

## ABSTRACT

# Autoimmune and Dystonia Distribution Characteristics of Cervical Dystonia Patients with Initial Resistance vs. Delayed Resistance vs. Responsiveness to Botulinum Toxin Therapy

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Initial resistance (1° NR) to botulinum toxin A therapy (Botox Rx) in cervical dystonia (CD) is characterized by at least two toxin exposures with EMG monitoring which produced weakness, atrophy and denervation, but no clinical improvement in dystonic symptoms. The phenomenon occurs in approximately 10% Botox Rx'd CD patients (Jankovic and Brin, NEJM, 1991).

Delayed resistance (2° NR) is characterized by no weakness, denervation or clinical improvements to Botox Rx after several earlier successful exposures. Many, but not all 2° NR have detectable Botox neutralizing antibodies (neut Ab). Some responding CD patients (Resp) have large Botox Rx dose and frequency without developing neut Ab (Duane, et al, *Movement Disorders*, 1995). Autoimmune antibodies (auto Ab), especially ANA, are more prevalent in CD than control patients (Duane, et al, *Neurology*, 1995). One-third of CD patients have extranuchal dystonia (CD+). This investigation studies whether 1° NR, 2° NR, Resp and neut Ab correlates with the presence of auto Ab or distribution of dystonic symptoms.

Fifty-three CD patients, 37 female/16male with mean age at study of 62 years had Botox Rx under EMG guidance at least twice. Eight were 1° NR, 14 2° NR, and 32 Resp. All had neut Ab assays at NorthView Pacific Laboratories and/or Boston University. Compared were gender, age at onset, duration of symptoms, duration of Botox Rx at last neut Ab titer determination, Botox Rx frequency including small booster doses, CD vs CD+ and presence of auto Ab (ANA, rheumatoid factor, thyroid). Neut Ab titers were classified as positive, equivocal (>40% but <70% animal survival) or negative. Statistical analysis was by G and t tests.

As expected, 1° NR had low dose and frequency of Botox Rx. The only comparisons with statistical significance were total dose exposure in Resp vs 2° NR (mean 1294 vs 2020 iu,  $p=.05$ ) and Resp vs 2° NR number of injections (mean 6.0 vs 10.2,  $p=.01$ ). One patient converted from positive Botox neut Ab with 2° NR to equivocal Neut Ab and Resp after one year's abstinence from Botox Rx.

In this preliminary investigation, the extent of dystonia and the presence of autoimmune antibodies does not influence the risk of Botox Neut Ab formation whereas total dose and frequency of exposure are correlated with 2° NR. However, eight of the 14 2° NR failed to demonstrate Botox neut Ab suggesting that either current assay techniques are insufficiently sensitive or other mechanisms induce 2° NR.

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