Letters to the Editor

Botulinum toxin-induced myopathy in the rat

Tomas Odergren

Department of Neurology, Karolinska Hospital, Stockholm, Sweden

Correspondence to: Tomas Odergren, Karolinska Sjukhuset, Neurologiska kliniken, Box 130, 171 76 Stockholm, Sweden

The article by Hassan et al. (1995) describing histological changes in rat muscle induced by a botulinum toxin injection raises several interesting points for the therapeutic use of botulinum toxin. The diminished fibre size detected up to 18 weeks post-injection should indicate that fibre atrophy persists at the usual time of clinical relapse of focal dystonia ~3 months after each botulinum toxin treatment (Jankovic, 1994). The degradation of neuromuscular junctions commencing 4 weeks after the botulinum toxin injections in the study supports previous evidence from Hassan et al. (1994) of an elimination of superfluous neuromuscular junctions in the restitution phase after botulinum toxin injections. Both these findings are compatible with EMG concentric and macro needle recordings in the sternocleidomastoid muscle of patients repetitively treated with botulinum toxin injections at clinical relapse of cervical dystonia (Odergren et al., 1994). The amplitude and duration of the registered potentials were diminished, whereas an increase of these parameters would have been anticipated judging from earlier reports of persistent profuse neuroterminal sprouting after botulinum toxin injections (Alderson et al., 1991). Thus the restitution of muscular function does not seem to be associated with electromyographic signs of immature reinnervation even in muscles exposed to repeated botulinum toxin injections.

The degenerative changes found in muscle fibres, which were interpreted as myotoxic effects of botulinum toxin by Hassan et al. (1995), raise obvious concerns for the long-term effects of therapeutic botulinum toxin injections. The injections in the studies by Hassan et al. (1994, 1995) caused total disuse of the rats injected limb for the first 6–8 weeks. The dose relative to muscle size was therefore presumably much higher than the doses used for therapeutic injections in humans, in which the aim is to weaken but not paralyse the injected muscle (Jankovic, 1994). The degenerative changes may therefore be less pronounced in muscles exposed to therapeutic botulinum toxin injections, especially if the degeneration is secondary to acetylcholine transmission blockade and ensuing trophic changes, rather than direct effects of, for example, proteolytic actions in the muscle fibre. The pursuit of the least effective dose of botulinum toxin in each treated muscle, as well as keeping treatment intervals as long as feasible for the individual patient are suggested by the findings.

References


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Reply

Sherif M. Hassan and Frans G. I. Jennekens

Laboratory of Neuromuscular Diseases, Department of Neurology University Hospital Utrecht, The Netherlands

Correspondence to: Frans G. I. Jennekens, Laboratory of Neuromuscular Diseases, Department of Neurology, University Hospital Utrecht, PO Box 85 500, 3508 GA Utrecht, The Netherlands

We are grateful for the opportunity, offered by the interesting letter of Dr Tomas Odergren, to comment upon a few implications of our study (Hassan, 1995) for the interpretation of the effect of botulinum toxin in human. We would first like to stress that it was not our aim to mimic in rat the changes induced by the toxin in human. We intended instead to elucidate the histological changes induced by botulinum toxin type A in muscle and nerve fibres. This is why we used a higher dose than commonly given in human. It appeared that some changes in the muscle fibres were secondary to functional denervation, whereas others were more likely to be due to a direct toxic (proteolytic) effect on the muscle fibres. The changes took some time to develop

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