PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	**A Botulinum Toxin A Treatment Algorithm for De Novo Management of Torticollis and Laterocollis**
AUTHORS	Hefter, Harald; Kupsch, Andreas; Müngersdorf, Martina; Paus, Sebastian; Stenner, Andrea; Jost, Wolfgang

The above paper was submitted to the Journal of Neurology, Neurosurgery and Psychiatry (JNNP) but declined for publication following peer review. The authors addressed the reviewer's comments and submitted the revised paper to BMJ Open. The paper was subsequently reviewed by a BMJ Open reviewer with access to the JNNP reviews.

ORIGINAL SUBMISSION – JNNP REVIEW

REVIEWER	***R. Kaji*** Tokushima University School of Medicine Tokushima 770-0530 Japan

GENERAL COMMENTS	This is an interesting study on treatment algorithm for treating cervical dystonia. Although the study is well conceived, there are several points to be clarified. #1 Cervical dystonia usually presents with combination of torticollis and laterocollis. How did the authors separate them into each, if combined. This is not very well stated. #2 The rating scale (Tsui score) is outdated, and TWSTRS is better. #3 The authors defined the algorithm at first, and analysis performed later. It would be ideal if they could compare the outcomes of at least a few of them and choose the best.

REVIEWER	***E.K. Tan*** Singapore General Hospital Department of Neurology Singapore General Hospital Singapore

GENERAL COMMENTS	This is an open-label, multicentre study on the effectiveness and safety of 500 U botulinum toxin A (Dysport®) following a standardized algorithm for 516 patients with torticollis and laterocollis. At week 4, mean Tsui scores had significantly decreased and these remained significantly below baseline at week 12 in both groups. The most frequent adverse events were muscular

	weakness and dysphagia. The authors concluded that Dysport 500 U is effective and well tolerated for the de novo management of a range of heterogeneous forms of CD, using a standardized regimen that allows tailored dosing based on individual symptom assessment. The report is clear and concise. The strength of this study is the sample size. The findings are largely confirmatory and this is an open label study. The authors need to provide more justifications to argue that previous dosing based on investigator judgement may produce variable results and could increase the adverse effect. Even though they have a pre-defined protocol in their study, it is still the investigators decision to identify and treat the most disabling symptom and to select the relevant injection protocol and also the need for EMG. At the end of the day, the individual investigator's experience will play a major role. As it is, the authors have not provided and compared the relevant experiences of the large number of investigators who were involved in this study. Unless all these info are provided and compared, this reviewer is not entirely convinced that this open label study which recommends a pre-defined treatment regime provides convincing evidence on the added value of this approach compared to what have already been reported in previous placebo controlled studies.

A further review was received for the JNNP version of the paper but the reviewer has declined to allow it to be published.

BMJ OPEN VERSION - REVIEW

REVIEWER	***Satoshi Kuwabara*** Department of Neurology, Chiba University, Chiba, Japan I have no conflicts of interest. Prof. Kuwabara is an associate editor for JNNP
REVIEW RETURNED	11-Jun-2011

GENERAL COMMENTS	The authors prospectively investigated the effects of botulinum toxin-A treatment for cervical dystonia, and demonstrated that a single dose of 500 U can be used effectively for the management when being injected according to a standardised algorithm. The findings of the present study support the use of one vial of 500 U as an appropriate starting dose, while the authors properly claimed the limitation that the algorism should not replace clinical judgment and individual patient assessment. This study is well-designed and provides useful clinical data on treatment for cervical dystonia