sensation	11 (8.5%)		
Blurred vision	12 (9%)		
Comorbidities	37 (29%)		
Disease disability (BSDI mean score)		0-3.17	1.1±1.0
Disease severity (JRS sum score)			
Eyelid spasms		0-8	3.0±2.4
Cheek spasms		0-8	3.7±2.2

Table 2. Psychosocial variable scores

Variable	Min	Max	Max Possible	Mean	SD
CDQ Total score	0	79	96	28.8	20.4
CDQ Stigma	0	95.8	100	37.8	28.3
CDQ Emotional wellbeing	0	83.3	100	24.9	21.9
CDQ Pain	0	41.7	100	8.4	10.9
CDQ Activities of daily living	0	95.8	100	37.3	25.6
CDQ Social/family life	0	54.2	100	11.0	14.2
DAS24 appearance concerns	12	76	96	37.0	13.7
TRI Subscales					
Decision satisfaction	9	45	45	35.5	5.2
Treatment concern	6	30	30	16.0	5.1
Cure	7	34	35	22.0	4.4
Treatment value	5	25	25	15.9	4.6
IPQR Subscales					
Identity	0	14	18	5.3	
Chronic timeline	6	20	20	16.8	3.5
Acute timeline	4	15	15	10.7	2.7
Emotional representations	5	25	25	14.3	5.1
Illness coherence	5	25	25	14.0	4.6
Treatment control	6	15	15	11.4	2.2
Positive personal control	4	18	20	9.4	3.5
Negative personal control	2	10	10	5.6	2.1
Illness uncertainty	3	15	15	9.3	2.5
Illness consequences	8	29	30	19.3	5.3
Psychological cause	5	23	25	12.3	4.9
Risk factor cause	6	22	30	12.1	4.2
Lifestyle cause	4	16	20	6.8	2.5
Chance or ageing cause	2	9	10	5.6	2.1
HADS Depression	0	17.5	21	5.2	4.2
HADS Anxiety	0	19	21	6.6	4.5

Table 3. Results of hierarchical multiple regression for CDQ24 Total Score

Outcome	CDQ Total				
Step	**1**	**2**	**3**	**4**	**5**
Gender	**0.22**	**0.16**	**0.16**	0.07	0.10
Age	-0.14	-0.13	-0.05	0.01	0.04
Relationship status	0.10	0.11	**0.18**	0.15	0.05
Housing	-0.09	-0.04	-0.03	0.00	0.04
Living situation	-	-	-	-	-
Experienced benefits	-	-0.03	0.03	0.01	0.01
BSDI	-	**0.34***	**0.28***	**0.22**	0.14
Diagnosis	-	-0.01	0.01	0.05	0.07
Treatment timing (months)	-	-0.09	-0.14	-0.12	-0.04
Last dose (units)	-	**0.20**	**0.16**	**0.14**	**0.11**
Previous cycles (total)	-	-	-	-	-
Laterality	-	-	-	-	-
JRS eyelid spasms	-	0.06	0.11	0.08	0.08
JRS cheek spasms	-	-	-	-	-
Comorbidities	-	-	-	-	-
DAS24	-	-	**0.37***	**0.27***	**0.20***
IPQR Illness identity	-	-	-	0.05	0.11
IPQR emotional representations	-	-	-	**0.23**	**0.16**
IPQR coherence	-	-	-	-0.01	-0.05
IPQR timeline cyclical	-	-	-	0.03	-0.01
IPQR consequences	-	-	-	**0.18**	**0.15**
IPQR uncertainty	-	-	-	0.07	0.06
IPQR timeline chronic	-	-	-	-	-
IPQR psychological causes	-	-	-	-0.03	-0.11
IPQR risk factor causes	-	-	-	0.01	-0.01
IPQR lifestyle causes	-	-	-	0.06	0.07
IPQR chance causes	-	-	-	-	-
TRI decision satisfaction	-	-	-	-0.03	-0.07
TRI treatment concern	-	-	-	0.07	0.01
TRI cure	-	-	-	-0.03	0.01
TRI treatment value	-	-	-	-0.04	0.00
HADS anxiety	-	-	-	-	**0.18**
HADS depression	-	-	-	-	**0.18**

***p*<0.001**

Table 4. Results of hierarchical multiple regression for each CDQ24 Subscale

Outcome	*CDQ Stigma*					*CDQ Emotional State*					*CDQ Pain*					*CDQ Activities of Daily Living*					*CDQ Social/Family Life*				
Step	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Gender	**0.25**	**0.22**	0.19	0.10	0.10	**0.29**	**0.23**	**0.21**	0.11	0.11	-	-	-	-	-	0.17	0.05	0.04	-0.02	-0.02	0.15	0.07	0.06	-0.02	-0.01
Age	-0.16	-0.14	-0.06	0.00	0.03	**-0.22**	**-0.17**	-0.10	0.00	0.03	-0.16	-0.12	-0.10	-0.06	-0.04	-	-	-	-	-	-	-	-	-	-
Relationship status	0.12	0.13	**0.19**	**0.17**	0.11	0.12	0.11	0.16	0.08	-0.06	-	-	-	-	-	-	-	-	-	-	0.09	0.12	0.15	0.09	0.05
Housing	-0.10	-0.05	-0.04	-0.01	0.01	-0.16	-0.11	-0.10	-0.05	-0.02	-0.17	-0.12	-0.12	-0.11	-0.09	-	-	-	-	-	-0.17	-0.11	-0.09	-0.06	-0.04
Living situation	-	-	-	-	-	-0.01	-0.05	-0.04	-0.09	-0.16	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Experienced benefits	-	-0.09	-0.02	0.01	-0.02	-	-0.07	0.00	0.00	-0.02	-	-0.02	0.00	0.00	-0.01	-	-0.07	-0.04	-0.01	-0.01	-	-	-	-	-
BSDI	-	0.17	0.12	0.00	-0.09	-	**0.23**	**0.18**	0.09	-0.01	-	0.18	0.16	0.04	-0.02	-	**0.59***	**0.57***	**0.50***	**0.44***	-	**0.33***	**0.29**	**0.20**	**0.13**
Diagnosis	-	-	-	-	-	-	-0.02	-0.01	0.04	0.07	-	-	-	-	-	-	0.13	0.11	0.13	0.08	-	0.03	0.02	-0.01	-0.06
Treatment timing (months)	-	-0.09	-0.12	-0.13	-0.04	-	-0.10	-0.13	-0.13	-0.02		-0.15	-0.16	-0.14	-0.09	-	-0.06	-0.06	-0.02	0.02	-	-0.13	-0.12	-0.11	-0.04
Last dose (units)	-	**0.22**	**0.17**	**0.14**	0.12	-	**0.16**	0.11	0.07	0.04	-	-	-	-	-	-	**0.14**	0.12	0.09	0.08	-	**0.22**	**0.19**	**0.15**	**0.14**
Previous cycles (total)	-	-	-	-	-	-	-0.12	-0.13	-0.08	-0.08	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Laterality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.23	0.22	0.23	0.18	-	0.06	0.04	-0.02	-0.08
JRS eyelid spasms	-	-	-	-	-	-	-	-	-	-	-	0.15	0.15	0.06	0.05	-	0.11	0.12	0.11	0.10	-	-	-	-	-
JRS cheek spasms	-	-	-	-	-	-	-	-	-	-	-	0.07	0.07	0.20	0.22	-	-	-	-	-	-	-	-	-	-
Comorbidities	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.02	-0.01	0.00	-0.02	-	-	-	-	-
DAS24	-	-	**0.49***	**0.37***	**0.32***	-	-	**0.45***	**0.30***	**0.23**	-	-	0.12	0.01	-0.03	-	-	**0.20**	0.10	0.08	-	-	**0.34***	0.15	0.11
IPQR Illness identity	-	-	-	0.03	0.06	-	-	-	-0.05	0.00	-	-	-	0.15	0.16	-	-	-	0.15	**0.17**	-	-	-	-0.02	0.00
IPQR emotional representations	-	-	-	**0.23**	0.20	-	-	-	**0.29**	**0.22**	-	-	-	0.06	0.01	-	-	-	**0.23**	**0.20**	-	-	-	**0.31**	**0.27**
IPQR coherence	-	-	-	0.08	0.05	-	-	-	0.00	-0.03	-	-	-	-0.11	-0.13	-	-	-	0.01	0.00	-	-	-	0.02	0.00
IPQR timeline cyclical	-	-	-	-	-	-	-	-	0.03	0.01	-	-	-	-	-	-	-	-	-	-	-	-	-	0.06	0.06
IPQR consequences	-	-	-	-0.03	-0.11	-	-	-	**0.22**	**0.18**	-	-	-	0.13	0.11	-	-	-	0.04	0.02	-	-	-	0.18	0.15

IPQR uncertainty	-	-	-	-0.03	-0.04	-	-	-	0.10	0.07	-	-	-	0.03	0.02	-	-	-	-0.03	-0.04	-	-	-	0.04	0.03
IPQR timeline chronic	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.04	0.04	-	-	-	-	-
IPQR psychological causes	-	-	-	0.08	0.07	-	-	-	0.06	-0.06	-	-	-	-0.09	-0.16	-	-	-	-0.10	-0.13	-	-	-	0.01	-0.06
IPQR risk factor causes	-	-	-	-0.01	-0.01	-	-	-	-0.02	-0.03	-	-	-	0.12	0.12	-	-	-	-0.03	-0	-	-	-	0.05	0.04
IPQR lifestyle causes	-	-	-	-	-	-	-	-	0.02	0.04	-	-	-	0.15	0.14	-	-	-	-	-	-	-	-	0.09	0.098
IPQR chance causes	-	-	-	-	-	-	-	-	0.01	-0.00	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
TRI decision satisfaction	-	-	-	-	-	-	-	-	-0.01	-0.05	-	-	-	-	-	-	-	-	-0.08	-0.09	-	-	-	-	-
TRI treatment concern	-	-	-	0.15	0.10	-	-	-	0.08	0.02	-	-	-	0.09	0.07	-	-	-	-	-	-	-	-	0.05	0.05
TRI cure	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.08	-0.1	-	-	-	-	-
TRI treatment value	-	-	-	-0.06	-0.08	-	-	-	-0.11	-0.09	-	-	-	0.01	0.02	-	-	-	0.03	0.03	-	-	-	-0.07	-0.07
HADS anxiety	-	-	-	-	0.14	-	-	-	-	**0.30**	-	-	-	-	0.17	-	-	-	-	0.01	-	-	-	-	0.06
HADS depression	-	-	-	-	**0.21**	-	-	-	-	0.15	-	-	-	-	0.10	-	-	-	-	0.16	-	-	-	-	0.20

***p*<0.001**