

PULSED CURRENT IONTOPHORESIS OF TYPE A BOTULINUM TOXIN FOR TREATMENT OF FOCAL HYPERHIDROSIS

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Introduction

Focal hyperhidrosis is a common disease with unknown etiology. There are some therapeutic approaches, all of which are relatively ineffective. Among these, local applications of metal salts (aluminium chloride) or tap water iontophoresis. More recently, local intradermal injections of type A botulinum toxin, a neurotoxin blocking the cholinergic stimulus of eccrine sweat glands, appear to offer an effective treatment option with few side-effects. Patient satisfaction rates are high. The procedure of injecting of type A botulinum toxin, however, shows a number of hindrances that limit its use. Among these, the so called needle fobia, and the strict requirements for sterility.

Because of the practical problems related to injections, we recently developed a pulsed current iontophoresis system that allows transdermal delivery of macromolecules without affecting their biological activity.

AIMS

In this study, we evaluated the feasibility of administering type A botulinum toxin by pulsed current iontophoresis for treatment of focal hyperhidrosis.

Preliminary experiments (Transdermal delivery of clostridium botulinum toxin type A by pulsed current iontophoresis, Pacini S., Gulisano M., Punzi T., Ruggiero M., AAD, Washington, 2007) were performed on Wistar rats.

After mild abrasion both on the selected skin areas and on control areas, type A botulinum toxin was applied onto the skin and the pulsed current 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 treated areas; specimens were then fixed and prepared for light microscopy observation. In order to evaluate the transdermal delivery and the distribution of type A botulinum toxin, immunohistochemistry reaction was performed.

To verify the integrity of the tissue, specimens underwent Haematoxylin-Eosin staining. The results show that pulsed current iontophoresis elicited the transdermal delivery of type A botulinum toxin.

The toxin was localized in association with striated skeletal muscles below the deep dermis; only a weak colour was observed in association with the epidermis (i.e. the site of application), and the dermis. Haematoxylin-Eosin staining revealed no significant alteration in the skin area where the treatment was performed.



After transdermal delivery, botulinum toxin type A was detected in association with skeletal muscles fibers.
Immunohistochemistry reactions : Panel A 200X, Panel B 400X panel C 400X (zoom)

Materials and Methods

To investigate the efficacy of pulsed current iontophoresis in delivering botulinum toxin type A through the skin for treatment of axillary focal hyperhidrosis in human, study were performed on 6 female patients.

The treatment session has been divided in 3 parts:

- Preliminary execution of Minor test (Fig.) for a quantitative evaluation of patient's sweating.
- Preliminary microdermoabrasion of the selected skin area to decrease patient's skin impedance (Fig.).
- Application of the type A botulinum toxin (**Vistabex®**, Allergan Pharmaceuticals), 50 units per side (under arm), 2cc saline solution diluted, driven in 10 (ten) minutes by a pulsed iontophoresis device, Fig., (**Mattioli Engineering Florence – Italy**) that is indicated for the transdermal administration of ionic drug solutions into the body for medical purposes and can be used as an alternative to injections (FDA approval N. K042590, Oct, 14th 2004). The control have been carried out after two weeks from the session performing a Minor test post-treatment.



Mattioli Engineering
Transderm® device

Results

The following results have been achieved:

Significant decreasing of the patient's under arm sweating (fig.) by control on Minor test.

Result Assessment : Good according to grade 3 from quartile evaluation scale (Between 51% and 75%)

Side effect : a light post treatment skin erythema

Complications: none.



Fig.1



Fig.2



Fig.3

Fig.1 preliminary Microdermoabrasion

Fig.2 Pre Test of Minor

Fig.3 Post Test of Minor

Conclusions

The present study proved the transdermal delivery of type A botulinum toxin (Vistabex® , Allergan Pharmaceuticals) through transcutaneous way using a pulsed Iontophoresis device. The main advantage using the present methodology is the complete absence of any pain and trauma associated to the high number of injections normally done in a mesotherapy setting together with the safety and easy use of the device. Finally it showed the possibility of delivery of a big molecule like botulinum toxin through the skin , opening the future applications with other high molecular substances in dermatology .

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Sponsored by: MATTIOLI ENGINEERING CORPORATION 8300 Greensboro Dr., Suite 800, McLean, VA 22102.