

EFFICACY OF BOTULINUM TOXIN FOR CERVICAL DYSTONIA. A COMPARISON OF METHODS FOR EVALUATION

T. Odergren, A. Tollbäck, RPT and J. Borg

From the Department of Neurology, Karolinska Hospital, Stockholm, Sweden

ABSTRACT. Twenty patients with cervical dystonia were treated during one year with repeated intramuscular injections of botulinum toxin. The outcome was evaluated comparing subjective global rating with relative changes in degree of pain on the Visual analogue scale (VAS), degree of dysfunction due to dystonia, and quality of life according to the Nottingham health profile (NHP). Objective measurement of dystonic position and movement ability was performed using a goniometer, semiquantitatively noted as scores according to Fahn and Tsui. Before treatment, the degree of impaired life quality on the NHP did not correlate with the Tsui score of dystonic posture, but significantly with the Fahn score ($p < 0.01$) which also includes data on pain. Significant improvement after treatment was seen for all parameters ($p < 0.05$). Global subjective rating correlated significantly with improved posture according to the Tsui score ($p < 0.05$), but not with reduced pain or degree of dysfunction. The results suggest that the efficacy of botulinum toxin in cervical dystonia is best evaluated using a combination of the VAS for pain and the Tsui score for dystonic posture and movement ability.

Key words: cervical dystonia, botulinum toxin, quality of life.

INTRODUCTION

Cervical dystonia, previously usually described as spasmodic torticollis, is a chronic condition of sustained or repetitive involuntary contraction of cervical muscles causing a dislocated head position (8). The condition is often complicated by pain and social disability including loss of capacity to work (2, 7). A prevalence of 89/million has been estimated, which makes cervical dystonia more common than more well-known neurological disorders such as Huntingtons' chorea or motor neuron disease (10). The delay to diagnosis is often several years with prior

misdiagnosis such as arthritis or psychiatric conditions (7).

During the last 5 years intramuscular injections with botulinum toxin have been established as the method of choice for focal dystonias, such as blepharospasm and cervical dystonia (11, 12). The efficacy has been demonstrated in placebo-controlled studies (6, 9), although lack of statistically significant objective effect also has been described (4). A uniform finding has, however, been clear subjective improvement of the majority of the patients in comparison with placebo, using various global rating scales. The duration of the effect is limited to about 3 months when the patients return for renewed treatment. In clinical practice the need for objective rating scores of the effect is evident. This is especially important since the pattern of dystonic muscle activation is very individual and has been shown to change after the introduction of botulinum toxin treatment (5).

The aim of this study was to ascertain to what extent a correlation could be seen between perceived treatment effect and the objective parameters of cervical dystonia that can be used in clinical practice for patients injected with botulinum toxin.

MATERIAL AND METHODS

Patients

The 20 patients who first completed at least one year of repeated botulinum toxin injections were included in the study. Mean age at completion was 57 years (range 42-78). The majority (13) were female, which is in agreement with larger studies (2, 7). Mean duration of dystonia was 16 years (range 3-35).

Nine patients were retired. Two patients were unable to work due to their dystonia, one due to other causes and the rest were working at the start of the botulinum toxin treatment.

Methods

Before the first treatment session all patients were instructed to complete the following forms:

Degree of pain due to cervical dystonia on the VAS 0-100.

Torticollis disability rating scale according to Fahn; ranking disability in all activities such as driving, working, reading and eating—maximal score 27 (3). Part 1 of the NHP questionnaire in the Swedish version (14). Total NHP score and six category scores regarding disturbance in emotional reactions, sleep, physical mobility; lack of energy, pain and social isolation each ranging from 0–100 were calculated.

At the first treatment session two status rating scales were completed by the same investigator:

A modified version of the Fahn torticollis score rating extent and direction of cervical and shoulder dislocation due to dystonia (max. score 6), presence of dislocation in relation to activity (max. score 4), duration and degree of dislocation (max. score 10), presence and degree of pain (max. score 10), presence of sudden spasmodic movement (max. score 10), and presence of tremor (max. score 2 points) or jerky movements (5 points)—for an aggregate max. score of 47 points (3).

The Tsui score reflecting the following variables:

A) Sum of the amplitudes of sustained dystonic movements in rotation, tilt and anteroposterior dislocation scored as: 0 = absent, 1 = < 15°, 2 = 15–30°, 3 > 30°.

B) Duration of sustained movements: 1 = intermittent, 2 = constant.

C) Shoulder elevation: 0 = absent, 1 = mild and intermittent, 2 = mild and constant, 3 = constant and severe.

D) Tremor; severity: 1 = mild, 2 = severe, multiplied by duration 1 = occasional, 2 = continuous.

Total score calculated as $(A \times B) + C + D$, maximal score 25 points (12).

The degree of disturbed posture in resting state and maximal active cervical movement in rotation, tilt and antero- and retroflexion, was measured by a goniometer (Myrinmeter, Olle Blomqvist Rehab-produkter AB).

After one year of repeated injections the patients completed the same forms as before treatment, with the addition of a global rating of effect. This was marked on a visual analogue scale ranging from -1 (deterioration) over 0 (unchanged) to +3 (total relief of symptoms). Based on previous experience the patients were presumed to have optimal effect of the treatment about 3 weeks after the last injection and were examined at this time by the same investigator as previously. This evaluation was done without examination of the results of the original scores, specific doses last given or discussing the subjective effect with the patient. The choice of one year of treatment for evaluation was arbitrary, but based on the experience that modifications of treatment to get an optimal result were most likely in the first three treatment sessions, i.e. within one year.

The doses of botulinum toxin were individualised primarily in response to distribution and degree of dystonic muscle activity. Total dose at last treatment given before evaluation ranged from 80–270 units of Botox (Allergan), mean 149. Two of the patients had after one previous injection experienced transient dysphagia as side effect, the others had not experienced any side-effects which affected the choice of dose. Statistical analysis was performed comparing pre- and posttreatment scores according to the Wilcoxon signed-rank test.

Correlation was performed regarding global evaluation and relative change in specific scores using Spearman's correlation coefficient analysis with adjustment for ties.

Mean values of the NHP total and category scores were calculated for comparison with age and sex adjusted group

control values for total and category scores, based on previous British studies on healthy subjects (14).

RESULTS

Three of the patients who did not improve on the Fahn score also ranked among the 4 patients who reported the least subjective effect on the global score.

Individual subjective and status scores for each patient are presented in Table I.

Global rating

Eighteen of the 20 patients noted improvement of at least +1 on the global rating scale. The median improvement was 1.5. Both the patients who reported negligible effects of the treatment also had low scores for pain on the VAS scale before treatment of 0 and 5 points, respectively.

Pain-VAS

The median pain VAS score of the whole group was reduced from 35.5 to 16.0 after treatment ($p < 0.01$). Neither large degree of pain pretreatment or a substantive reduction of pain was, however, a prerequisite for marked subjective improvement.

Fahn disability rating scale

A reduced score on the degree of functional impairment was found in 17 of the patients, median value before start of treatment 11.0 – after 8.5 ($p < 0.01$). One of the 2 patients who were on sick-leave due to dystonic symptoms was able to return to full time work schedule.

Nottingham health profile

The median NHP questionnaire total score was 28.5 before treatment, with a wide range from 0–85. The mean scores for each category were at least twice that of the control value except for sleep disorder, although some subjects with cervical dystonia consistently had scores at or below the mean values of the control group.

The patients perception of health in the NHP questionnaire total score before treatment had

Table I. Subjective global effect, pre- and posttreatment values of pain, function and status scores and reduced dislocation after treatment

(F=female, M = male, Age in years)

Sex	Age	Subj. score	Pain (VAS scale)		Dysfunction		NHP		Fahn score		Tsui score		Reduced dislocation
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
F	42	2.8	15	5	4	1	0	2	18	15	4	0	5
F	64	2.0	67	28	13	13	40	41	30	20	10	6	20
F	61	2.0	35	17	17	15	53	19	23	18	10	8	20
F	49	2.0	0	0	7	3	10	3	24	0	10	0	15
F	46	2.0	58	27	11	11	54	37	26	24	6	3	15
M	43	2.0	75	0	15	5	36	0	28	12	10	8	20
F	46	1.8	62	15	11	6	14	4	22	17	4	4	5
F	77	1.5	32	35	12	8	57	44	28	22	14	8	5
M	63	1.5	26	19	9	6	3	6	27	28	14	16	15
M	57	1.5	36	0	9	5	17	13	21	10	8	2	15
M	55	1.5	50	20	11	9	14	8	21	19	14	4	20
F	48	1.5	48	41	19	14	30	25	32	29	18	14	20
F	47	1.5	72	53	9	7	42	27	34	27	14	10	10
F	78	1.0	97	32	21	15	85	71	33	23	14	14	0
M	65	1.0	10	12	14	11	44	38	26	24	11	15	0
F	62	1.0	2	0	11	3	9	9	21	20	10	12	5
F	61	1.0	5	0	17	15	12	5	18	18	12	12	0
F	47	1.0	70	56	15	12	28	10	30	27	14	14	15
M	69	0.2	0	0	5	9	0	0	16	18	10	10	15
M	74	0.0	5	0	4	2	29	14	18	19	10	12	5
Median	1.5		33.5	16.0	11.0	8.5	28.5	11.5	25.1	19.5	10.0	9.0	12.5

significant correlation to the investigators evaluation using the Fahn ($r = 0.64$, $p < 0.01$) but not the Tsui score ($r = 0.25$).

The median combined score of the NHP questionnaire was reduced to 11.5 after treatment ($p < 0.01$).

The separate categories that showed the most

substantive reductions of the mean values were lack of energy, emotional reaction and pain (Fig. 1).

Status scores according to Fahn & Tsui, respectively

The median value of the Fahn score before treatment

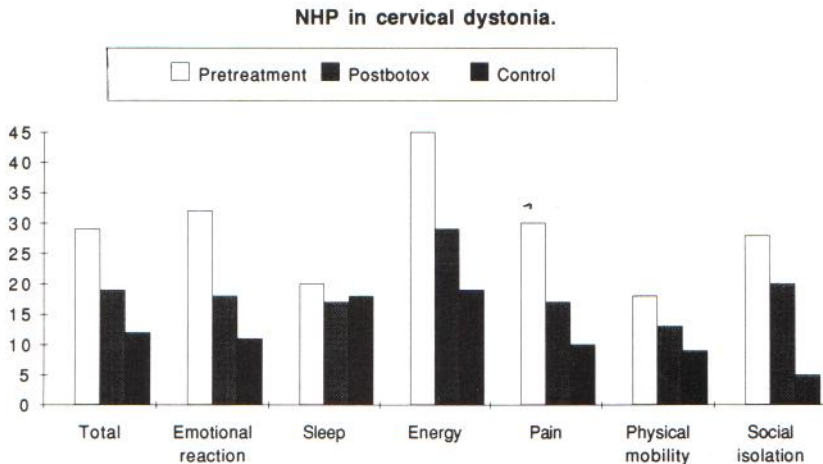


Fig. 1. Mean values of total and category scores of the Nottingham health profile for subjects with cervical dystonia before and after treatment with botulinum toxin and an age and sex matched control group as calculated from reference values (see Methods).

was 25.1 – after 19.5 with a reduction seen in 16 of the treated patients ($p < 0.01$).

The status score of Tsui demonstrated an improvement in 11 of the treated patients, with a reduced median score from 10.0 to 9.0 ($p < 0.05$).

A reduced dislocation (mainly in rotation) was measured with the goniometer in all but 3 of the treated patients, although this was not always reflected in the semiquantitative scoring of either the Fahn or Tsui scales.

Correlation of subjective and objective variables of treatment efficacy

Three of the 4 patients who did not improve on the Fahn score were also to be found among the 4 patients who reported the least subjective effect on the global score. The 7 patients who reported the least subjective improvement were all among the 9 patients who did not improve on the Tsui scale.

Factors contributing to the patient's evaluation of the treatment could be expected to be reduction of pain, normalization of posture and regained ability to perform daily activities. Correlation coefficients were determined between the global rating and the relative reduction (as percentage) of respectively pain VAS (restricted to the 18 patients who had pain before treatment, $r = -0.04$), dysfunction score ($r = 0.15$) and Tsui score ($r = 0.70$). The relationship was significant for the Tsui score ($p < 0.01$), but not for the other two parameters. A smaller ($r = 0.62$) but still significant ($p < 0.01$) correlation was found between global rating and reduction of the Fahn score.

DISCUSSION

The subjective effect found in the present study is in agreement with earlier studies finding improvement of 70–90% of subjects treated with botulinum toxin (6, 11, 12). The Fahn status showed good correlation with the patients, perception of health disturbance on the NHP questionnaire, presumably partly due to the inclusion of pain and other anamnestic data in this score.

The dystonic dislocation *per se* as scored according to Tsui did not significantly correspond with the subjective evaluation of health before treatment.

The Tsui score, on the other hand, measures

improvement of posture, which seems to be a key determinant of the perceived treatment effect.

This does not imply that reduced pain is an unimportant aspect of the subjective effect in most patients, but it underlines the importance of status scores reflecting dystonic posture to correctly evaluate the treatment effect.

Low sensitivity of marginal subjective improvement is, on the other hand, a limitation of the Tsui score, as earlier indicated in studies which failed to demonstrate any objective improvement (5). Small improvements seem to be more reliably detected with the Fahn score. The correlation with the global rating of improvement was not, however, superior to the Tsui score. Since the Fahn score is more time consuming, a combination of the Tsui score and degree of pain on the VAS score therefore seems to be a good basis for follow-up of treatment effect in combination with palpation of engaged muscles in the dystonic movements. When comparing different patient groups, however, the Fahn score seems more valid in relation to the patients perception of their condition.

The magnitude of impaired life quality (measured by the NHP) due to cervical dystonia prior to treatment with botulinum toxin was in our study group comparable to earlier studies on subjects with angina pectoris awaiting coronary bypass surgery (1).

The Swedish version of the NHP questionnaire has been demonstrated to have good reliability and validity for chronic conditions such as hip arthrosis and heart failure. The weighting of the questions in the various categories is similar to that of the English version (14).

Similar results regarding subjects with angina pectoris have been noted in studies on both Swedish (14) and British subjects (1). The British reference values should therefore be comparable to those of a Swedish group of similar age and sex composition.

Improvement of perceived health in the NHP questionnaire has been reported as a sign of efficacy after coronary bypass surgery (1) and hip arthroplasty (13).

The relative effect of the various interventions is hard to compare, since the groups are dissimilar regarding age and sex composition. The treatment with botulinum toxin demands repeated injections about every 3 months, which probably in itself has some negative effect on the subjective health evaluation.

If botulinum toxin treatment is introduced early

after the start of dystonic symptoms the social isolation and loss of ability to work may in many cases be avoided.

In some patients this pattern may be hard to break after many years of illness, regardless of the local effect of the injections. This underlines the importance of early detection and treatment of patients with cervical dystonia among those with cervicalgia and restricted neck movement.

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Address for offprints:

Tomas Odergren, M.D.
Department of Neurology
Karolinska Hospital
S-104 01 Stockholm