

TREATMENT WITH BOTULINUM NEUROTOXIN IMPROVES ACTIVITIES OF DAILY LIVING AND QUALITY OF LIFE IN UPPER LIMB TREMOR

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INTRODUCTION. Botulinum neurotoxin's (BoNT) degree of effectiveness on upper limb tremor is subject to debate: although this treatment reduces the amplitude of the tremor in essential tremor (ET)¹⁻¹⁰, a clear functional benefit has not been demonstrated. This limited benefit was explained by the occurrence of side effects and by a slight improvement in kinetic tremor. The non-optimal methodology used in pioneer studies also may explain the lack of benefit. Few studies have assessed etiologies of upper limb tremor other than Parkinson's disease (PD) and ET^{6,11-15}.

OBJECTIVE. The objective of the present study of a cohort of patients with upper limb tremor (due to various etiologies) was to assess the effectiveness of repeated BoNT injections on activities of daily living (ADL) and quality of life (QoL).

METHODS. We retrospectively examined the medical records of consecutive patients treated with BoNT injections for upper limb tremor. The choice of the target muscles was mainly based on a clinical examination, although EMG was sometimes used to select one muscle among several with similar actions.

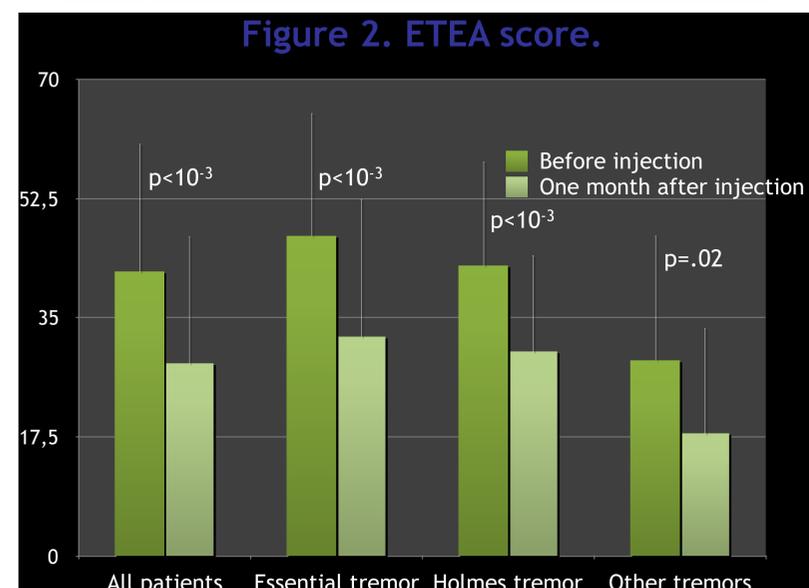
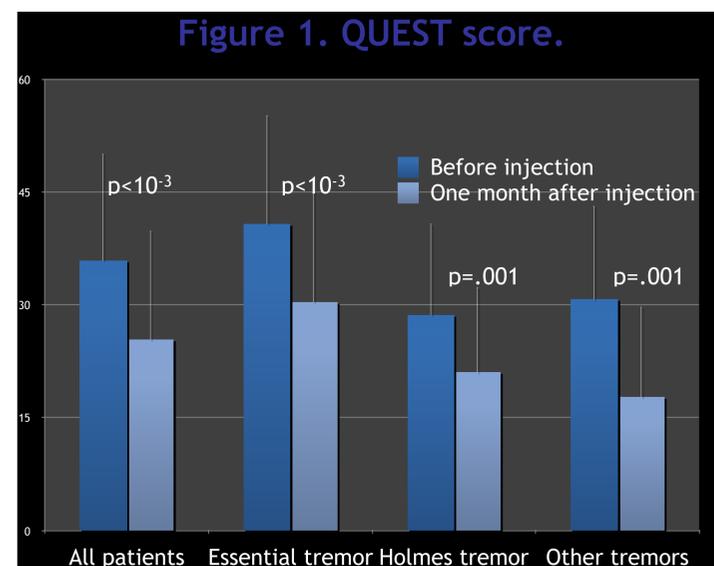
The following data were collected with regard to QoL and ADL: the QUEST¹⁶ and Essential Tremor Embarrassment Assessment (ETEA)¹⁷ on the day of the last injection and one month after the last injection (via a 'phone call). We also recorded the patient-rated Clinical Global Impression - Improvement (CGI-I)¹⁸. For quantitative variables, the Shapiro-Wilk test was used to study the normality of the data distribution, and intergroup comparisons were performed using Student's t-test or the Mann-Whitney U test. For qualitative data, intergroup comparisons were performed using the chi-squared test or Fisher's exact test. All quantitative data were quoted as the mean+/-standard deviation (median; range).

RESULTS. A complete data set was obtained in 38 subjects (25 men, 13 women; age 63,74+/-14,53 years). The etiologies of the tremor were ET (n=21), Holme's tremor (HT) resulting from focal, cerebral lesions (n=8), primary writing tremor (n=4), idiopathic dystonic tremor (n=4) and Parkinson's disease (n=1). The number of injection cycles was 12.45+/-12.74. The posology of the last injection was 136.24+/-97.58 U OnabotulinumtoxinA. The posology of BoNT (per limb) was higher in HT (216.13+/-127.93) than in ET (95.43+/-54.07) ($p < 10^{-3}$). The most distal muscles were more targeted in ET (74.40%) than in HT (44.16%) ($p < 10^{-5}$). The most proximal muscles were more frequently targeted in HT (41.96%) than in ET (16.35%) ($p < 10^{-8}$). QUEST, ETEA and CGI-I scores are summarized in Figure 1, Figure 2 and Table 1.

CONCLUSIONS. The results of the present study demonstrated an improvement in ADL (according to the ETEA) and QoL (according to the QUEST) in a group of patients with upper limb tremor one month after BoNT injections. Improvements were also observed in ET and HT subgroups.

To the best of our knowledge, BoNT's efficacy on upper limb tremor has never been specifically studied in patients with HT. We suggest that injections in the shoulder girdle muscles play a key role for successful treatment.

The good results obtained here and in other studies prompt us to think about the role of BoNT treatment within the overall therapeutic strategy. In ET, the question of second-line treatment frequently arises because beta-blockers and primidone - the two main oral medications in this condition - have limited functional benefit¹⁹ or fail to reduce the tremor in 30% of the patients²⁰. There are no guidelines on how many oral medications should be tried before considering BoNT injections or neurosurgery. Treatment with BoNT has a good short- and long-term safety profile and the side effects are always transient, which is not the case with neurosurgery. Despite several limitations (mainly the retrospective design), our study described the outcome of BoNT injections under "real-life" treatment conditions, and gave long-term results. In the future, a double-blind, placebo-controlled study including long-term evaluation (for example over 3 cycles of injections) would be of value because some patients improve after several injections or need to decrease BoNT dose because of side effects.



Population	Side effects (weakness)	CGI-I
All (n=38)	18.42% (n=7)	2.08+/-0.97 2 (0-4)
Essential tremor (n=21)	9.52% (n=2)	2.24+/-1.04 2 (0-4)
Holmes tremor (n=8)	12,50% (n=1)	2.13+/-0.99 2 (0-3)
Other tremors (n=9)	44.44% (n=4)	1.67+/-0.71 2 (1-3)

Table 1. Side effects and patient-related CGI-I (mean+/-standard deviation; median (range)) one month after the last injection.

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