treat infant botulism patients has demonstrated its continued safety, efficacy and US cost-effectiveness.

Keywords: Botulism immune globulin (Human); BabyBIG®; Infant botulism; Botulinum toxin
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24. Analgesic effects of Botulinum toxin A in an inflammatory pain model in rats: Comparison of Dysport® and Botox®; synergistic interaction with morphine

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The analgesic effect of Botulinum toxin A has been already demonstrated in different experimental models of pain. The aim of the present study was to compare the efficacy of Dysport® and Botox® on inflammatory pain induced in rats by a sub-plantar (s.p.) injection of carrageenan (2 mg/0.1 ml) in the right hind paw. Hyperalgesia was assessed by measurement of the withdrawal threshold of each hind paw in response to mechanical stimulus (Randall & Selitto pressure test). In this model, Dysport® and Botox® elicited a comparable analgesic effect (ED50: 22 and 28 U/kg, respectively) when administered (s.p.) in the right hind paw 3 days before carrageenan administration. In this model, intraperitoneal injection of morphine induced a dose-dependent analgesic effect with an ED50 of 0.6 mg/kg. When a non-active dose of morphine (0.3 mg/kg) was tested in animals pre-treated 3 days before with a non-active dose of Dysport® (10 U/kg), a significant analgesic effect was observed. Considering that large doses of morphine result in side effects and tolerance, this result suggests that Botulinum toxin A may have morphine sparing effects.

Keywords: Botulinum toxin; Pain; Morphine; Carrageenan
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25. Xeomin® displays lower potency and is neutralized by anti-BOTOX® antibodies

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Xeomin® [Merz; 150 kDa Botulinum type A toxin (BoNT/A)] and BOTOX® [Allergan; 900 kDa BoNT/A complex] were compared, to assess the degree of similarity between these products in terms of potency and antigenicity. Potency was evaluated in the Digit Abduction Score (DAS) mouse assay. Full-range dose–response profiles were achieved with 3 lots of each product, with similarity between lots for a given product. Between products, however, the mean potency of Xeomin® was ~50% lower than that of BOTOX®. Subsequently, studies were conducted to investigate whether rabbit-derived, BOTOX®-neutralizing antibodies (nAbs) could also neutralize Xeomin®. Equi-efficacious, near-maximal doses (ED94) were selected for each product lot from the DAS potency profiles. Each ED94 dose for each lot was combined 1:1 with either naïve serum (control) or nAbs and then evaluated in the DAS assay. As expected, anti-BOTOX® nAbs inhibited each of the BOTOX® lots near-maximally (average DAS inhibition ~85% of matched control). Similarly, anti-BOTOX® nAbs also inhibited each lot of Xeomin® near-maximally (average DAS inhibition ~90%). These results suggest that inhibition of the 150 kDa toxin is the common basis for neutralization for both products. With lower potency and similar antigenicity, Xeomin® is not dose-equivalent to BOTOX® and would not be expected to be effective in BoNT/A-resistant subjects.

Keywords: BoNT/A; Potency; Antigenicity; Neutralization; Mouse
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26. An histological assessment of diffusion of different botulinum neurotoxin type A formulations injected in the mice leg

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Botulinum neurotoxin type A (BoNT/A) is largely employed in the therapy of a wide array of human syndromes characterized by a hyperactivity of peripheral cholinergic nerve terminals. In this study we determined the extent of diffusion of three different commercial preparations of botulinum neurotoxin type A by developing a high sensitive test based on Neural Cell Adhesion Molecule (N-CAM) expression in muscle. N-CAM is an integral membrane glycoprotein which accumulates on muscle fiber membrane after denervation and is not expressed in muscle under physiological condition. This analysis allowed us to monitor the functional diffusion of BoNT by identifying the muscle fiber paralyzed by the toxin.

Methods: Swiss webster CD1 mice were injected with Botox®, Dysport® or Xeomin® in a 1:4:1 ratio in the tibialis anterior of both hindlimbs (sx with one formulations and dx with another). In another set of experiments each mouse were injected with one of the three toxin formulations in one hind limb muscle and the contralateral muscle was used as control. A similar set of experiments was performed by injection of gastrocnemius and quadriceps femoris muscle. Further, immunohistological and immunoblot analyses were used to examine the expression of N-CAM in mice muscles injected.

Results: Our data indicate that the three formulations exhibit a very moderate diffusion in nearby muscles from injected site and only Dysport® shows a slightly wider mobility than Botox® and Xeomin®.

Keyword: BoNT/A N-CAM
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