

Effective treatment of frontal hyperhidrosis with botulinum toxin A

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Summary

Background Focal hyperhidrosis is a common condition mostly confined to the axillae, palms and soles. In some individuals, predominantly men, increased sweating of the forehead may be the major complaint and may interfere with the person's quality of life. Botulinum toxin A has been shown to be a very effective treatment for focal hyperhidrosis of the axillae and palms.

Objectives To assess the response in 10 men suffering from frontal hyperhidrosis treated with botulinum toxin A.

Methods Botulinum toxin A Botox[®] was injected at multiple sites evenly distributed over the forehead (mean dose 86 mouse units).

Results The mean \pm SEM amount of sweat was significantly reduced, 4 weeks after treatment, from 173.8 ± 38.6 mg min⁻¹ to 53.7 ± 17.6 mg min⁻¹. The effect lasted at least 5 months in nine of the 10 patients. All patients subjectively judged the treatment as very effective. Minor side-effects included painful injections and a transient weakness of forehead muscles without ptosis.

Conclusions In this study, we provide evidence that botulinum toxin A is an effective and safe treatment for frontal hyperhidrosis.

Key words: botulinum toxin A, sweating, therapy, wrinkles

Focal hyperhidrosis is a common condition characterized by an excessive production of sweat, which mainly affects the axillae, palms, soles and forehead. The cause of essential focal hyperhidrosis is unknown, and the sweat glands and their innervation do not show any morphological abnormalities.^{1,2} A dysfunction of the central sympathetic nervous system, possibly of hypothalamic nuclei, or of prefrontal areas or their connections, is suspected.^{1,2} A positive family history for the condition in 30–50% of patients suggests a genetic background.³ Treatment of focal hyperhidrosis includes the use of metal salts such as aluminium chloride, tap water iontophoresis and, in refractory cases, surgical procedures such as suction curettage or sympathectomy.

Recently, botulinum toxin A has proved to be a very effective treatment for focal hyperhidrosis of the axillae and palms. Botulinum toxin A is produced by the anaerobic bacterium *Clostridium botulinum*. Hypohidrosis or anhidrosis is a well-known effect of botulism

and was described by the German romantic poet and physician Justinus Kerner in 1822.⁴ This effect formed the basis for the use of botulinum toxin A as a therapy for hyperhidrosis. Botulinum toxin A was shown to abolish physiological sweating in the axilla and the back of the hand for 6–11 months in healthy volunteers;⁵ many subsequent publications also reported good results with the use of botulinum toxin A injections in focal hyperhidrosis of the axillae^{6–9} or palms,^{6,7,10,11} and in gustatory sweating.¹² This report describes the use of botulinum toxin A in frontal hyperhidrosis.

Patients and methods

The study was performed in accordance with the Declaration of Helsinki. Patients were recruited from a nation-wide questionnaire for patients who wrote to our clinic regarding focal hyperhidrosis. Of the 261 patients answering the questionnaire, about 20% complained of facial sweating. The condition seemed to affect considerably more men than women. We

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selected 10 severely affected men and offered them treatment with botulinum toxin A. The median age was 41 years (range 26–59). None had underlying thyroid disease or diabetes mellitus. All patients felt embarrassed by the sweating of the forehead, eight by having to wipe their face often and four by the dripping of sweat into their eyes. The most common reported triggers of sweating were stress, excitement, physical activity and heat. The median age at onset of the sweating on the forehead was 16 years (range 12–47). The hairy scalp and the temporal regions were also involved in five patients, and three patients had hyperhidrosis of the nose, chin or cheeks. Written consent was obtained from all patients prior to injection.

The area of sweating on the forehead was visualized by Minor's iodine-starch test and documented by a photograph before and after injection. Gravimetric quantification of the amount of sweating was performed using three coffee filters (size 4, Melitta, Minden, Germany) placed on the forehead. The filters were weighed on a scale (BP1215, Sartorius, Göttingen, Germany) before and after gravimetry and the difference in weight was calculated. Twenty to 30 injection points evenly distributed over the entire forehead were marked. The distance between two injection points ranged from 1 to 1.5 cm. At each injection point 3 mouse units of botulinum toxin A (Botox[®], Allergan, Ettlingen, Germany) were injected intracutaneously, as previously described.^{6,7,10} A mean \pm SEM of 86 ± 2.9 mouse units Botox[®] was injected per patient. To prevent drooping of the eyelid, the caudal strip about 1 cm above the eyebrow was not treated. The patients were evaluated again after 4 weeks by Minor's iodine-starch test and gravimetric assessment. They were also asked to complete a separate questionnaire focusing on epidemiological aspects and subjective ratings of sweating and their satisfaction with treatment.

Results

Sweat production significantly decreased in all patients, as shown with Minor's iodine-starch test (Fig. 1a,b). Gravimetry showed a markedly reduced sweat production from 173.8 ± 38.6 mg min⁻¹ (mean \pm SEM) before treatment to 53.7 ± 17.6 mg min⁻¹ 4 weeks after treatment (Fig. 2). The reduction was highly significant ($P < 0.005$). In three of the patients a partial disability in frowning of the forehead was noted at the visit 4 weeks after treatment. Two other patients

reported that they had noticed a partial disability in frowning of the forehead prior to the review appointment. This disability disappeared after 1 week in one patient and after 3 weeks in the other patient. In all five patients this impairment was limited to a maximum of 8 weeks. Other side-effects included pain of injections. No infections, haematomas or ptosis were observed.

Five patients were extremely satisfied with the treatment, four were satisfied and one was content. All patients reported a significant reduction in sweating on the forehead after treatment and all expressed their desire to repeat the treatment. Asked to quantify their annoyance by the frontal sweating on a scale from 0 (not at all) to 10 (very much), the patients rated it 9.5 before and 2.9 after treatment. To date (5 months after treatment), all but one of the patients are still satisfied with the therapeutic effect. One requested further injections after 4 months.



Figure 1. Minor's iodine-starch test performed on the forehead (a) before and (b) 4 weeks after treatment with botulinum toxin A. Note the clear demarcation of injected areas.

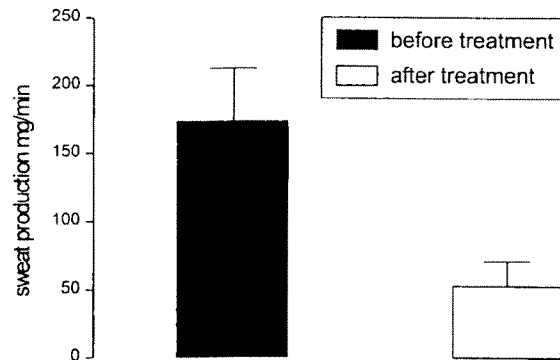


Figure 2. Gravimetric assessment of mean frontal sweat production before (black column) and 4 weeks after treatment (white column) in 10 patients. Values are given in mg min^{-1} . Bars indicate SEM. The reduction in sweat production is highly significant ($P < 0.005$).

Discussion

In our study, botulinum toxin A injections proved to be an effective and safe treatment for frontal hyperhidrosis. The amount of sweating was markedly reduced, as shown by Minor's iodine-starch test and by gravimetric assessment. All patients were content with the treatment and expressed their wish to have the injections performed again. The side-effects included pain of injections and partial disability in frowning of the forehead in half the patients. This impairment was limited to a few weeks and can be alleviated by using multiple injections and small injection volumes. Ptosis did not occur in any of the patients.

Botulinum toxin acts via an inhibition of the release of acetylcholine from the cholinergic nerve fibres. The duration of the effect is limited, due to transiently sprouting nerve fibres and a restoration of the original end-plate.¹³ In nine of our 10 patients, the treatment effect lasted at least 5 months. According to our experience, the effect of botulinum toxin A in axillae and palms also lasts an average of 4–8 months.⁷ As the nerve fibres innervating the muscles are also cholinergic, botulinum toxin A has also been used as an effective treatment for diseases with muscular hyperactivity such as dystonia¹⁴ and wrinkles.¹⁵ Its effect in muscles is shorter lived than in sweat glands. The exact reason for this difference is not known, but it might perhaps result from more active sprouting of nerve fibres in muscles than in sweat glands.

Facial hyperhidrosis appears to be a special form of focal hyperhidrosis. According to our data, it occurs in about 20% of patients suffering from focal

hyperhidrosis and seems to affect more men than women. The elicitation factors are similar to those described¹⁶ for hyperhidrosis in other localizations. Patients affected by facial hyperhidrosis may suffer greatly from the condition, especially when being confronted in public. On a subjective rating scale, our patients were greatly relieved after treatment with botulinum toxin A. In conclusion, we provide evidence that botulinum toxin A is a safe and very effective treatment for frontal hyperhidrosis.

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