

## LETTERS TO THE EDITOR

# INAPPROPRIATE CITATIONS USED TO DESCRIBE THE PHARMACOLOGY OF BOTULINUM TOXIN TYPE A PREPARATIONS IN CLINICAL USE\*

Sir,

The recent European consensus published by Wissel et al. (1) is a well-documented report on the current use of botulinum toxin type A (BoNT-A) in adult spasticity. However, the authors describe the pharmacology of BoNT-A preparations by citing two publications that must be interpreted with caution.

Firstly, the paper of de Almeida & De Boule (2) has been cited, which included preclinical and clinical data supposed to differentiate BoNT-A preparations with respect to their diffusion characteristics. Pickett et al. (3) have subsequently clarified several sources of confusion in this work, including the absence of a role for the neurotoxin-complex size in diffusion of product, inappropriate unit ratios of different products being compared, and inappropriate animal studies cited for comparing BoNT-A products.

Secondly, a publication by Chapman et al. (4) has been cited, which included a review of clinical uses of BoNT-A products by analysing 57 papers and concluded a significantly lower rate of dysphagia following Botox® compared with Dysport®. However, of the papers reviewed by Chapman et al. (4), only 3 are direct comparisons between both BoNT-A preparations. Odergren et al. (5) conducted a well-designed study and concluded that the safety profiles of both toxins were not significantly different. Ranoux et al. (6) also conducted a well-designed, cross-over study in which Dysport® was more efficient than Botox®, although with a somewhat higher incidence of minor adverse effects. Their findings suggested that a unit conversion ratio between Dysport® and Botox®, starting from 3 U of Dysport® to 1 U of Botox®, was certainly too high, as recently corroborated by several publications (7–9) (2.5:1, 1.57:1 and 1.3–1.6:1, respectively). The third suitable paper included by Chapman et al. (4) was from Bihari (10) and is a less robust observational study with a heterogeneous population (blepharospasm, hemifacial spasm and cervical dystonia), making the conclusions highly questionable.

We consider the conclusions of the papers in the pharmacology section included by Wissel et al. (1) to be invalid because of obvious weaknesses in methodology together with inappropriate incorporation of incorrect pharmacological information from earlier publications.

\*This letter is written independently of the connection of the authors with Ipsen Company.

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RESPONSE TO LETTER TO THE EDITOR BY ZAKINE ET AL.  
ONGOING DISCUSSION ON THE PHARMACOLOGY OF BOTULINUM TOXIN TYPE A FORMULATIONS:  
CONCLUSIONS OF ADULT SPASTICITY CONSENSUS ARE CORRECT IN THIS RESPECT

We would like to acknowledge that variations in the methodologies used in clinical studies can undoubtedly account for differences observed in either efficacy or side-effects between botulinum toxin type A (BoNT-A) formulations. We are well aware of the limitations in previously published clinical studies and of the ongoing debates that have further added to the confusion. Indeed, the recent papers cited by Zakine, Pickett and Maisonobe (3, 8, 9 above), also have their limitations. They were, however, published after our Consensus Paper was submitted to this journal, but continue to add to the developing debate.

The objective of the consensus was to review the published literature and to provide statements of best practice based on this literature and supplemented by expert opinion informed by clinical experience. Expert opinion, based on clinical experience, is at this stage invaluable for making sense of conflicting evidence, to resolve confusion and for offering guidance to less experienced injectors. The issue of migration of BoNT-A is

of key importance, particularly where there is a need to treat multiple problems of spasticity and when the use of effective doses in multiple muscles is more likely to expose differences in side-effects between formulations.

As stated in the consensus, clinical studies comparing the migration of Botox® and Dysport® have not been carried out in patients with spasticity. Therefore, it seems valid that, until such studies are available, we examine the best published evidence in other indications, supplemented by our clinical experience in adult spasticity, in order to steer our less-experienced colleagues.

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