

ABSTRACT

A Paradigm for Assessing the Role of Botulinum Toxin Antibodies in Delayed/Secondary Non-Response

D.D. Duane, M.D. and A.M. Pickett, Ph.D.

Arizona Dystonia Institute/Arizona State University · Scottsdale / Tempe, Arizona, U.S.A.
Speywood Pharmaceuticals, Ltd., Maidenhead, Berkshire, England

An estimated 5% to 15% of cervical dystonia patients treated with botulinum toxin later lose the clinical benefit of such treatments. Whether the loss of benefit is secondary to circulating antibodies to the toxin (Toxin Ab) or other mechanisms (Duane et al, *Mov't Dis*, 1995) is not clear. How helpful the determination of circulating Toxin Ab may be in clarifying patient nonresponse at the muscle and/or the central dystonic mechanism level requires elucidation. For assisting future research addressing these issues, the following classification and paradigm of assessment of patient response and antibody determination is suggested:

Response: I-No local muscle response, i.e., no weakness, atrophy or EMG evidence of toxin-induced membrane change. II-No clinical improvement in patient pain, cervical range of motion, or posture despite evidence of muscle weakness, atrophy and/or EMG evidence of toxin-induced membrane change. III-Good clinical (more than 30%) improvement in dystonic symptoms and signs. A-Peripheral muscle weakness and atrophy with injection outside the site of clinical involvement. B-No peripheral muscle weakness or atrophy at site injected remote to the clinical area of interest. If within the first two injection series, primary (initial). If from >2 series, secondary (delayed). For example; IB- The patient is resistant and may have demonstrated antibodies to the commercial toxin employed; whereas, IIA raises the question that resistance may be non-Ab mediated. If such non-response occurs with the initial two trials of toxin treatment, the patient may be referred to as a *primary nonresponder*, with the description: *diffuse muscle/dystonia, neck/dystonia, dystonia or peripheral muscle nonresponse*. IIA is a *primary clinical dystonia nonresponder*. If the nonresponse is observed after several successful series, *secondary nonresponse* is the suggested term specifying whether the nonresponse is at the muscle (neck or peripheral) or the clinical effect on the dystonic process.

Toxin Ab titer: The specific toxin administered is to be indicated, i.e., A, B, or F. 1- In vitro Ab determination. 2- In vivo Ab determination. Challenge toxin in the in vivo determination to be indicated: a) purified toxin, b) Botox[®], c) Dysport[®], d) BotB[®]. For example, A2b represents presence of A antibody in which the commercial toxin used was Botox[®]. Titer determination should be designated: 1) absent or 2) present. If present, the titer level indicated as: a) low, b) intermediate, c) high.

Utilizing such a strategy of specific indication of patient response, antibody measurement including correlation with evidence of peripherally-induced weakness should permit clarification as to whether patient nonresponse is antibody mediated, related to other level muscle or central mechanisms.

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