PostScript

CORRESPONDENCE

Dysport produces intrinsically more swallowing problems than Botox: unexpected results from a conversion factor study in cervical dystonia

Defining a conversion ratio between Botox and Dysport mouse units to compare their therapeutic potencies has puzzled neurologists for years: initial studies used inadequate clinical models, such as blepharospasm, hemifacial spasm, or spasmodic dysphonia, which are extremely dose insensitive with respect to their therapeutic outcome and side effects. A later study used cervical dystonia as a more sensitive model, but referred to independent patient groups, thus provoking criticism because of vast interinvidual cervical dystonia differences. By using cervical dystonia and applying a crossover design, the study by Ranoux and colleagues[1] certainly has methodological advantages over previous ones. However, it has its own flaws: with durations of action in the Dysport 1:4 group ranging from 0 to 491 days and a substantially larger standard deviation in this than in any other group, the Dysport 1:4 group obviously contains at least one, if not more, patients with clearly abnormal and unusual responses, thus erroneously overestimating this group's duration of action. The Dysport 1:3 group with a normal range of durations of action, was not significantly different from the Botox group. The meaning of a duration of action of 0 days in the Botox group and in the Dysport 1:3 group remains unclear. With the pain score in the Botox group being substantially lower than in the Dysport groups, the analgesic effect of Botox may well be underestimated. Additionally, by using the Tsui Scale rather than the Toronto Western Spasmodic Torticollis Scale[2] to monitor the motor effects of cervical dystonia and patient estimates of the beginning of the waning of the therapeutic effect as a measurement for duration of action, the raw data are subject to criticism. Unusual therapy parameters, such as average Botox doses of 100 MU only and single injection points per target muscle, may also have biased the results. The latter is particularly interesting as the side effect profiles reported may indicate a wider tissue penetration for Dysport than for Botox.

Another aspect of the Ranoux *et al* study, however, is much more exciting: cervical dystonia treatment with Dysport has been noted to produce more swallowing difficulties than cervical dystonia treatment with Botox. In the light of the conversion ratio discussion, the logical argument was usually that Dysport was relatively overdosed compared to Botox. The Ranoux *et al* study suggests that this may not be true. Instead, with a dose independent fivefold higher incidence of swallowing difficulties, Dysport must be intrinsically different from Botox.

Determination of conversion factors with clinical models is a never ending story. Measuring the biological effect of different botulinum toxin preparations directly within the target muscle may be a perspective for the future.[3] With the advent of NeuroBloc/MyoBloc, the conversion factor discussion has become even more complex: apart from different therapeutic potencies, completely different side effect profiles[4] now have to be taken into account.

D Dressler
Department of Neurology, Rostock University, Gehlsheimer Str. 20, D-18147 Rostock, Germany

Correspondence to: Dr D Dressler; dirk.dressler@med.uni-rostock.de

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Authors' reply

We appreciate Dr Dressler's interest in our study.[1] We agree that determining most appropriate conversion factors may be a "never ending story", although therapeutic trials are designed to make the story more rational. Certainly, measuring the biological effect of the botulinum toxin preparations directly within the muscle will not replace randomised clinical trials. We also agree with Dr Dressler's remarks concerning adverse events due to Dysport and Botox injections. We were surprised by the fact that, for the same efficacy, dysphagia was more frequent with Dysport than with Botox. Nevertheless, this reflects the experience of many injectors and could be explained by a different diffusion pattern of the two products.

We would like to reply to the several criticisms raised by Dr Dressler. As we mentioned in the results section, an unexpected long duration of action was observed in some patients. This was the case in the three groups, so the duration of action was not specifically overestimated in a single group, namely the Dysport 1:4 group. In this group, the range of duration of action was 46–491, in fact, and not 0–491 as mentioned by Dr Dressler. In fact, "0", as mentioned in the ranges for both the Botox and the Dysport 1:3 groups (table 2), means that one patient in each of these groups never reported any improvement. We do agree that the longer duration of action observed with Dysport was only a non-significant tendency, and needs to be confirmed by other studies. One should not forget, however, that our study was not designed to compare durations of action of the three regimens; this was only a secondary outcome measure.

Although the baseline pain score was lower in the Botox group than in the Dysport groups, the difference was not statistically significant, and we do not think this marginal difference may have artificially modified the final results. Contrary to the contentions of Dr Dressler, self evaluation of therapeutic efficacy by patients is an important tool in all randomised trials and is certainly desirable, when appropriate. In cervical dystonia, it appears to be both the best and the easiest way to assess the duration of action of injections, and this has already been used by others. We assume that the choice of the Tsui Scale as the main judgement criterion was suitable, as it has been widely used in previous studies and substantially contributed to the assessment of botulinum toxin efficacy in cervical dystonia. It was shown to be equivalent to the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) for assessment of improvement of cervical dystonia following treatment, especially when used together with the TWSTRS pain scale,[2] as in our study.

With regard to treatment doses, we do not agree that an average dose of 100 Botox units is unusual. Most of our patients presented with pure rotatory torticollis and the muscle couple splenius capitis-sternomastoid was usually treated. In our experience, 100 Botox units (104 in this study, range 70–180, table 1) are sufficient to treat the great majority of such patients. Furthermore, several recent studies support the hypothesis that low dose botulinum toxin treatment may be as beneficial as a high dose regimen.[3 4] In our study, we wanted the dose to be the only parameter to change within an otherwise standardised protocol of injection. Single site injection close to the motor point of the muscle is an easily reproducible technique and this is why it was chosen. To date, no study has found multiple site injections to be more effective than single site injections.

D Ranoux, M Zuber
Service de Neurologie, Hôpital Sainte-Anne, Paris, France

C Gury
Pharmacie, Hôpital Sainte-Anne, Paris, France

Correspondence to: Dr D Ranoux, Service de Neurologie, Hôpital Sainte-Anne, 1 rue Cabanis, 75 674 Paris Cedex 14, France; ranoux@chsa.broca.inserm.fr

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Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression

I read the interesting paper by Vroomen and colleagues[1] concerning the utility of clinical