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LETTERS TO THE EDITOR

BOTULINUM TOXIN TYPE A AND TYPE B FOR SIALORRHOEA IN PARKINSON'S DISEASE: A CASE FOR SWITCHING THERAPY?

Sir,

Over the last 20 years, botulinum toxin A (BTX-A) has been used to treat a variety of conditions involving muscle overactivity. Recent reports have indicated that BTX-A is both safe and effective in the treatment of persistent pathological conditions caused by dyskinesia (1) and many autonomic dysfunctions characterized by acetylcholine-mediated process, such as sialorrhoea (2–4) and hyperhidrosis (5). In particular, sialorrhoea affects about 10% of patients with Parkinson's disease (PD). Current treatment for sialorrhoea is unsatisfactory with respect to the side-effects of anticholinergic drugs and salivary gland radiation, while surgical treatments are invasive. However, in an open-label study of 18 patients with PD with diurnal drooling, we have demonstrated that a total dose of BTX-A of about 80 mouse units (MU) in a 1 ml volume, administered to the parotid glands via 2 distinct injections under ultrasound guidance (3), is effective and safe (4).

Although treatment with BTX-A is effective and safe, it needs to be repeated periodically and some patients develop secondary immune resistance (6) or do not obtain effective control of symptoms. Failure to respond to treatment on 2 successive occasions, without evidence of their condition worsening, suggests a developing insensitivity to BTX-A (7). In many patients, the cause of this secondary non-responsiveness is unknown. Since botulinum neurotoxin is a large protein, frequent dosing (8) or the administration of high cumulative doses (9) contribute to antibody formation. In clinical practice, the choice of dose and frequency of injections are designed to minimize antibody formation (10).

In cervical dystonia, botulinum toxin type B (BTX-B) has been shown to be an effective treatment for BTX-A-resistant patients (11, 12). Development of BTX-B began in the early 1990s with interest in its use for treating patients with cervical dystonia, approved by the Food and Drug Administration (FDA) in the USA. The intracellular targets of BTX-A and BTX-B are different (synaptosome-associated protein (SNAP-25) and vesicle-associated membrane protein (VAMP) or synaptobrevin, respectively) (13, 14). As a result, neutralizing antibodies developed against one serotype have not been reported to block the biological activity of another serotype.

We describe here the case of a 65-year-old man with sialorrhoea, with a diagnosis of PD (stage III Hoehn & Yahr) made 6 years previously. After unsuccessful treatment with oral anticholinergics, he was treated with BTX-A for 2 years to reduce sialorrhoea. The dose of BTX-A (Botox, Allergan, Inc., Irvine, CA, USA) injected into each parotid gland ranged from 25 to 50 mouse units (MU) in a 1 ml volume. We used a 1 ml syringe with a 26-gauge needle, and 2 injection points. The injections were placed in the parotid glands using a linear electronic ultrasound probe Technos of 7.5–13 MhZ (Esaote, Genoa, Italy). The Drooling Severity Scale and Drooling Frequency Scale were used to calculate the drooling score, considering the sum of the scores for severity and frequency of drooling (15). At first measurement, this patient presented a total score of 8. After starting treatment with BTX-A, the total score reduced progressively. However, in the second year after the commencement of treatment, the total score was not reduced, with the same result obtained even when the total dose was increased. This failure can be explained by the production of antibodies to BTX-A. The patient was therefore treated with a total of 1000 MU of BTX-B (NeuroBloc, Elan Pharmaceuticals, San Diego, CA, USA), in a 1 ml volume, divided into 2 sites and injected into each parotid gland, using the same ultrasound guidance as for BTX-A. After an effect latency of 3 days, there was a reduction in total drooling score (from values in the range 8–9 to values in the range 4–5). In this patient, with this dosage, the duration of effect was 3–4 months. No side-effects were noted, and after 3 years of treatment with BTX-B there are still therapeutic effects.

Published studies concerning BTX-B treatment for sialorrhoea in PD differ in the selection of patients and in methodology, and they report different efficacy and side-effects (16, 17). In fact, in almost all studies, BTX-B has been found to be as efficacious as BTX-A, but the duration of action of BTX-B has generally found to be shorter than that of BTX-A. Since BTX-B may produce the same effects, but not be disabled by neutralizing antibodies to BTX-A, it may be a possible therapeutic option for patients who have antibody resistance. Therefore, given the efficacy and safety of BTX-B in the management of sialorrhoea in PD, we propose switching therapy from BTX-A to BTX-B in patients who are non-responders or poor responders to BTX-A. Nonetheless, large clinical trials on BTX-A-resistant patients with sialorrhoea secondary to PD are required to address this issue definitively.

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