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EDITORIAL COMMENTARIES

Botulinum toxin in muscle spasticity

Botulinum toxin type A has been widely used in focal dystonias for more than 10 years, but it is also undoubtedly of benefit in the relief of spasticity,[1] a far commoner cause of motor impairment and neurological disability. The injection technique, by contrast with more traditional peripheral nerve blocks, requires little special equipment and can be learnt relatively easily. Thus it seems likely that botulinum toxin is destined to become much more widely used for this indication, although good evidence on which to base management decisions for busy clinicians is lacking.

There is uncertainty about the best delivery method regarding optimum dilution and the number of injection sites per muscle, but the toxin seems to diffuse adequately to produce dose dependent weakness. Dosage is usually estimated according to clinical judgement and the relative mass of the target muscle, but objective evaluation has always been difficult. In the paper by Hyman *et al* (this issue, pp 707–712) a careful attempt has been made to inform current, rather arbitrary, clinical practice with a properly controlled and randomised dose ranging study of hip adductor spasticity in multiple sclerosis.[2] These authors conclude that the optimal dose divided between both legs is around 500–1000 Units of the Dysport preparation, although evidence for a dose-response effect was not statistically significant.

Double blind studies often show less impressive effects than open label studies because of protocol constraints about which muscles to inject and doses to be used. The same is true of multicentre investigations using a very heterogeneous subject population. Nevertheless, it is salutary to note that the outcome measures improved in the placebo treated group almost as much as in those that received active treatment. Expressed differently, the effect size was relatively small and difficult to detect despite using a good range of appropriate measures.

Smaller doses injected into upper limb muscles are effective at relieving pain as well as spasticity after stroke

and can, paradoxically, actually increase grip strength by unmasking underlying voluntary movement.[3] It is claimed that the treatment may break the vicious cycle whereby chronic spasticity shortens muscles and increases spasticity further, permitting residual volitional movement to bring about active stretching. If supplemented by regular passive stretching by orthoses and intensive physiotherapy, benefit may last much longer than the duration of any paralysis induced by botulinum toxin and perhaps may even be permanent.

Such functional gains cannot be expected in patients with established spasticity, limited or no active movement at the target joint, and a static or progressive condition such as multiple sclerosis. Because of the relatively high cost, using large doses of botulinum toxin every few months to weaken several large powerful proximal lower limb muscles might seem prohibitively expensive. The challenge now is to undertake comparative cost-utility studies with increased physiotherapy, use of adductor wedge orthoses, or older techniques that seem to have fallen out of fashion such as obturator nerve blocks, before botulinum toxin is adopted uncritically as the treatment of choice.

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Impaired cognitive performance in drug free users of recreational ecstasy (MDMA)

In the paper by Gouzoulis-Mayfrank *et al* (this issue, pp 719–725)[1], the authors provide evidence that even moderate use of the recreational drug methylenedioxymethamphetamine (MDMA) may lead to cognitive decline in otherwise healthy young people.

This amphetamine derivative (known widely as ecstasy, XTC, or E, but also as Adam, clarity, or essence) is widely used by young people throughout western Europe and the United States. The popularity of the drug has been enhanced by its close association with particular forms of music and dance venues and, despite well publicised cases of MDMA associated death, by the widely held belief that MDMA is a "safe" drug. Indeed, many users think that with better management the dangers associated with the acute effects of MDMA can be removed.[2 3] This is based on the false premise that the danger lies in poor control of environmental temperature and "bad" or adulterated drug, which with better quality control, can be eliminated. As can be seen from the introduction to the paper by Gouzoulis-Mayfrank *et al*, the scientific literature paints a very different picture, with evidence from animal studies in particular of potent neurotoxic effects of MDMA itself on central serotonergic (5-HT) systems. Although many have vigorously contested the applicability of these results to the human condition, a growing body of data is sufficient to raise legitimate concern that negative consequences of exposure to MDMA, although manifest in subtle alterations in cerebral function in the short term (as described by Gouzoulis-Mayfrank *et al*), might develop into major deficits over longer periods of time. These may possibly be exacerbated by interaction with normal aging processes, or as a result of exposure to stress[4 5] and are likely to include cognitive dysfunction and mood disturbances. Even if these long term effects are confined to particularly susceptible people, the very scale of current usage is such that this could represent a major healthcare problem.

The initial studies indicating the dangers of MDMA were performed over a decade ago. Unfortunately in the intervening years we have experienced a sharp decline in the public acceptance of evidence based on animal experiments, and only now are data emerging from human studies which show clear parallels between the laboratory and clinical experience. Those who have been warning of the dangers of MDMA for some time will take scant comfort from having been proved right.

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