Effect of transdermal botulinum toxin on sweat secretion in subjects with idiopathic palmar hyperhidrosis

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SIR, We explored whether a simple unassisted transdermal delivery of botulinum toxin type A (BTX) is effective for treating palmar hyperhidrosis.

Palmar hyperhidrosis is common and troublesome. Nonsurgical treatments include topical antiperspirants, iontophoresis, anticholinergic drugs and botulinum toxin injections. Most antiperspirants contain 1–2% aluminium salts and, although convenient and effective, require repeated application and can irritate skin.[1] Iontophoresis, although effective,[2] has disadvantages of requiring frequent, lengthy treatment and potential skin allergy.[1] Oral anticholinergic drugs are largely ineffective because of undesirable side-effects.[1] BTX injections are highly effective in treating palmar hyperhidrosis with effects lasting 6 months.[3–5] However, pain associated with injection is a major limitation. Surgical procedures such as thoracic sympathectomy are fairly effective but high rates of compensatory hyperhidrosis are a major negative side-effect.[6]

We have previously postulated that BTX can be administered topically, either with or without assistance by procedures such as iontophoresis or sonophoresis.[7]

This prospective study was performed at the National University Hospital, Singapore. Informed consent was obtained from 16 subjects aged 20–50 years with idiopathic palmar hyperhidrosis. The hospital ethics board reviewed and approved the study.

Exclusion criteria were diabetes mellitus, polyneuropathy, anticholinergic medication, pregnancy and thyrotoxicosis. Caffeinated substances were withheld 6 h prior to testing.

Subjects received 100 units of BTX (Botox®; Allergan, Irvine, CA, U.S.A.) in saline solution transdermally on the right (dominant) hand, heated with a thermal lamp before testing to achieve maximal opening of sweat pores and thus permit better BTX entry. Saline solution served as a control to the left hand. Tight-fitting powder-free plastic gloves were worn and the fluid was carefully squirted into the palmar glove side along the inside of the sleeve and the wrist tied off to prevent leakage. Gloves were worn for 2 h and subjects instructed to rub the palms to maximize BTX absorption.

Sweat production was assessed using the Quantitative Sweat Measurement System (Q-Sweat; WR Medical Electronics Co., Stillwater, MN, U.S.A.) and the starch–iodine sweat test. Assessments were made 1 h prior to BTX application and at weeks 2, 4, 8, 16 and 24 following BTX application.

Q-Sweat parameters included baseline sweat volume and percentage increase in poststimulation sweat volume. The starch–iodine sweat test rated sweating on a scale of 1–3: 1, sweating absent; 2, 50% sweating; 3, 80% or more sweating.

Patients rated their hand sweating prior to BTX application and at weekly intervals for the first 2 months followed by monthly intervals for the remaining 4 months. Patient Sweat Scoring, subjective sweat assessment, used an analogue scale of 0–100 points: 0, no sweating; 100, most severe form of sweating.

Sweat output parameters were compared between BTX and saline solution. Both subjective and objective parameters of sweat production collected from all 16 patients showed this technique of delivering BTX through the skin not to be effective. There was no statistically significant improvement ($P > 0{\cdot}01$; Mann–Whitney test) at 2 and 24 weeks post-treatment in all subjects (Fig. 1).

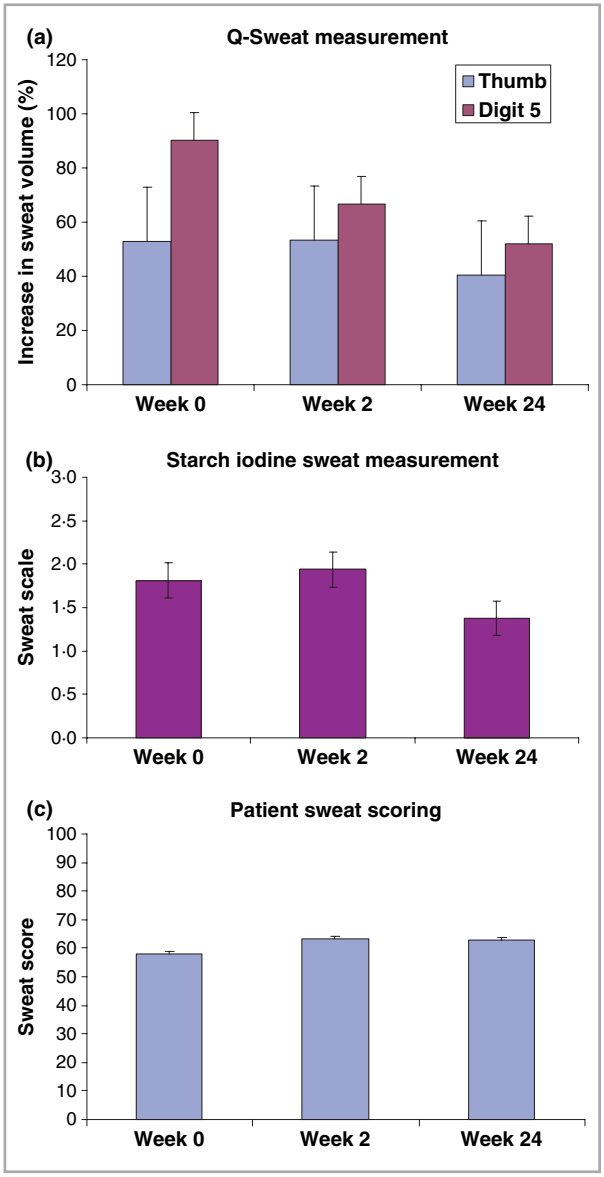

Fig 1. Subjects with transdermal botulinum toxin type A applied. (a) No significant improvement in sweating was observed at weeks 2 and 24 in the thumb and digit 5. Sweat measurements by (b) starch–iodine testing and (c) patient individual sweat scoring also did not show any significant effect.

Several factors may account for this. BTX adhesion to syringes or gloves could lead to protein adsorption or denaturation and hence reduce BTX efficacy. However, gloves were nonmedicated and nonpowdered, and plastic syringes are routinely used to administer reconstituted BTX solution. We also considered whether bubbling and agitation during reconstitution and application could lead to denaturation. This is unlikely as the 900-kDa BTX molecule is a stable protein.[8]

Rather, we suggest that the main reason for the negative findings of this study is related to two factors. To be effective, BTX needs to reach the sweat glands via the sweat ducts. This journey, 2–5 mm long, commences at the sweat pores, follows the relatively straight distal duct section and requires negotiating the densely coiled duct section proximal to the sweat glands.[9] BTX therefore has a relatively large distance to travel from the skin surface to the active site, the secretory portion at the proximal end. The winding portion of the sweat ducts may necessitate an additional driving force to be applied to ensure BTX delivery to the sweat gland. Iontophoresis of BTX has been shown to be effective in palmar hyperhidrosis for periods of up to 3 months.[10]

Second, but likely to be less important, is the relatively large size of the BTX molecule. The 900-kDa size of the protein complex may reduce the diffusion rate through the sweat ducts.[8]

Our study fails to show an effect of a simple transdermal application method of BTX in the treatment of palmar hyperhidrosis. Future efforts for devising simpler, less painful application of BTX will need to improve transdermal methods of delivery to the dermal sweat glands. One possible method to improve delivery would be by using smaller BTX molecules such as Xeomin® (Merz Pharma, Frankfurt am Main, Germany) which is 150 kDa as compared with the 900-kDa Botox® used in this study.[8]

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Key words: *botulinum toxin type A, palmar hyperhidrosis, quantitative sudometry, starch–iodine, transdermal*

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Every cloud has a silver lining?

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Sir, The recent report of generalized argyria secondary to topical silver sulfadiazine in a patient with dystrophic epidermolysis bullosa[1] was very interesting. However, the Greek word for silver was misspelt, with a ν substituted for the correct υ. Previous educational trends banished Latin and ancient Greek from the classroom for many years; however this downward trend may now have reversed.[2] Neglect of ancient history and languages in educational curricula was the cause of a recent demonstration in London, which was addressed (in Latin) by Boris Johnson.[3] Might I suggest that a dermatologist volunteer to vet such Latin and ancient Greek terms when they are used in the *British Journal of Dermatology*? Two senior dermatologists with classical educations immediately come to mind. Sadly, misprints appearing in journals are all too frequently copied (as can be evidenced by the various published spellings of the names making up the 'Z-N' stain).

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Key words: *Greek, silver, spelling*

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