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 interindividual cervical dystonia differences. By using cervical dystonia and applying a crossover design, the study by Ranoux and colleagues¹ 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 Scale² 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 profiles⁴ now have to be taken into account.

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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.^{3–5} 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.

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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 colleagues¹ concerning the utility of clinical

evaluation in patients with sciatica and suspected lumbosacral nerve root compression. While the study appears generally well done, I am concerned about several aspects of the calculations and the interpretation of some of the results. Firstly, the reported odds ratio for "male sex" appears to have been inverted; from the information presented it should be 0.55 and not 1.8. Secondly, the authors are inconsistent with rounding or truncation of reported values for the odds ratios; while some values were appropriately rounded, others were truncated where it appears that they should have been rounded up (for example, typical dermatomal distribution, less pain on standing or walking, less pain on lying down, history indicating root compression according to investigator, and paresis). Thirdly, there seem to be minor errors in several of the reported odds ratios or confidence intervals (for example, sports activities, finger to floor distance >25 cm, and hypalgesia); it is not clear if this relates to unreported missing values or something else, but the small magnitude differences based on the reported raw data do not substantially change the conclusions. Fourthly, the authors report a significant univariate odds ratio for the straight leg raise test (OR = 2.3, $p < 0.05$), yet because this test did not appear in the stepwise multivariate model, they concluded that "We were struck by the fact that the straight leg test was not a predictor of root compression. This test may indicate nerve root tension or irritation, but not necessarily nerve root compression." Stepwise multivariate regression techniques can be helpful in selecting a good predictive multivariate model, but must be used and interpreted with caution, particularly in the presence of collinear variables. Correlated explanatory variables can interfere with attempts to find the "best" or even a satisfactory regression model. Furthermore, such techniques can yield biologically implausible models, can select irrelevant "noise" variables, and can fail to select biologically important variables. They are more appropriate for prediction (that is, anticipating the results in a future subject) than explanation.

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Superficial temporal artery pseudoaneurysm following craniotomy

We read with interest the letter by Lee *et al* describing a case of postoperative superficial temporal artery pseudoaneurysm.¹ Although we agree that this complication is rare, we do not agree with their statement, "such a complication after cranial surgery has not previously been reported". Having recently submitted an identical case to a different journal, we too have reviewed the literature and feel obliged to share our experience.

In 1985, Rousseaux *et al* reported a case of an STA pseudoaneurysm that developed following a craniotomy for frontal lobe meningioma resection.²

In 1988, Shimoda *et al* reported a case of multiple STA pseudoaneurysms following a craniotomy.³ Their haemophilic patient sustained a golf ball injury to the left temporal region, which resulted in an intraparenchymal haematoma. An emergent left temporal craniotomy was performed. Forty days after surgery, two separate STA pseudoaneurysms were identified over the incision scar and treated by endovascular embolisation. Although it is conceivable that the golf ball was responsible for the pseudoaneurysms, the relation of the pseudoaneurysms with the incision scar is compelling evidence that they were the result of the craniotomy.

In 2000, an additional case of an STA pseudoaneurysm that developed after a craniotomy was reported by Tsutsumi and colleagues.⁴

Given the number of craniotomies performed each year along the course of the STA, the occurrence of this complication is exceedingly low, but not unreported.

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BOOK REVIEW

Clinicians guide to sleep medicine

Edited by N J Douglas (Pp 242, £29.99).
Published by Edward Arnold Publishers,
London, 2002. ISBN: 0340 742054

As the preface to this book states, the last 30 years has seen a rapid growth in the awareness of sleep disorders. In particular epidemiological studies have shown that obstructive sleep apnoea/hypopnoea syndrome is a prevalent disease that causes significant mortality. However, as readers of this journal will be well aware, not all sleep problems are respiratory related and any clinician working in this area needs to be familiar with all types of sleep disorders in order to make a differential diagnosis. A strength of this book is that it provides basic information on all common clinical sleep presentations; for each a brief outline is backed up with key references.

The author is an international authority on sleep related breathing disorders, and indeed many of the recent randomised placebo controlled trials showing symptomatic improvements following the treatment of obstructive sleep apnoea/hypopnoea syndrome have been carried out in his laboratory. Therefore it is not surprising that the book provides an authoritative overview in this area. The non-respiratory sleep disorders are less well

covered; although, it could justifiably be argued that this bias merely reflects the lack of research in these disorders. Areas where there is a lack of evidence to support clinical practice are clearly stated.

In summary, this is highly readable book that and provides practical information for those interested in broadening their knowledge of the management of with patients that present with common sleep disorders. Above all it makes the crucial point that education is the key for those working in this area—this simple book is likely to be a valuable resource for those seeking such an education.

Mary Morrell

Panayiotopoulos syndrome, a common and benign childhood epileptic syndrome

Edited by C P Panayiotopoulos (Pp 158, 345.00). Published by John Libbey, Eastleigh, 2002. ISBN 0 86196 619 8

Dr Panayiotopoulos has written this monograph cum swan song about the syndrome that he has put on the diagnostic map and to which his name has been attached. This childhood syndrome certainly breaks many "epilepsy rules". The seizures usually start with autonomic symptoms nausea, retching, or vomiting and evolve to altered awareness usually only after several minutes. Tonic deviation of the eyes follows, lasting many minutes, which may evolve into hemiconic or tonic clonic seizures. Sometimes children suffer atonic seizures "ictal syncope", another atypical form. About half of patients have seizures, which last more than half an hour—technically status epilepticus—and yet prognosis is good, and one third of affected children only ever experience one episode, the median number is three. The EEG often shows occipital spikes but the spikes may also be elsewhere and in one third are multifocal, usually a poor prognostic sign in epilepsy but not in this benign syndrome. There is often fixation-off sensitivity: electrographic paroxysms which appear when the child is in complete darkness or in light but is not visually fixating. They are abolished by fixation, irrespective of ambient illumination.

He argues the case for a benign focal seizure susceptibility syndrome, including this condition and benign epilepsy with centrotemporal spikes as different expressions of a related underlying tendency.

In his book Dr Panayiotopoulos describes his syndrome in detail including all the clinical and electrographic variants, with numerous case histories. His clinical experience is manifest in the text, which presents his personal views. The main criticisms of the book are the quality of the publishing, with variable print quality and illustrations and that it requires substantial padding to turn this relatively narrow topic into a whole book. However, it will be a reference source for anyone wishing to appreciate the subtleties of this syndrome.

Mark Manfred

Neuropsychological interventions, clinical research and practice.

Edited by Paul J Eslinger. (Pp 254, £38.00).
Published by Guilford Press, New York, 2002.
ISBN 1-57230-744-7

As the editor of this book says, at one time those who reported psychometric testing data

in relationship to a particular lesion location or disease process were considered more experimental and scientific, where rehabilitators were perceived as seeking a therapeutic effect from atheoretical and non-experimental approaches. Although this attitude is still prevalent in some quarters, the respectability of neuropsychological rehabilitation would appear to be on the increase. Several books on the topic have been published in recent years so why bother to buy or read this one? The main difference is that this book focuses on ideas, models, and methods driving current research into neuropsychological rehabilitation. The authors of each chapter were asked to address the question "How is research in this area conceptualised, scientifically framed, and experimentally advancing?" (p 13).

The book is comprised of 14 chapters (12 from North America and 2 from Europe) in three sections namely Foundations of Neuropsychological Interventions; Models of Intervention for Neuropsychological Impairments, and Future Directions (only 1 chapter in this section). The book is sound and contains some helpful and clinically relevant information. What I felt was lacking, however, was the integration of the work on different neuropsychological impairments into a sensible whole. If a person is referred for rehabilitation, we need to address the cognitive, psychosocial, behavioural, and emotional sequelae together and not address the individual problems piecemeal. A chapter on integrating theory and practice from a number of models, theories, and frameworks would have been welcomed. Nevertheless, there is much of value here for those engaged in the practice of rehabilitation or wanting to know the current state of play.

Barbara Wilson

Neuronavigation and neuroanatomy

Edited by Wolfgang Seeger, Josef Zwintner (Pp 419, EUR 248). Published by Springer-Verlag, New York, 2002. ISBN 3 211 83741 8

The increasing use of frameless neuronavigation constantly poses new challenges to neurosurgeons. Its aim is to create a linkage between digital image data and anatomical structure. This provides increasing 3-D orientation and hopefully thereby making operative interventions less traumatic, more precise, and also avoids external frames for stereotactic biopsies. Its increasing use in skull based surgery has particularly aided this multidisciplinary and interdisciplinary branch of surgery. The major drawback has been that the localisation, achieved at the

onset of surgery, as a result of intraoperative movement of brain (brain shift) will considerably reduce the accuracy of surgical targets. Therefore checks during the procedure are essential if safe and effective surgery is to be carried out. To date, mathematical modelling and real time data acquisition have not resolved this dilemma. The book provides some 200 pages of drawings which provide guidance for individual plans and to neuronavigational surgery by providing landmarks in the form of both points and shapes. It also provides some advice on surgical technique and approaches. It is useful both for the individual using neuronavigational techniques and also for those carrying out more traditional surgery.

As an atlas it is more of a reference book and reflects the experience of two very senior authors. The drawings are in colour, and although schematic, cannot be faulted in their purpose. If I were to make any criticism then I feel that the book is large and that there is a fair amount of wasted space, but this is entirely in keeping with the format of an atlas and perhaps a different layout would not have provided the clarity the authors were seeking to achieve. As a reference book it will prove both useful to individual surgeons and also to libraries.

James Van Dellen

Magnetic resonance imaging in dementia

By J Valk, F Barkhof and P Scheltens (Pp 353; £129.50). Published by Springer, Heidelberg, 2002. ISBN 3 540 41731 1

This lavishly illustrated book provides a lucid and up to date account of magnetic resonance in the dementias. It is a timely as well as an informative book. Dementia represents an epidemic of staggering proportions for countries with ageing populations: almost 20% of those over the age of 80 years have dementia. Neurologists, psychiatrists, and neuroradiologists will increasingly be involved in the investigation of dementia and magnetic resonance imaging (MRI) will be a key element in that process. Recent European and American guidelines now recommend MRI or computed tomography (CT) at least once in the assessment of all patients with dementia.

In the opening chapters, a succinct summary of the scope of magnetic resonance technology in dementia is provided, including overviews of modern MRI techniques, magnetic resonance spectroscopy, and functional imaging. Individual disorders are covered in subsequent chapters, under the broad but

appropriate headings of neurodegenerative disorders, disorders primarily affecting white matter, vascular dementias, and miscellaneous dementias. This classification proves to be a useful means of approaching the wide variety of diseases causing dementia, and to have particular relevance in terms of the imaging findings. The authors also strike the right balance between adequately discussing the commoner causes of dementia without neglecting the exotica. The illustrations of the MRI features of some of the less common dementias may be particularly valuable to leaf through when faced with a patient with an unusual scan.

However this book is far from being just an atlas of MR images in dementia. Its strength is that for each disease or condition, the clinical features, pathology, and where appropriate, genetics and treatment options are elegantly and concisely discussed. Even without the illustrations, it therefore proves to be an excellent textbook of dementia. The addition of numerous fantastically reproduced MR images, often accompanied where appropriate by MR spectra and line drawings, make this an invaluable and fascinating textbook for anyone with an interest in either dementia or neuroradiology. The rapid development of the field means this book should appeal to those in training or trained. Furthermore its illustrations are such that it would not seem out of place on your coffee table.

Jonathon Schott, Nick Fox, Adam Waldman

Mosby's color atlas and text of Neurology, 2nd edition.

Edited by G D Perkin (Pp 324, £28.95). Published by Elsevier Science, London, 2002. ISBN 0 7234 3208 2

There are now too many neurology textbooks available with little to choose between them. Hardly a publishing house does not have one! However, this is a reference text with a difference since it is also a colour atlas. There are excellent illustrations on virtually every page. Its only rival is Parson's colour atlas which is less comprehensive. This book is aimed at medical students and MRCP candidates. It is too detailed for medical students. MRCP candidates whom I showed it to liked its concise detail but felt that it could be improved with more emphasis on practical approach and differential diagnosis. It is well written with good summary lists and is a welcome addition despite the existing choice of neurology textbooks. It is reasonably priced and would be very useful to illustrate teaching sessions!

David Bateman