Use of iontophoresis or phonophoresis for delivering onabotulinumtoxinA in the treatment of palmar hyperidrosis: a report on four cases *

Tratamento da hiperidrose palmar com onabotulinumtoxinA veiculada por iontoforese ou fonoforese - Relato de casos

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Abstract: Idiopathic palmar hyperhidrosis is a common disease that exerts a considerable effect on patients' quality of life. The definitive treatment of this condition (sympathectomy) is associated with some adverse effects and surgical risks. Drugs such as onabotulinumtoxinA can be percutaneously delivered by phonophoresis or by iontophoresis and may be useful in the treatment of hyperhidrosis. In this paper, the authors describe four cases in which an objective and subjective improvement in sweating was seen following 10 daily sessions of phonophoresis or iontophoresis. No adverse effects were reported. The clinical results achieved with treatment were maintained over 16 weeks of follow-up after the end of treatment. Percutaneous drug delivery techniques should be perceived as an option for the treatment of dermatologic conditions.
Keywords: Botulinum toxins, type A; Hyperhidrosis; Iontophoresis; Phonophoresis

Resumo: Hiperidrose palmar idiopática é doença frequente, que tem grande impacto na qualidade de vida dos pacientes, e seu tratamento definitivo (simpatectomia) associa-se a risco cirúrgico e efeitos adversos. Fármacos, como onabotulinumtoxinA, podem ser veiculados percutaneamente por iontoforese ou fonoforese e contribuir no tratamento da hiperidrose. Os autores apresentam quatro casos em que houve melhora objetiva e subjetiva da sudorese após dez sessões consecutivas de iontoforese ou fonoforese, sem evidências de efeitos adversos. Os resultados clínicos mantiveram-se por 16 semanas de observação após a interrupção do tratamento. Técnicas de veiculação percutânea de medicamentos devem ser percebidas como opções nos tratamentos dermatológicos.
Palavras-chave: Fonoforese; Hiperidrose; Iontoforese; Toxinas botulínicas tipo A

Hyperhidrosis is sweating in excess of that required for thermoregulation. It is estimated to affect between 0.3 and 1.0% of young people, with symptoms often beginning in infancy and adolescence. A family history has often been demonstrated, with the 14q11.2-q13 gene being associated with palmar hyperhidrosis. The condition affects both males and females, principally individuals of Japanese descent. [1-3]

There are idiopathic primary forms and those that occur secondary to hyperthyroidism, menopause, obesity, panic syndrome, alcoholism, neoplastic conditions or medication. The condition may affect the skin of the entire body or be limited to the palmoplantar region, axillae, inframammary, inguinal, intergluteal or craniofacial regions. The palmoplantar and axillary forms are predominant. It is affected by emotions and negatively affects the individual's quality of life. [1,2]

The effects of palmar hyperhidrosis are underestimated by clinicians and few patients receive effective treatment. Intradermal infiltration of

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onabotulinumtoxinA (BTX) is effective; however, it is associated with significant local discomfort. [1,4]

Normally, percutaneous penetration of drugs is restricted by the epidermis. Iontophoresis and phonophoresis are noninvasive methods of administering molecules through the skin, facilitating their penetration through hair follicles or sweat ducts. Iontophoresis uses low-intensity electricity to transport drugs through the gradient formed. Phonophoresis uses ultrasonography to increase the percutaneous absorption of drugs. [5,6]

Four healthy university students with bilateral primary palmar hyperhidrosis, who had not been submitted to any previous treatment, were selected. The condition was determined by the starch-iodine test (Minor's test). The study was approved by the institution's internal review board (794/2007).

Two patients were submitted to the iontophoresis protocol, using galvanic micro-current (Physiotonus Microcurrent, Bioset) with 0.4 – 0.5 A of current applied for 15 minutes on each hand for ten consecutive days.

Two patients were submitted to phonophoresis using a 3MHz therapeutic ultrasound device (Avatar I - Esthetic- KLD) in continuous mode, with 1MHz frequency and 0.4 W/cm^2 intensity, for 10 minutes in each hand for ten consecutive days.

A bottle of BTX (Botox 100 UI, Allergan, Inc.) was dissolved in 1.5 ml of sterile saline solution, after which 200 g of carbopol gel 1% was added. The preparation was stored in a refrigerator and used for all the sessions.

The results were evaluated subjectively by the patients and qualitatively by the investigator (HAM), who was blinded with respect to the patients' identity and who evaluated photographs of Minor's test results using a visual analog scale that ranged from 0 to 10.

Case #1: A 25-year old male university student who had had hyperhidrosis for five years, which increased in intensity with physical activity and stress, preventing him from practicing muscle training. He also mentioned that the condition affected his personal relationships. He was submitted to phonophoresis and reported a subjective improvement of 70% (Figures 1A and 1B). The evaluation conducted by the investigator rated his improvement at 80% (from 10 to 2 points).

Case #2: A 27-year old male university student reported having had hyperhidrosis for 10 years, increasing in intensity when he practiced physical activity. He mentioned that the condition also affect-

Figure 1: Pacient #1. Minor's test conducted before treatment (A) and following 10 phonophoresis sessions with onabotulinumtoxinA in carbopol gel (B). Patient # 2. Minor's test conducted before treatment (C) and following 10 phonophoresis sessions with onabotulinumtoxinA in carbopol gel (D)

ed his work. He was submitted to phonophoresis and reported a subjective improvement of 100% (Figures 1C and 1D). The investigator's evaluation rated his improvement at 80% (from 5 points to 1).

Case 3: A 19-year old female university student, who had had hyperhidrosis for seven years. She reported that the condition became worse during physical activity and mentioned that it interfered with her work. She was submitted to iontophoresis and reported a subjective improvement of 100% (Figures 2A and 2B). The investigator's evaluation rated her improvement at 80% (from 10 to 2 points).

Case 4: A 23-year old female university student, who had had palmar hyperhidrosis for one year, the condition becoming worse during stress, emotional situations and physical activity. She mentioned that it interfered with her work. She was submitted to iontophoresis and reported a subjective improvement of 70% (Figures 2C and 2D). The investigator's evaluation rated improvement at 66% (from 3 points to 1 point).

None of the patients reported any adverse effects resulting from the treatment and all the results were maintained over 16 weeks of follow-up after completion of the sessions.

Clinical and surgical options exist for the treatment of palmar hyperhidrosis. Aluminum chloride (20-30%) is the most common topical treatment; however, its occlusive effect is limited and it causes local irritation as do tannic acid, methenamine, formaldehyde, boric acid, resorcinol, glutaraldehyde and potassium permanganate. [7]

Systemic anticholinergic drugs such as glycopyrrolate, propantheline, benztropine and oxybutynin reduce body perspiration; however, they are associated with mydriasis, constipation, dry mouth, blurred vision and urinary retention. Calcium channel blockers, benzodiazepines and indomethacin have also been described for the treatment of palmoplantar hyperhidrosis. [7]

Tap water iontophoresis has been used for decades; nevertheless, its mechanism of action is unknown. The addition of anticholinergic agents to the water increases the therapeutic efficacy of this technique. [8]

Intradermal infiltrations of BTX (types A and B) are effective options; however, they are limited by their cost and by the local discomfort, and may result in transitory alterations to the fine movements of the hands. [4,7]

T2-T3 thoracic sympathectomy is an alternative solution for palmar hyperhidrosis; however, it is asso-

Figure 2: Pacient #3. Minor's test conducted before treatment (A) and following 10 iontophoresis sessions with onabotulinumtoxinA in carbopol gel (B). Patient # 4. Minor's test conducted before treatment (C) and following 10 iontophoresis sessions with onabotulinumtoxinA in carbopol gel (D)

ciated not only with surgical risks, but also with distant alterations (50-70%) such as compensatory sweating on the trunk and face, gustatory sweating, dysgeusia and arrhythmias. [9]

Since iontophoresis and phonophoresis cause no adverse effects, are relatively inexpensive and since the technique of percutaneous administration of other drugs such as anesthetics, anti-inflammatories and corticoids has already been well established, the use of these techniques for the administration of BTX in the treatment of palmar hyperhidrosis is fully justified.

The report of long-lasting success with the topical treatment of axillary hyperhidrosis with BTX strengthened the conviction of percutaneous absorption and the possibility of using BTX delivered through iontophoresis and phonophoresis. [10] Taking palmar hyperhidrosis into consideration, the ease of application with these methods and the absence of any adverse effects are favorable characteristics that should be emphasized.

Techniques of percutaneous drug administration should be perceived as options for dermatological treatments. Regimes of application, means of diffusion, the number of sessions and the drug concentrations are variables that may modify their performance. It was not, however, possible to compare the efficacy of the two methods in these cases.

These favorable results should stimulate others to design randomized, double-blind, placebo-controlled clinical trials with long follow-up periods and expressive sample sizes to clarify the role of these techniques in the treatment of hyperhidrosis. ❑

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