Introduction

Sweating is the mechanism by which homeotherms control body temperature. The hypothalamus controls the internal temperature through receptors sensitive to heat and cold. When homeostasis deviation occurs, the thermoreceptors located below the epidermis send impulses through the afferent pathway to the hypothalamus, which promptly makes the physiological changes efferent so that the thermal equilibrium returns².

The hypothalamus is a region of the central nervous system (CNS) that performs functions such as regulation of emotions, thermal sensations, sensations of pain, and activates the endocrine system with the goal of homeostasis.

It operates through the peripheral nervous system (PNS), nerves and ganglia, and its response may be the autonomic nervous system (ANS) sympathetic or parasympathetic³.

Autonomic nervous system (ANS) controls glandular, cardiac and neural secretions, and is divided into sympathetic (ANS-S) and parasympathetic (ANS-P) secretions. The ANS-S is responsible for active responses such as fight or flight, has preganglionic fibers, called nicotinic, which has as neurotransmitter acetylcholine (Ach) and postganglionic nerve fibers that has neurotransmitter called noradrenaline. However, in the case of sweat gland secretions, the preganglionic neuron is Ach, that is, in this case the response is cholinergic²,³,⁴. Vasodilation is of great importance for this process, as the sweat gland receives...
more water and electrolytes that pass through the duct towards the surface of the skin.\textsuperscript{5,6}

Hyperhidrosis is the production of sweat above the amount considered normal, caused without external stimulation, that is, excessive sweating is produced both in heat and cold, in situations of anxiety, nervousness or not, in physical activities or not in an autonomous way and uncontrollable way. Its origin is still unknown.\textsuperscript{7,8}

It can occur in the plantar, palmar, craniofacial or axillary regions and can also affect several regions simultaneously. Although it does not trigger any physical illness, the affected individuals feel uncomfortable and frustrated, since hyperhidrosis generates consequences in the day to day: normal activities such as handshake in the form of length, personal, professional, intimate relationships cause embarrassment\textsuperscript{9,10,11}. Primary hyperhidrosis is localized, and onset of symptoms may occur in childhood, adolescence or adulthood, and there may be linkage with genetic factors.\textsuperscript{10} Secondary hyperhidrosis is due to a primary disease such as hyperthyroidism, menopause, or due to hormonal disorders that trigger the increase of sweating. In this case, it is essential to treat the primary disease so that hyperhidrosis ceases\textsuperscript{11,12}.

Among sweat treatment or control options are topical products such as specific astringent deodorants. There is also oral treatment with medications, or through invasive procedures such as the application of botulinum toxin type A (BTX-A)\textsuperscript{13,14,15}.

\textit{Clostridium botulinum} is a gram-positive anaerobic bacillus with oval spores. Its natural habitat is soil, dust and marine sediments, and its spores survive at high temperatures, germinate under anaerobic conditions and produce the botulinum toxin.\textsuperscript{15,16}

The botulinum toxin used clinically is type A, which is the most used and the most studied both clinically and aesthetically. However, botulinum toxin type B has been recently studied and it has shown considerable therapeutic and aesthetic effects; due to this, type B toxin is already being marketed in the USA.\textsuperscript{4,6}

The ophthalmologist Alan B. Scott began in 1960 studies for the use of BTX with the objective of an alternative treatment to the surgical correction of strabismus. This study was approved for human intake by the Food and Drug Administration (FDA) in 1977, obtaining a positive therapeutic result.\textsuperscript{4,6}

In 1990, the National Institutes of Health (NIH) introduced BTX-A into the list of the most efficient and safe medicines. Although it is a toxin, BTX-A is a great option for the treatment of some pathologies.\textsuperscript{17,18} The application of BTX-A for therapeutic purposes, as in the case of hyperhidrosis, is one of the safest, most effective and almost non-existent side-effects according to scientific research. The onset of effects occurs from three to eight days and its durability is generally 6 months to 1 year, depending on the degree of the pathology.\textsuperscript{19}

Before to commercialization, the purification of BTX-A should be performed by industry, thus avoiding the risk of adverse effects and increased antigenicity. The process consists in passing the solution of the culture by precipitation in acidic media until the formation of a free crystalline complex of the ribonucleic acids and contaminating materials. Later, this complex is filtered, redissolved in saline and associated with albumin and hemagglutinin, which aims to stabilize and protect the active component.\textsuperscript{14}

The mechanism of action of BTX-A is the cleavage of a membrane protein of the postganglionic neuron, called SNAP-25, important for the function of the synaptic vesicles. Thus, ACh remains in the vesicles, accumulating in the neuron due to irreversible blockade and it cannot be released to go to the nerve terminal. There is, therefore, an inhibition of the stimulus for sweat production. The nerve terminal and the sweat glands remain uninjured.\textsuperscript{4,9,10,16}

The process takes place in stages: first BTX-A binds to the nerve terminal through its heavy chain. Following binding, internalization takes place via receptor-mediated endocytosis. The terminal membrane couples the toxin-receptor, forming a vesicle containing BTX-A into the nerve terminal, and from this vesicle the light chain will be released into the cytoplasm. The light chain is responsible for the cleavage of the vesicular SNAP-25 enzyme, thus preventing the release of ACh and consequently chemical deprivation by reducing muscle contraction and blocking glandular secretions. The nerve terminal remains intact, the synthesis and storage of Ach continue to stimulate sprouts of lateral axons, which reestablish a new neuromuscular junction (JNM), thus maintaining its normal activity.\textsuperscript{4,9,18,21,22}

The effect is temporary and reversible, as neural shoots form as a second outlet to Ach; then, after a time, the neurotransmitter is released through the new shoots, thus resuming its original activity.\textsuperscript{4,9,21}

In the literature, no cases of compensatory hyperhidrosis involving BTX-A have been reported, and an improvement in the psychological and emotional state has been reported that reflects on people's daily lives.\textsuperscript{7,12,13,23} However, overdosage may cause local, generalized and profound neuromuscular paralysis.\textsuperscript{22} Research has shown that adverse reactions are usually minimal and, when they do occur, they are temporary and, most of the time, only at the site of application. These reactions were characterized by schistosomiasis, pain, edema, bleeding, inflammation, pruritus, paresthesia, sensitivity, hypersensitivity, hemorrhage and irritation, with hours duration, which were not very relevant.\textsuperscript{22,24} The objective of this study was to report, through the follow-up of a case study, the relationship between the life quality of a patient before and after 30 days of the application of botulinum toxin type A for the treatment of hyperhidrosis.

Materials and Methods

The case study was descriptive, relating the treatment of hyperhidrosis with a possible improvement in a patient life quality. The study was carried out with only one volunteer as object of study, added to the bibliographical research with concrete information based on books, articles and electronic journals with public content of pertinent scientific literature.
The procedure was performed in the city of Jundiaí-SP, at the Day Hospital Nova Plástica Clinic. The team consists of doctors, nurses, dentists and biomedicals, and the facilities are suitable for invasive procedures and even plastic surgeries, regulated by the Local Surveillance (VISA).

A qualified professional for the present procedure, medical plastic surgeon (CRM 90204), performed intradermal applications for the first time in the patient’s palmar region. The patient signed the Written Informed Consent Form (WICF) and answered the questionnaire on life quality assessment.

The type of botulinum toxin was type A, manufactured by Allergan, known as BOTOX (batch: C4330C3; expiration date: October 2019).

Data collection was performed using a closed life quality questionnaire for only one patient suffering from hyperhidrosis in the palmar region, before treatment and 30 days after application, in order to evaluate the results of the procedure. The questionnaire was standardized and adapted from Baroncello et al., containing closed questions, on a scale from ‘0’ to ‘4’, with 0 being considered poor and 4 being excellent. (APPENDIX A). The points of the questions were summed up and the result was evaluated as follows: the closer to 100, the better life quality.

This study was approved by the Research Ethics Committee of the Paulista University (UNIP) CAAE: 90793718.0.0000.5512 under the number: 3,285,629.

Case Report

A 22-years-old male, clinically diagnosed with primary hyperhidrosis, sought treatment complaining of embarrassment and frustration due to bilateral palmar hyperhidrosis, which began in adolescence. This, after signing the WICF, opts for treatment through the intradermal application of BTX-A.

Treatment Protocol

1. Signature of the WICF;
2. Answer to the life quality questionnaire before treatment of BTX-A for palmar hyperhidrosis adapted from Baroncello et al.;
3. Anesthesia: Topical anesthetic in the affected region;
4. Assepsia of the bilateral palmar region;
5. Marking the points in pencil (Figure 1);
6. Application of BTX-A in the demarcated area (Figure 2);
7. Recommendations: Do not tighten the region; not to perform physical activities after the next 24 hours;
8. Follow-up in the next four weeks and after 30 days answer another questionnaire to evaluate the life quality after the application.

Figure 1: Marking of points (before intervention)

Source: Prepared by the author (2019)
Results and Discussion

Before the treatment reported here, the patient answered the life quality questionnaire and the score was 28 points out of 100, reaffirming that hyperhidrosis is a pathology that caused the patient serious psychological and social problems⁷. In a study by Baroncello et al. (2014)¹ with 51 patients with primary hyperhidrosis in the palmar, axillary and axillary-palmar regions, before undergoing surgical intervention, the reported complaints were also of a decreased life quality due to hyperhidrosis¹⁴.

Tamura et al. (2011)¹² carried out a study with seven patients with plantar hyperhidrosis treated with BTX-A. The post-application results were satisfactory, with reduction of sweating with onset of effect between 48 to 72 hours, and complete effect after one week. In the present report, the action of BTX-A started 72 hours after application and its full effect was observed in the second week after the procedure.

Reis et al. (2011)¹³, in a 10-year retrospective analysis of individuals with hyperhidrosis treated with botulinum toxin, evaluated 39 patients treated between July 2000 and July 2010. The results were satisfactory, treatment was considered safe and effective. 95.3% of the patients reported being very satisfied and there was no compensatory hyperhidrosis. Of the 39 patients, 2 reported pain at the application site, the same occurred with one single patient in the present study, where the symptom lasted at most four hours. The sum of points in the life quality of the volunteer of the present report after 30 days of application of BTX-A was 90 points out of 100, therefore, there was a decrease in sweating and improvement in life quality. The patient was fully satisfied with the outcome of the treatment.

Lessa and Fontenelle (2011)²⁵ reported the case of a 20-years-old boy with symptoms of social phobia and psychiatric disorders who had an independent diagnosis of palmar, plantar and axillary hyperhidrosis. The complaint was of discomfort and desire to avoid social situations due to excessive sweating. The cognitive-behavioral treatment was performed for social phobia, which did not present positive results. BTX was then applied to the axillary region, and in the first week the patient presented improvement of the symptoms, which was maintained in a progressive manner until the fourteenth week, resulting in the absence of social phobia due to BTX application.

Andrade et al. (2011)²⁶ reported a case involving four volunteers, all of whom had bilateral palmar hyperhidrosis. All felt interference in personal, professional, and emotional relationships due to hyperhidrosis, as in the current case study. Two of the participants were submitted to treatment with BTX-A conveyed by iontophoresis, and the other two were BTX-A conveyed by phonophoresis. Both results were satisfactory, the decrease in sweating was on average 76.5% and there were no adverse effects.

Dias et al. (2001)²⁷ reviewed the literature on the efficacy of BTX in hyperhidrosis from six studies with patients with hyperhidrosis. Satisfactory reduction in sweating, as well as side effects that lasted for hours and satisfaction with treatment, were reported in all cases. Among them, there were two studies on hyperhidrosis in the palmar region, one of them with four individuals. Two of these individuals had muscle weakness of the transient thumb. In the other study with twenty volunteers, all had pain only during the application of BTX, and four complained of temporary muscle weakness.

The description of the present case study is consistent with what has been reported in the literature and corroborates with the results demonstrating that the treatment of BTX-A for hyperhidrosis is efficient and has a positive impact on patient’s life quality.
Conclusions

In the present report, although temporary adverse effects occurred, no compensatory hyperhidrosis was reported, which resulted in improved life quality and patient satisfaction. Therefore, the therapeutic use of botulinum toxin type A for primary hyperhidrosis decreased sweating, had temporary side effects and significantly improved the patient life quality. These data corroborate with the related literature.

Acknowledgement

To the team of Day Hospital Nova Plástica, mainly to Dr. Paulo Martin, for the authorization and aid in the execution of the study.

References

19. Oliveira IM. Use of botulinum toxin in Gingival Smile Cosmetics. Aracaju [Internet]. Aracaju: University of Tiradentes; 2014 [quoted 2018 Oct. 03]. 9 p. Available at: http://openrit.grupotiradentes.com/xmlui/bitstream/handle/1940/USO%20DA%20TOXINA%20BOTUL%C3%81NI%20NA%20%COSM%C3%81TIC%20DENTAL%20A%20%200GENIVAL%20%2028UNIT%3E%2029.pdf? Sequence = 1
Appendix A - Life quality questionnaire relating to hyperhidrosis before and after treatment with botulinum toxin type A, applied to the patient, adapted from Baroncello et al.¹

Name:
Coming from:
Natural:
Birth:
Age:
Gender: M () F ()
Telephone:

Clinical Data:

1. Location of hyperhidrosis:
   () Axillary
   () To plant
   () Palmar
   () Facial skull

2. How long does the treatment last in months?
   () Less than 12 months
   () More than 12 months

3. Did you have compensatory hyperhidrosis?
   () Yes
   () Not

4. If positive for compensatory hyperhidrosis, it is:
   () Acceptable
   () Disturbing
   () Debilitating

5. Were you satisfied with the treatment?
   () Unsatisfied
   () regular
   () good
   () great

6. Did you experience any side effects?
   () Pain
   () Esquimoses
   () Decrease in strength
   () Anything

7. How do you evaluate your life quality before and after treatment:

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life quality</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Decreased sweating</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

8. With regard to this set of functions or acts, how would you rate your life quality in the following items:

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorite hobby</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Playing sports</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Being with friends</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Socially dancing</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Wearing sandals</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

How to Cite this Article: Caroliny Scarlett Pardo Muraro, Sabrina de Almeida Marques, Ana Beatriz Carollo Rocha-Lima, Denise Aparecida Gonçalves de Oliveira, Erika Simone Lopes, Cristina Tischer Ranalli Aparecido, Claudia de Moura, Veronica Cristina Gomes Soares. "Botulinum Toxin Type a in the Treatment of Hyperhidrosis: Case Study" Weber Medicine & Clinical Case Reports (ISSN:2449-1624), Vol. 7 (1) 2019, Article ID wmccr_267, 1247-1253
9. With regard to partners, how would you rate your life quality in relation to the act of:

<table>
<thead>
<tr>
<th>Activity</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wear socks</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Handicrafts</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Write</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Picking objects</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Shaking hands</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

10. How would you rate the sweating excessively:

<table>
<thead>
<tr>
<th>Activity</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>It was necessary to justify</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Observed demonstrations of rejection</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>He wanted to leave the place</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>He tried to keep distance from other people</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

11. How would you rate your life quality of when you were:

<table>
<thead>
<tr>
<th>Activity</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indoors</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>In hot environments</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Tense or worried</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Thinking about it</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>With problems at school or work</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Wearing colorful clothes</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Before the tests</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Before public performances</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>

Total before treatment:

Total after treatment:

Caption: Poor 0; Bad 1; Regular 2; Good 3; Excellent 4. Score classification between 0 to 100. The closer to 100, the better the life quality.