Duration of efficacy increases with the repetition of botulinum toxin A injections in primary axillary hyperhidrosis: A study in 83 patients

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Background: Intradermal injections of botulinum toxin are effective but transitory in primary axillary hyperhidrosis. These injections are repeated when the symptoms recur. The reported duration of efficacy is variable, from 2 to 24 months, but it is unknown how the duration of efficacy changes when injections are repeated.

Objective: In this retrospective study, we aimed to evaluate changes in the duration of efficacy of botulinum toxin injections (Dysport, Ipsen, Boulogne-Billancourt, France) with the repetition of injections in patients with axillary hyperhidrosis.

Methods: From May 2001 to April 2012 inclusive, 83 patients were treated with a dose of 125 U per underarm. We compared the duration of effect of the first and last toxin injections.

Results: The median duration of efficacy for the first injection was 5.5 months, whereas that for the last injection was 8.5 months. The difference between these 2 durations is statistically significant (P = .0002).

Limitations: Although retrospective and based on the declarative, this work is the first to our knowledge to highlight this benefit of treatment and to evaluate botulinum toxin over such a long period (11 years).

Conclusion: There appears to be an increase in the duration of efficacy of botulinum toxin A injections with the repetition of injections in patients with primary axillary 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 2013;69:960-4.)

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

Hyperhidrosis is excessive production of sweat. It affects 1% to 3% of the population, with a sex ratio of 1, and its prevalence is highest between the ages of 25 and 64 years.[1,2] It can have major psychosocial repercussions for patients.[3-6] 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 the 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. Options include topical medications (most commonly aluminium chloride), iontophoresis, botulinum toxin injections, systemic medications (including glycopyrrolate and clonidine), and surgery.[8] Endoscopic thoracic sympathectomy is one possibility for invasive treatment and frequently causes compensatory hyperhidrosis.[9-11] Most other reported complications are postoperative pain, pneumothorax, segmental atelectasis, and transient Horner syndrome.[12] It is

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Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication August 2, 2013.

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Published online September 16, 2013.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2013.08.002

also an expensive treatment. Intradermal injections of botulinum toxin are used as a second-line treatment and have been shown to be effective,[13] by blocking the presynaptic release of acetylcholine. These injections are repeated when the symptoms recur. They have been reported to be effective for about 2 to 24 months,[3,14-23] but nothing is known about the change in the duration of efficacy with repeated injections. The aim of this retrospective study was to evaluate the change in the duration of efficacy of botulinum toxin injections for axillary hyperhidrosis with the repetition of injections.

CAPSULE SUMMARY

- Injections of botulinum toxin are effective but transitory in primary axillary 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 long-term effectiveness. Patients can expect a decreased need for injection sessions over time.

METHODS

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

All these patients had axillary hyperhidrosis detected by Minor test.[24] 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 axillary skin. All the patients had experienced treatment failure for first-line treatment with antiperspirants based on aluminum salts with concentration at 20%, with major psychosocial repercussions. 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 underarm sweating is never noticeable and never interferes with my daily activities"; a score of 2 corresponds to "my underarm sweating is tolerable but sometimes interferes with my daily activites"; a score of 3 corresponds to "my underarm sweating is barely tolerable and frequently interferes with my daily activites"; and a score of 4 corresponds to "my underarm 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.[13]

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/wk, age of onset <25 years, positive family history, cessation of focal sweating during sleep).[25] 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, Ipsen, Boulogne-Billancourt, France), at a dose of 125 U per underarm. The botulinum toxin (250 U) was diluted in 1.25 U of saline and delivered with a syringe fitted with a 30-G needle. In total, 12 to 13 intradermal injections of 0.05 mL of Dysport (Ipsen) (10 U), separated by a distance of 1 to 2 cm, were carried out for each underarm (about 120-130 U/underarm). Subsequent sessions were performed at the patient's request, when the symptoms recurred with a moderate discomfort (HDSS score >2/4) with a positive Minor test result. The HDSS and Minor test scores 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 the last injections of botulinum toxin. We determined median values rather than means, because the median is considered much more reliable than the mean for analyses of time intervals, which are generally asymmetrically distributed. Indeed, the presence of an extreme value for a single individual has a considerable effect on the mean, but little or no effect on the median.

We used the nonparametric Wilcoxon matched pairs test 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.[26]