Botulinum toxin in plantar hyperhidrosis assessed by a digital imaging system

Toxina botulínica em hiperidrose plantar avaliada através de sistema de imagens digitais

Original Article

ABSTRACT

Introduction: Hyperhidrosis is a condition characterized by an excessive and uncontrolled production of sweat; the most current treatment is botulinum toxin.

Objective: Botulinum toxin type A acts through a transient block of acetylcholine release in the cholinergic autonomic fibers to reduce sweating. Its use is increasing as patients learn about its efficacy.

Methods: Patients (n = 7) were treated with botulinum toxin with a total dose of 100 U. We analyzed patient and physician assessments and digital photography images using Image-Pro, a digital imaging system®.

Results: Patients presented an average clinical improvement of hyperhidrosis of 73%, which was photographically documented.

Conclusions: There is no need to use higher doses of botulinum toxin to obtain good results.

Keywords: botulinum toxins; hyperhidrosis; hiperidrose/therapy.

RESUMO

Introdução: *A hiperidrose é uma doença caracterizada pela transpiração excessiva e descontrolada, sendo a toxina botulínica o tratamento mais atual. Objetivo: A toxina botulínica do tipo A age através do bloqueio transitório da liberação da acetilcolina nas fibras colinérgicas autônomas, reduzindo a transpiração. O emprego desse tratamento tem aumentado à medida que os pacientes reconhecem a eficácia da substância.*

Métodos: *Sete pacientes foram tratados com uma dose total de 100U de toxina botulínica. Os resultados foram avaliados com base nas opiniões dos pacientes e dos médicos, e em fotografias digitais analizadas por sistema Image Pro®.*

Resultados: *Os pacientes apresentaram, em média, uma melhora clínica da hiperidrose da ordem de 73%. O processo foi documentado fotograficamente.*

Conclusões: *Não há necessidade da utilização de doses altas de toxina botulínica para a obtenção de bons resultados.vitiligo; avaliação; protetores de raios solares.*

Palavras-chave: *toxinas botulínicas; hiperidrose; hiperidrose/tratamento.*

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INTRODUCTION

Hyperhidrosis is characterized by excessive and uncontrolled production of sweat, being a condition of unknown etiology.[1] It typically occurs in areas with a greater concentration of sudoriferous glands (axillae, palms and soles of the feet.[2]

Excessive sweating, which occurs in 0.1-0.5% of the population, seems to have an associated genetic component in 30-50% of cases.[3-6] It usually starts when patients are in their 20s or 30s.[4,5]

Sudoriferous glands have sympathetic innervation; acetylcholine is the neurotransmissor.[7] Such glands play an important role in thermoregulation, and are activated by brain stimuli, such as those generated in situations of anxiety.[2,7] In individuals with hyperhidrosis, the glands are morphologically normal; however there seems to be an abnormal neurological response to stimuli in the hypothalamic centers.[2]

Hyperhidrosis is clinically diagnosed, based on the patient's history and physical examination, and identified by excessive sweating.[1] It is necessary to exclude secondary causes of hyperhidrosis, including obesity, menopause, the use of antidepressants, endocrinopathies (hypoglycemia, hyperthyroidism, pheochromocytoma) and neuropathies that involve a lack of autonomic dysfunction (syringomyelia, focal central nervous system lesions).[7] Other rare conditions associated with hyperhidrosis include Ross and Frey syndromes and localized unilateral segmental hyperhidrosis.[8-9]

Given its effects on patients' social lives, hyperhidrosis entails psychological implications.[4,11] Other consequences include dehydration and skin maceration, which may be associated with secondary infections.[4,5,12] Dyshidrosis and contact dermatitis are other possible complications.[13]

Several treatments have been used, including topical products such as aluminium chloride – which frequently causes local irritation – and agents that stain the skin – such as glutaraldehyde, formaldehyde (sensitizing), tannic acid and methenamine.[4,11,14-16] As with the use of topical products, systemic cholinergic agents also have limited effectiveness, in addition to the same side effects, such as dry mouth, blurred vision, urinary retention, constipation and palpitations.[2,4,11] A further alternative is iontophoresis, which has been reported to be effective in individuals that have both the palms and soles of the feet affected. However this treatment is uncomfortable and requires a great number of treatment, maintenance and control sessions.[1,4,7,11] The surgical options for the axillary region include the direct total excision of the glands – an alternative that is no longer used due to the resulting unattractive scars and reduced mobility – and the curettage of the glands. While curettage seems to lead to satisfactory results, further studies are required.[2,4,7,11] Endoscopic sympathectomy is a good option in cases involving the palms; this treatment is less affective in the axillae.[1,4] The most frequent side effect is compensatory hyperhidrosis, which can occur in nearly all cases, mainly in the back, abdomen and legs. Gustatory sweating can also occur in up to 50% of patients.[4,17,18] Other complications include recurrence (in up to 7.5% of cases), Horner syndrome, pneumothorax, pneumonia and neuralgia.[4,7,13,17-19] Lumbar sympathectomy can be performed in the plantar region, however it is associated with a risk of impotence.[11]

Botulinum toxin type A causes a transient blockage of acetylcholine release in the cholinergic autonomic fibers.[1,4] Intradermal injections are applied at multiple points in the affected area, with improvement observed in 2-10 days.[3,4] The decrease in sweating is verified after 3-14 months.[18] Many studies in the literature describe the successful use of botulinum toxin in cases of axillary and palmar hyperhidrosis, as well as case studies of craniofacial hyperhidrosis, gustatory sweating and Ross syndrome. Regarding its use in the plantar region, there are very few reports published.[12,20,21] Our experience with the use of botulinum toxin to treat plantar hyperhidrosis is presented in this study.

METHODS

The present study, which complied with the ethical principles of the Helsinki Declaration, included 7 patients (5 women and 2 men). The exclusion criteria were age less than 12, pregnancy or breastfeeding, patients with organic causes of hyperhidrosis, neuromuscular diseases, use of medications that may interfere in neuromuscular activities, and concomitant treatment for hyperhidrosis. All patients were diagnosed with plantar hyperhidrosis based on clinical history and the Minor test (starch-iodine).[12]

The contents of a 100 U lyophilized botulinum toxin A (Botox,) vial was diluted in 5 ml of 0.9% sterile saline solution. A 2.5% lidocaine-prilocaine cream (EMLA,) was applied to the site, which was then covered with plastic film for one hour. Each sole of the foot received 25 intradermal injections (2U per point) with a 30 G1/2 needle, roughly 2 cm apart from each other.

The subjective analysis of the treatment was using a patient questionnaire that assessed the beginning and stabilization of the reduction in sweating, the percentage of reduction, the beginning of compensatory sweating in other sites, as well as the level of satisfaction with the treatment.

The objective analysis of the percentage of sweating reduction was performed before treatment and at 2, 4 and 12 weeks after treatment using the Minor test and comparing images obtained using software to evaluate digital images (Image-Pro Plus,, Media Cybernetics, Inc, Bethesda, Maryland, USA). For each image the percentage of dark area (with sweating) was compared to the total area of the plantar region. That percentage was then compared with subsequent pictures. The relative reduction in sweating was calculated as the difference between the pre- and post-treatment percentages of dark areas.

RESULTS

Patients' ages ranged between 14 and 42, with the majority reporting the beginning of the condition in childhood, at ages from 7 to 15. All patients presented hyperhidrosis in the palmar regions, 2 patients presented the condition in the geni-

tal area, 2 in the nasal region and one in the axillae. One patient had undergone endoscopic thoracic sympathectomy, with improvement of the palmar hyperhidrosis and the beginning of compensatory hyperhidrosis in the trunk.

In the subjective assessment, patients described improvement within 1-3 days. Improvement of 40-100% (average 73%) was reported (Images 1 and 2). Two patients described increased sweating on the hands. All patients were satisfied with the treatment, except for one, who had previously undergone sympathectomy, who described sweating (not treated) on the top of the foot and reported "still having wet feet." When asked if they would undergo the same treatment again, four patients answered positively while the other three, including the patient mentioned above, gave negative answers due to the pain involved.

A reduction in sweating was observed in all cases in the visual assessment of the Minor test. The quantitative evaluation of the reduction was performed through the digital analysis of the test's photographic images (Image 3). The first assessment took place between 2-3 weeks (average 2.4 weeks) after treatment, with a mean reduction of 48% in the sweating in the plantar area. The last assessment was performed at 15-23 weeks (average 18.7 weeks), with a mean reduction of 66% in the same area (Figure 1).

DISCUSSION

Authors report the beginning of the botulinum toxin action within 48-72 hours, with a complete effect after one week.[9,12,22] The duration of the treatment described in the literature ranges from 5 months (in the axilla)[2,23] to 10 months (in the plantar region)[20] up to 12 months (in the palmar region and in patients with gustatory sweating).[9,12,24-27] In the cases presented in this study, patients reported that the treatment took effect within 1 to 3 days, with no symptoms for up to 23 weeks (average 18.7 weeks).

Although patients described few side effects, the main adverse effect was pain during the application, which prevented two patients in our study from repeating the treatment.[12,25,27] The methods proposed to reduce pain include ice or liquid nitrogen packs, topical anesthetics and infiltrative anesthetic block. [21,25,26,27]

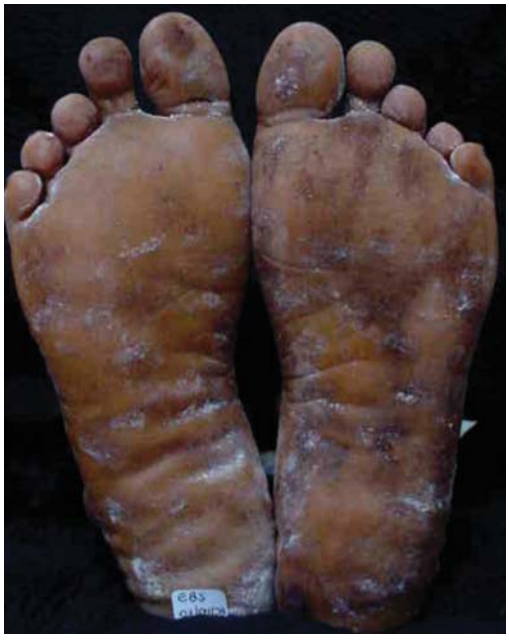


Figure 1 - Pre-treatment Minor test

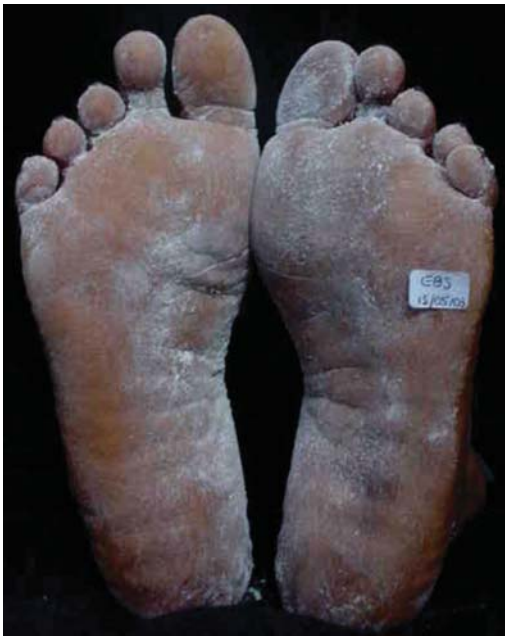


Figure 2 - Post-treatment Minor test

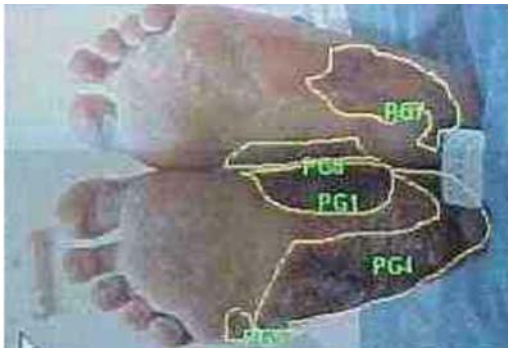
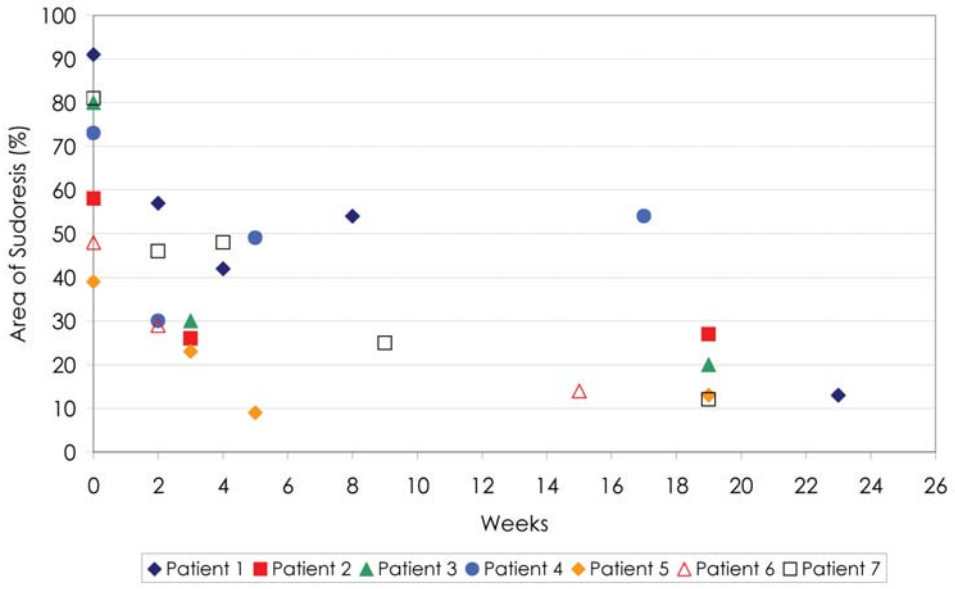


Figure 3 - Evaluation of treated areas with digital photography and Image Pro® system



Graph 1 - Evaluation of treated areas with digital photography and Image Pro® system

Vadoud-Seyedi and others described the use of Dermojet to apply the toxin in order to reduce pain, and reported an acceptable level of pain in 3 patients.[20] Other side effects described less frequently are painless hematomas,[12] muscular weakness,[1,21,25,27] headache,[1] and dry skin on the hands.[21] While compensatory hyperhidrosis is described in several sites,[1,5] many authors did not observe this effect.[2,12]

The study demonstrated that patients are generally satisfied with the treatment and would repeat it when symptoms return and/or would recommend this therapy.[1,2,21] One patient was dissatisfied due to persistent sweating in non-treated adjacent areas.[24]

The doses used by the authors who performed treatment in the plantar region are similar to those applied by Vadoud-Seyedi and others and Naumann and colleagues:[12,20] 100 UI per patient (3 UI for every 2 cm (4 cm^2), amounting to 42-48 UI per plantar region).[12] Naumann and colleagues indicated that the optimal dose of botulinum toxin type A is the amount that effectively reduces sweating to physiologically normal levels for the longest possible time, while causing minimal side effects. The authors stated that some patients required individual adjustment of doses for optimal results to be achieved.[18]

The authors who described treatments of the plantar region did not calculate the reduction in sweating in percentage terms. The reduction was measured using the Minor test and/or the gravimetric quantification of sweating.[12,20,21] In the cases described in the present study, reductions of 48 and 66% were verified, respectively, in 2 to 3 weeks (average 2.4 weeks) and in 15 to 23 weeks (average 18.7 weeks) after the treatment.

The authors demonstrated that, unlike in previously analyzed cases, reduced doses of botulinum toxin type A led to satisfactory results, thus reducing costs and allowing patients to afford the treatment. ●

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