TRANSDERMAL DELIVERY OF CLOSTRIDIUM BOTULINUM TOXIN TYPE A BY PULSED CURRENT IONTOPHORESIS

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Botulinum toxin is composed of a neurotoxin, which is classified immunologically into types A to G, and non-toxic components including hemagglutinin. The therapeutic possibilities of botulinum toxin type A are manifold and certainly not yet fully exhausted. The toxin is now being administered not only in focal dystonia and focal spasticity but also in several other medical fields. Tremors, hyperhidrosis, rhinitis, achalasia, hemifacial spasm, blepharospasm, anal fissure and aesthetic corrections are only several of the numerous fields where this neurotoxin can be used.

Type A botulinum toxin has a molecular weight ~150 000 Da; it is a highly potent inhibitor of the neurotransmitter release from the peripheral nerve terminus. The mechanism of action involves the cleavage of proteins associated with the process of exocytosis. The classical method of administering botulinum toxins is by injection. In this study we evaluated the possibility of administering type A botulinum toxin by pulsed current iontophoresis. Experiments were performed on male Wistar rats; after a mild abrasion of the selected skin area and of a control area, the toxin was applied onto the skin and the iontophoresis treatment was performed (current intensity waveform showed bursts of alternate symmetric 5 mA square pulses; electric treatment was performed for 10 min). Biopsies were taken both from control and from treated areas; specimens were then fixed and prepared for light microscopy observation. To evaluate the transdermal delivery and the distribution of type A botulinum toxin, immunoistochemistry reaction was performed. In order to verify the integrity of the tissue, specimens underwent classical Haematoxylin-Eosin staining. Our results show that iontophoresis allowed the transdermal delivery of type A botulinum toxin; the toxin appeared clearly localized in association with striated skeletal muscles localized below the deep dermis; only a weak colour was observed in association with the epidermis (i.e. at the site of application) and the dermis.

Haematoxylin-Eosin staining revealed no significant alterations in the skin area where iontophoresis was performed.

Thus, we hypothesize that pulsed current iontophoresis allows the transdermal delivery of type A botulinum toxin; this simple procedure can satisfy the request for a wide use of neurotoxins in medicine and surgery.