Journal of Pakistan Association of Dermatologists. 2023;**33(3)**:1677-1680.

Case Report

Fractional CO_2 Laser-assisted botulinum toxin type a delivery for primary palmar hyperhidrosis: A case report

Sarah Diba, Yuli Kurniawati, Odelia Jovita Jusuf Fantoni

Department of Dermatology and Venereology, Faculty of Medicine, Sriwijaya University; Dr. Mohammad Hoesin General Hospital, Palembang, South Sumatera, Indonesia.

Abstract Primary palmar hyperhidrosis (PPH) can be challenging for both patient and physician. Botulinum toxin type A (BTX-A) injection has been shown to be useful in treating PPH, whilst it causes pain and discomfort in most of the patient. Herein, we report a male patient with PPH who had shown a promising outcome after being treated with fractional CO_2 laser-assisted BTX-A delivery with no adverse effects.

Key words
Primary palmar hyperhidrosis; Laser-assisted drug delivery; Botulinum toxin type A; Fractional CO_2 laser.

Introduction

Management of PPH can be challenging for both patient and physician. Botulinum toxin type A (BTX-A) injection has been successfully performed for PPH despite its effect on pain sensation at site of injection and weakness in palmar muscle strength. Hence, other technique such as fractional CO_2 laser as laser-assisted drug delivery (LADD) for topical BTX-A has been developed.

Case report

A 29-year-old male with PPH for 13 years was treated with fractional CO_2 laser-assisted BTX-A delivery. At baseline, hyperhidrosis disease severity scale (HDSS), visual analog scale (VAS) hyperhidrosis and dermatological quality of life index (DLQI) scores were 3, 9 and 11 respectively; and positive starch-iodine was found on both palms (**Figure 1**). Two sessions of this treatment were performed on the right palm and 50 units BTX-A solution was applied immediately on each session at two weeks interval. The follow-up was observed every 2 weeks for the first 2 months, then every month for the next 2 subsequent months afterwards (**Table 1**). The peak anhidrotic effect was seen in 2-6 weeks after the last treatment. At week 6, HDSS, VAS hyperhidrosis and DLQI were improved; and starch-iodine test was negative on the treated side. Moreover, the anhidrotic effect of BTX-A started to subside in the 3rd month of treatment with the effect fully diminished in the 4th month.

Discussion

Primary palmar hyperhidrosis causes excessive sweating which can interfere with daily activities and decrease patient's quality of life. Injection of BTX-A is one of the modalities in treating PH. This patient had received

Address for correspondence
Dr. Odelia Jovita Jusuf Fantoni
Department of Dermatology and Venereology, Faculty of Medicine, Sriwijaya University; Dr. Mohammad Hoesin General Hospital, Palembang, South Sumatera, Indonesia.
Email: odeliajfantoni@gmail.com

Figure 1 Starch-iodine test (a) baseline (b) after 6 weeks.

Table 1 Assessment of therapeutic response using HDSS, hyperhidrosis VAS and DLQI.

Assessment	*Baseline*		*Week 2*		*Week 4*		*Week 6*	
	Left	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*
HDSS	3	3	3	3	3	2	3	1
VAS hyperhidrosis	9	9	9	6	9	4	9	1
DLQI	8	8	8	6	8	4	8	2

antiperspirant which is the first line therapy, but he did not experience any improvement thus intradermal BTX-A injection was preferred. However, pain associated with injection is a major limitation. Therefore, fractional CO_2 laser-assisted BTX-A was used in this case.

Botulinum toxin type A has large molecules measuring ~900 kDa and is a water-soluble protein, thus transdermal absorption is difficult and requires injection.[1,2] Molecules which are hydrophilic or too large (>500 kDa) to penetrate the stratum corneum must be encapsulated in liposomes, injected or administered systemically.[3] Chow and Wider-Smith reported that topical BTX-A did not produce an anhydrous effect on PPH.[2] Fractional ablative laser can function as LADD that breaks the skin barrier thereby increasing the penetration of topical drugs during clinical application. Laser-assisted drug delivery was chosen as it can increase drug penetration, minimally invasive and quick recovery.[4,5]

Botulinum toxin type A acts by inhibiting the release of neurotransmitter acetylcholine in postganglionic sympathetic nerves of the sweat glands.[6,7] Light chain of the toxin is released into nerves and bind to soluble N-ethylmaleimide sensitive factor attachment protein receptor (SNARE) protein, which inhibits the exocytosis of neurotransmitter acetylcholine.[7] This protein is required for the release of acetylcholine from vesicles at motor nerve endings, resulting in chemodenervation of motor nerves and autonomic nerves, causing skeletal muscle or eccrine sweat gland activity to be inhibited.[6–8]

Botulinum toxin type A therapy for PPH requires about 100 to 150 units in one palm, with a peak onset of anhidrosis in five to seven days.[7] The effect of anhidrosis lasts for 4-12 months.[6,7] Treatment of PPH with fractional CO_2 laser-assisted BTX-A delivery less painful than BTX-A injection therapy.[9] However, time management needs to be taken into account as it requires one hour of topical anesthetic application before laser.[10] In this case, the right palm was applied BTX-A 50 units per application twice with two weeks interval.

The use of CO_2 fractional lasers can increase permeability and penetration depth of topically applied drugs.[4,9] Thermal damage caused by fractional lasers forms a microscopic treatment zone (MTZ) which provides an access pathway

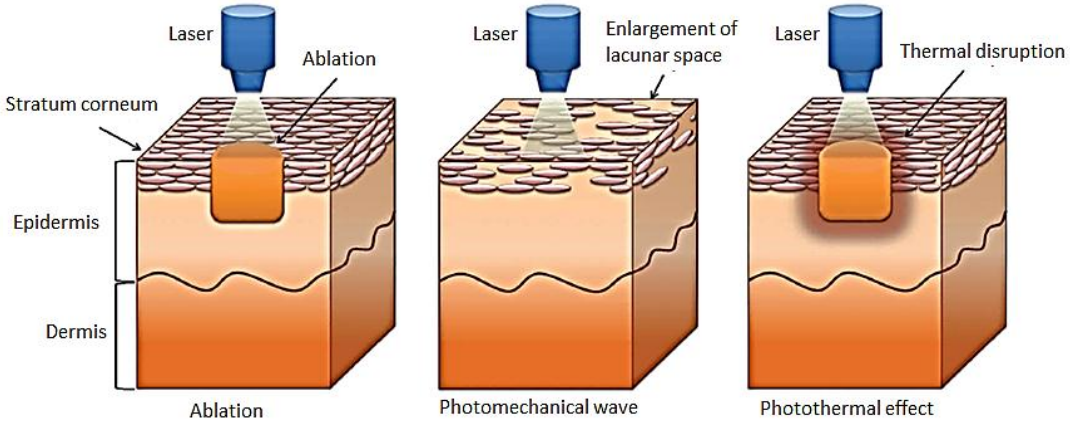

Figure 2 Mechanisms of laser-assisted drug permeation. [5]

for drug molecules. Fractional lasers create smaller wound sizes, thus epithelial regeneration is faster.[4] Fractional laser therapy as LADD increases the penetration of topical drugs into the stratum corneum, epidermis and dermis.[4] In this case, the therapy to be given is BTX-A 100 topical units on right palm using CO_2 fractional laser as LADD since intact stratum corneum is impermeable to molecules larger than 500kDa.

The mechanisms of laser-assisted drug permeation, including direct ablation, photomechanical waves, and photothermolysis effects (**Figure 2**).[5] Fractional ablation penetrates skin barrier through the formation of micropore, thus drug molecules can pass through the formed microchannels.[5,9] Another mechanism is through photomechanical waves which can cause an increase in superficial skin permeability through expansion of intercellular space and intracellular lipids. The third mechanism is photothermal which destroys the skin barrier through the transformation of light energy into heat when absorbed by the chromophore, causing denaturation and coagulation resulting in drug penetration into the skin.[5,11] Drugs can reach deeper layers of the skin to the dermis which is called vertical diffusion. Drugs can also diffuse into surrounding tissues through lateral diffusion.[5] Topical drug administration with LADD technique helps drug molecules penetrate the outermost barrier of the skin, which is stratum corneum, thereby allowing drug reaches deeper layers of the skin through transepidermal and transappendegeal pathways.[9,10]

Junsuwan *et al.* used fractional CO_2 laser-assisted BTX-A delivery in the left palm of 3 patient with PPH. A total of 100 units topical BTX-A was applied with energy 12.5 mJ, pulse duration 950 s, scan size 10x10 mm, resulting in a decrease in VAS hyperhidrosis compared to baseline 54.1 %, 83.4%, and 58.4% at 2, 6, and 10 weeks, respectively, after the first session.[10]

The most common side effects in LADD technique, including erythema, edema, moderate-severe pain, and hyperpigmentation.[9] The use of BTX-A can cause palmar muscle weakness.7,14 We noted some discomfort that disappears about 30 minutes after the laser, but no other side effects were found.

Fractional CO_2 laser-assisted BTX-A delivery had shown a promising outcome in improving excessive sweat production for PPH without significant adverse effects. It appears to be a feasible alternative in treating PPH.

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