Duration of efficacy increases with the repetition of botulinum toxin A injections in primary palmar hyperhidrosis: A study of 28 patients

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Background: Intradermal injections of botulinum toxin are effective but transitory in primary palmar hyperhidrosis. These injections are repeated when the symptoms recur. We do not know how the duration of efficacy changes when injections are repeated.

Objective: In this retrospective study, we aimed to investigate the change in the duration of efficacy of botulinum toxin A (Dysport, Ipsen, Boulogne-Billancourt, France) with the repetition of injections in patients with primary palmar hyperhidrosis.

Methods: From May 2001 to April 2012, 28 patients were treated with a dose of 250 U of botulinum toxin A per palm. We compared the duration of efficacy of the first and last toxin injections.

Results: The median duration of efficacy was 7 months for the first injection and 9.5 months for the last, the difference being statistically significant (P = .0002).

Limitations: Study limitations include a relatively small number of patients treated at a single center and evaluated retrospectively.

Conclusion: To our knowledge, this study is the first to report a significant increase in the duration of efficacy of botulinum toxin A injections with the repetition of injections in patients with primary palmar hyperhidrosis. The reasons for this effect may be linked to the mechanism of action of botulinum toxin, and may improve our understanding of its pharmacologic effects. (J Am Acad Dermatol 2014;70:1083-7.)

Key words: axillary; botulinum toxin; duration of efficacy; hyperhidrosis; increase; repetition of injections.

Hyperhidrosis is excessive production of sweat affecting 1% to 3% of the population, with a sex ratio of 1, and is most prevalent among those aged 25 to 64 years.[1-3] It can have major psychosocial repercussions for patients.[4-6] It is mostly idiopathic (primary) but may be associated with an underlying disease. It is localized in 90% of cases,[7] but it may also be generalized. The regions of the body most affected are the underarms, palms of hands, soles of feet, forehead, and inguinal folds. Sweat is secreted and excreted by the eccrine sweat glands, which are innervated by cholinergic fibers, paradoxically, via the sympathetic system. The first-line local treatments are antiperspirants based on aluminium salts, which often prove ineffective, and iontophoresis. Intradermal injections of botulinum toxin are used as a second-line treatment and have been shown to be effective[8] by blocking the presynaptic release of acetylcholine. These injections are repeated when the symptoms recur. Treatment has been reported to be effective for about 2 to 22 months, but nothing is known about the change in

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the duration of efficacy with repeated injections.[9-15] Endoscopic thoracic sympathectomy is a possible invasive treatment, which is offered in severe cases, after the failure of other medical treatments. It frequently causes compensatory hyperhidrosis. It is also an expensive treatment. The aim of this retrospective study was to evaluate the changes in the duration of efficacy of botulinum toxin injections for palmar hyperhidrosis with the repetition of injections.

CAPSULE SUMMARY

- Injections of botulinum toxin are effective but transitory in primary palmar hyperhidrosis.
- We report a significant increase in the duration of efficacy of botulinum toxin with the repetition of injections.
- This finding provides additional evidence about the long-term effectiveness. Patients can expect a decreased need for injection sessions over time.

METHODS

We included all eligible patients followed up for primary palmar hyperhidrosis and seen between May 2001 and April 2012 in dermatology consultations at Le Mans Hospital in France for treatment with botulinum toxin.

All the patients had experienced failure for first-line treatment with antiperspirants based on aluminum salts with concentration at 20% and/or iontophoresis, with major psychosocial repercussions.

All these patients had palmar hyperhidrosis detected by Minor test.[16] In this test, 2 g of iodine and 4 g of potassium iodide in alcohol to 100 mL is painted over the skin area. After it has dried, a fine starch powder is applied. Sweat causes the color to turn dark blue. The result is measured over 5 minutes at room temperature and at rest. In all cases the iodine-starch test made it very easy to identify the location of excessive sweating in the palmar skin (Fig 1).

All had a Hyperhidrosis Disease Severity Scale (HDSS) score of more than 2/4, indicating severe hyperhidrosis and that sweating interfered with activities of daily living. It is a disease-specific scale for hyperhidrosis that provides a qualitative measure of the severity of the patient's condition based on how it affects daily activities. A score of 1 corresponds to: "my palm sweating is never noticeable and never interferes with my daily activities"; a score of 2 corresponds to: "my palm sweating is tolerable but sometimes interferes with my daily activites"; a score of 3 corresponds to: "my palm sweating is barely tolerable and frequently interferes with my daily activites"; and a score of 4 corresponds to: "my palm sweating is intolerable and always interferes with my daily activites." The validity and reliability of the HDSS were proved, and the use of this scale is recommended by the Canadian Hyperhidrosis Advisory Committee.[8]

The exclusion criteria were myasthenia and pregnancy. All patients underwent a pretreatment evaluation consisting of a clinical examination, objective excessive sweating, with criteria of primary hyperhidrosis (focal, visible, excessive sweating of at least 6 months' duration without apparent cause with at least 2 of the following characteristics: bilateral and relatively symmetric, impairs daily activities, frequency of at least 1 episode per week, age of onset <25 years, positive family history, cessation of focal sweating during sleep).[17] An evaluation, including a clinical examination, thyroid palpation, and determinations of glycemia and thyroid stimulating hormone, was carried out to exclude cases of secondary hyperhidrosis.

All patients were treated with a first injection of botulinum toxin A (Dysport) at a dose of 250 U per palm. The botulinum toxin (500 U) was diluted in 2.5 mL of saline and 1-mL syringes fitted with a 30G needle were used for the injections. In total, 25 intradermal injections of 0.05 mL of botulinum toxin A (10 U) were administered, separated by a distance of 1 to 2 cm, into each palm and the fleshy parts of the fingers. We offered the patients pain relief, based on the inhalation of an equimolar mixture of nitrogen and oxygen or hypnoanalgesia, during the injection sessions. Subsequent sessions were performed at the patient's request, when the symptoms recurred with moderate discomfort (HDSS score >2/4) with a positive Minor test result. The HDSS score and Minor test result were evaluated at each visit. During these successive sessions, the duration of efficacy of the previous injection was evaluated by asking the patients how long it took for the symptoms to recur.

We compared the median duration of efficacy of the first and last injections of botulinum toxin. We determined median rather than means, because the median is considered more reliable than the mean for analyses of time intervals, which are generally asymmetrically distributed. Indeed, the presence of an extreme value in 1 individual has a considerable effect on the mean value, but little or no effect on the median value.

We used nonparametric Wilcoxon matched pair tests to compare the durations of efficacy between the first and last injections, with a significance threshold of 5%. Statistical analyses were carried out with R software.[18]