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Quantitative Assessment of Botulinum Toxin Treatment in 43 Patients with Head Tremor

*†Jörg Wissel, *Florian Masuhr, *Ludwig Schelosky, *†Georg Ebersbach, and †Werner Poewe

*Department of Neurology, Virchow Clinic, Charité, Berlin, Germany and †Department of Neurology, University Clinic, Innsbruck, Austria

Summary: We treated 43 patients who had head tremor as the major complaint with local botulinum toxin type A (Btx A) injections into neck muscles: 29 patients were classified as suffering from tremulous cervical dystonia (TCD), and 14 had head tremor without dystonia (HT). All patients were clinically assessed by means of the Tsui scale and a 4-point pain scale at baseline and follow-up visit. Quantitative recordings of head tremor with a bidirectional accelerometer system (horizontal and vertical planes) placed on the forehead were obtained before and 2–3 weeks after Btx A injections. Muscle selection for an injection was based on the visible and palpable tremor oscillation in the involved neck muscles and on analysis of standardized simultaneous electromyographic recordings of six cervical muscles. Patients with HT received mean total doses of 400 units (U) of Dysport (Btx A) (range, 160–560 U) distributed between the two splenius capitis muscles. Patients with TCD received a mean total dose of 500 U Dysport (range, 320–720 U) injected into a mean of 3 muscles (range, 2–4 muscles). The condition of all patients with HT and of 26 of the 29 patients with TCD improved subjectively. The total on the Tsui scale as well as pain scores decreased significantly ($p < 0.05$) following treatment. Latency of onset, duration of improvement, and side effects showed no significant difference in HT and TCD. Amplitude of HT decreased significantly for both groups following treatment. The mean dominant peak frequency in TCD and HT was slightly less than 5 Hz and did not change significantly after treatment. **Key Words:** Head tremor—Essential tremor—Cervical dystonia—Botulinum toxin.

Head tremor as a feature of essential tremor is difficult to treat and frequently less responsive to propranolol, primidone, or other agents known to ameliorate essential tremor (ET). Head tremor is also a well-known feature in cervical dystonia (CD), where it usually responds to local injections of botulinum toxin (1). In polygraphic recordings, up to 50% of patients with CD show brief head tremor episodes (2,3).

Following botulinum toxin type A (Btx A) treatment of CD, the responder rate range is 53–90% (4). The magnitude of score changes, especially tremor scores, is less well documented, and the effects on tremor frequency have not been investigated.

We therefore studied the tremolytic efficacy of local Btx A injections both in patients with head tremor without dystonia (HT) and in patients with tremulous CD (TCD) by using clinical ratings and quantitative head tremor measurements. Furthermore we compared tremor frequencies before and after treatment.

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Address correspondence and reprint requests to Prof. W. Poewe at Universitätsklinik für Neurologie, Anichstraße 35, A-6020 Innsbruck, Austria.

PATIENTS AND METHODS

A total of 43 consecutive patients with head tremor as the major complaint were included in the study and treated with Btx A (Dysport) injections. In 14 cases [12 female and two male; mean age, 52.1 years (range, 30–93 years), and mean duration of disease, 14.3 years (range, 2–30 years)], head tremor was not associated with any postural abnormality or dystonic electromyographic (EMG) activity during spontaneous head position or movements (Fig. 1) (2,3). Of these 14 patients, who were classified as having HT, six had an additional postural hand tremor ($n = 3$) and/or a positive family history ($n = 5$) that suggested a diagnosis of ET, whereas no definitive nosologic classification of HT was possible in eight.

A total of 29 patients [23 female and six male; mean

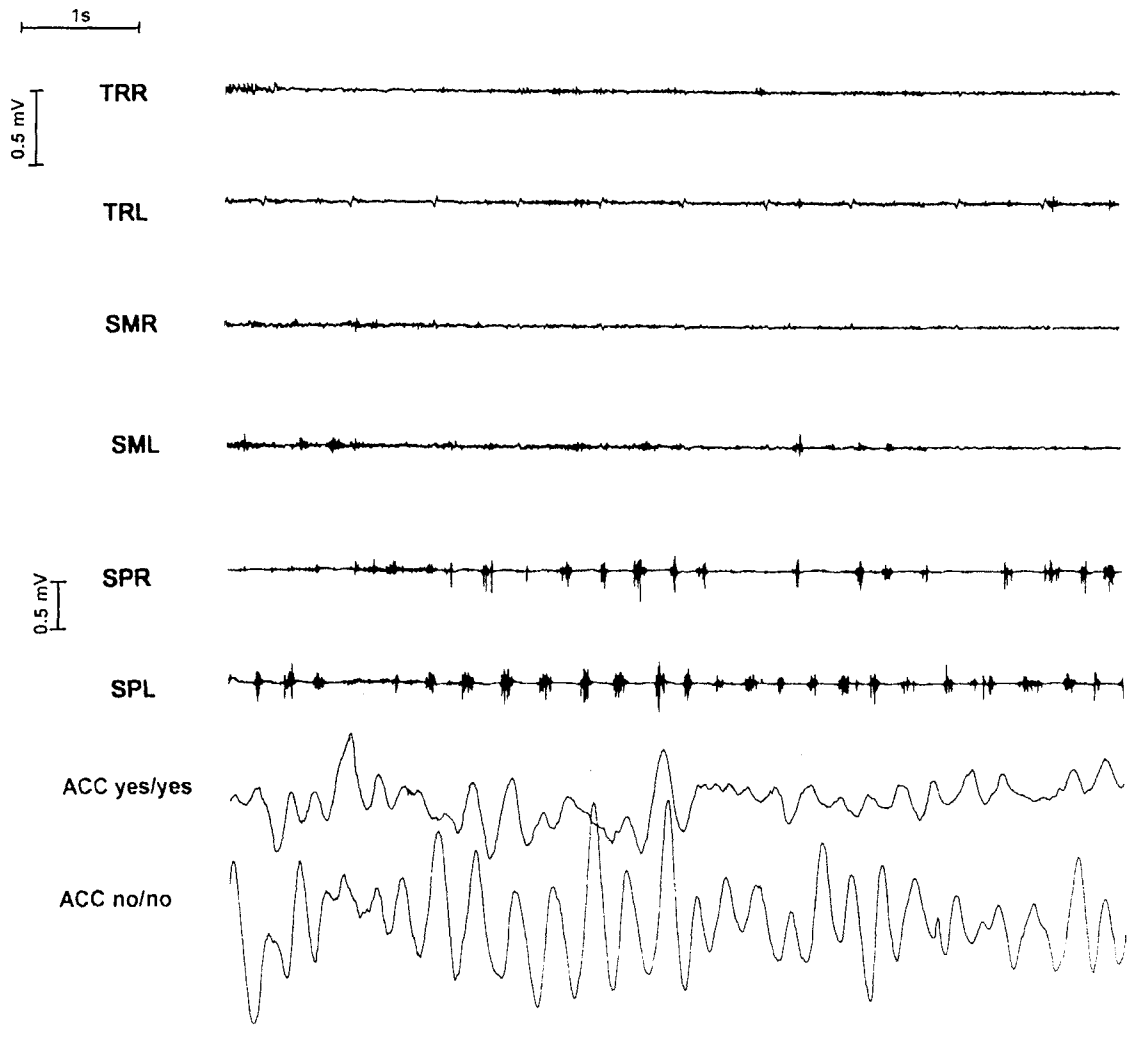

FIG. 1. Multichannel electromyographic recording of six prime head movers (bilateral splenius capitis, sternocleidomastoid, and trapezoid muscles) and bidirectional accelerometric signals (head movements in vertical and horizontal planes) of a 43-year-old woman holding her head spontaneously in the midline with marked no–no head tremor. *TRR,* trapezius right; *TRL,* trapezius left; *SMR,* sternocleidomastoid right; *SML,* sternocleidomastoid left; *SPR,* splenius capitis right; *SPL,* splenius capitis left; *Acc,* accelerometer; *yes/yes,* vertical plane; *no/no,* horizontal plane.

age, 53.8 years (range, 30–82 years); and mean duration of disease, 8.7 years (range, 1–54 years)] had mild but clear-cut postural deviation in addition to head tremor and were classified as cases of TCD with typical asymmetrical dystonic EMG activity (Fig. 2). Two patients with TCD had additional dystonic features (one blepharospasm and one writer's cramp), and one of them had a family history of dystonia. Six patients had additional postural hand tremor, and one of them had a family history of tremor.

Muscle selection for injection was based on visible head deviation and palpable tremor oscillation in involved neck muscles, and on the analysis of polygraphic EMG recordings (2,3) of six prime head movers: bilateral splenius capitis, sternocleidomastoid, and trapezoid muscles (see Figs. 1 and 2). The Tsui scale (5) and a 4-point pain scale (0 = no, 1 = mild, 2 = moderate, and 3 = severe pain) were evaluated at baseline and 2–3 weeks after treatment.

Quantitative recordings of the head tremor were obtained before and 2–3 weeks after the Btx A injections. Head movements in the horizontal (no–no) and vertical (yes–yes) planes were recorded with a bidirectional accelerometer system placed on the forehead while the patients were sitting in a comfortable chair.

The accelerometer system consisted of two piezoresistive accelerometers (ICS, MN, U.S.A.) with a range of ±2 G (±19.62 m/s^2) each, which were attached in a right-angled position to each other. Digitalization of the accelerometer data was performed by a digital signal pro-

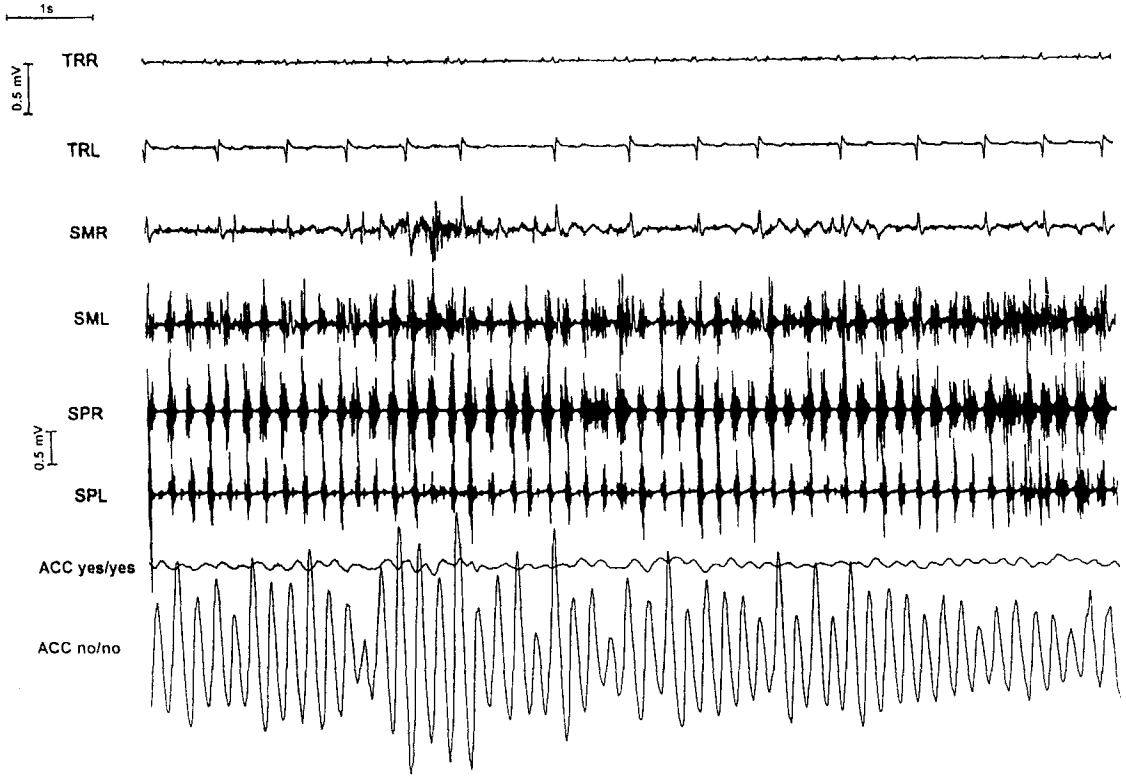

FIG. 2. Multichannel electromyographic recording of six prime head movers (bilateral splenius capitis, sternocleidomastoid, and trapezoid muscles) and bidirectional accelerometric signals (head movements in vertical and horizontal planes) of a 54-year-old woman with a marked no–no head tremor and cervical dystonia. Spontaneous head position with involuntary turning of the head toward the right (30°–40°) and mild tilt to the left (5°–15°). *TRR,* trapezius right; *TRL,* trapezius left; *SMR,* sternocleidomastoid right; *SML,* sternocleidomastoid left; *SPR,* splenius capitis right; *SPL,* splenius capitis left; *Acc,* accelerometer; *yes/yes,* vertical plane; *no/no,* horizontal plane.

cessor-based analogue/digital system over a 30-s period with a sample rate of 50 Hz. Further, FFT (fast Fourier transform, which transforms from the time domain into the frequency domain) estimations were performed with Hypersignal Workstation software. The data obtained by spectrum analysis were displayed for every plane on two orthogonal axes in which the root-mean-square magnitude of the frequency components (y-axis) were plotted as a function of their frequency (x-axis). Measurements were taken of the dominant frequency and its magnitude (peak power) expressed as power of acceleration [$(m/s^2)^2$].

The accelerometer data showed a parametric distribution when tested with the Kolmogorov–Smirnov test ($p > 0.05$). Statistical significance was tested by paired t tests for clinical and accelerometer data. Since the tremor amplitudes for the two accelerometer planes were correlated, the results were summed and a single statistic was applied.

RESULTS

The mean dose and the number of muscles injected in patients with TCD [mean dose, 500 units (U) of Dysport] were greater than in HT patients (mean dose, 400 U Dysport). All patients with HT received only bilateral injections into the splenius capitis muscles, whereas most patients with TCD received injections into three neck muscles: splenius capitis (n = 32), sternocleidomastoideus (n = 18), trapezius (n = 17), levator scapulae (n = 10), or semispinalis cervicis (n = 7) muscle.

The condition of all patients with HT and all but three patients with TCD improved subjectively. The mean Tsui score at 2–3 weeks following treatment in patients with TCD and HT decreased significantly ($p < 0.001$; TCD from 10.2 to 5.2 and HT from 3.1 to 1.1).

The mean baseline pain scores were higher in TCD patients than in HT patients. Pain reduction following treatment was significant ($p < 0.05$) in both groups (HT from 1.0 to 0.4 and TCD from 1.5 to 0.8). Mean response latency was 7 days for patients with HT and 8.6 days in the TCD group. The mean duration of improvement was slightly shorter in patients with HT (HT, 8.5 weeks vs TCD 9.2 weeks). The frequency of subjectively mild and transient side effects (local pain, neck weakness, and dysphagia) was equally distributed (HT 40% vs TCD 39%).

In all patients, the head oscillations in the horizontal plane were greater than those in the vertical plane. The mean dominant peak frequency of the no–no head tremor before treatment was slightly slower in TCD patients (4.5 Hz) than in HT patients (4.8 Hz). Treatment with Btx A had no significant impact on tremor frequencies, as shown in Table 1. The combined statistical analysis of the tremor amplitudes of the mean peak power before treatment and after treatment showed a significant reduction in both groups ($p < 0.05$ for the HT group and $p < 0.001$ for the TCD group; Table 2).

TABLE 1. *Quantitative head tremor measurement: mean dominant frequency*

	Mean peak frequency (Hz)	
Tremor	HT (n = 14)	TCD (n = 29)
Yes–yes baseline	4.3 (2.0–8.8)	4.2 (2.0–6.6)
No–no baseline	4.8 (3.5–7.8)	4.5 (2.0–6.6)
No–no posttreatment	4.8 (3.2–7.9)	4.5 (2.3–6.7)

HT, head tremor without dystonia; TCD, tremulous cervical dystonia.

TABLE 2. *Quantitative head tremor measurement: mean peak power of the dominant frequency (summed results of the tremor amplitudes for the two accelerometer planes)*

	Mean peak power [$(m/s^2)^2$]	
Tremor	HT (n = 14)	TCD (n = 29)
Baseline	0.079 (0.0016–0.2900)	0.088 (0.0006–0.4908)
Posttreatment	0.0255[a] (0.0003–0.1184)	0.0253[b] (0.0002–0.1970)

HT, head tremor without dystonia; TCD, tremulous cervical dystonia.
[a] $p < 0.05$.
[b] $p < 0.001$.

DISCUSSION

Botulinum toxin injections are now considered to be the most effective treatment for several types of focal dystonia. Using subjective response grading, and clinical and objective tremor measurements, the present study shows that botulinum toxin injections into neck muscles are an effective treatment both for patients with TCD and for patients with HT. Previous studies on the efficacy of Btx A treatment in CD have universally included patients with head tremor episodes. Only limited information is available about Btx A efficacy on head tremor. In a study by Jankovic and Schwartz (1), 42 of 51 tremor patients had disabling head tremors of various types (essential, dystonic, or combined). While reporting a global improvement in 67% of all head tremor patients, these authors did not specifically address the question of Btx A responsiveness in subgroups of head tremor. In a double-blind placebo-controlled trial, Pahwa et al. (6) recently studied the efficacy of Btx A treatment in 10 patients with an essential head tremor and failed to demonstrate significant improvements according to subjective response parameters, clinical ratings, and accelerometric measurements of head tremor. Nevertheless, half of their patients treated with Btx showed clinically judged improvements following treatment, compared with only 10% in the placebo group.

In the present study, subjective response, clinical ratings, and accelerometric measurements of head tremor amplitude showed significant improvement of similar magnitude both in TCD patients and in patients with HT. There were no differences in Btx A responsiveness between clearly dystonic head tremors and essential or unclassified head tremors.

All cases in the HT group of this series had previously received a variety of pharmacologic treatments (propranolol, primidone, trihexyphenidyl, or tiapride) for varying periods of time without showing a significant improvement. Nevertheless, all of them responded subjectively and objectively to a significant degree to Btx A injections. The present results therefore suggest that Btx A injections are equally useful for treating dystonic and nondystonic head tremors.

Accelerometric measurements showed a significant reduction in the tremor amplitudes in both groups. The tremor frequencies assessed by a computer-based frequency analysis, however, did not change significantly. Since the presumed mechanism of tremor reduction is the weakening of the contracting muscles, one would indeed not expect changes in the tremor frequency.

In addition to the tremolytic reduction effect, most patients reported a significant reduction in pain. This applied not only to patients with TCD, but also to a subgroup of HT patients with intermittent cervical pain associated with head tremor.

Adverse effects were only mild and transient, and no specific medical intervention was necessary. Frequency of side effects in TCD patients is in accord with those in previously published series of botulinum toxin treatment for CD (4). The higher incidence of dysphagia in TCD patients (n = 5) than in HT patients (n = 2) is probably due to the higher doses injected and to injections in the sternocleidomastoid muscle in TCD patients. The increased incidence of local postinjection pain in HT patients (n = 4) than in TCD patients (n = 2) might represent different subjective pain thresholds in two pa-

tient groups with different baseline pain severity (1.0 in IHT patients vs 1.5 in TCD patients).

Local Btx A injections appeared to be an effective and safe approach for treatment of patients with disabling head tremor irrespective of its underlying pathophysiology.

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