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Comparing Botox® and Xeomin® for axillar hyperhidrosis

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Abstract Recently, Xeomin®, a novel botulinum toxin (BT) type A drug became available. Separation of complexing proteins reduced the size of its BT component, thus potentially affecting its tissue diffusion, adverse effect profile and therapeutic properties. We report the first use of Xeomin® in an autonomic indication. A total of 46 patients (34 females, 12 males, age 32.7 ± 13.2 years, disease duration 14.2 ± 12.0 years) with symmetric bilateral idiopathic axillar hyperhidrosis and a previously stable Botox® treatment received 50 MU of BT in 5 ml of 0.9% $NaCl/H_20$ in each axilla. The patient, the injector and the observer were unaware of which axilla received Xeomin® and which Botox®. The therapeutic effect as measured from the BT application to the onset of its decrease lasted 3.2 ± 1.4 months and was excellent in 89% and good in 11% of the patients. Side-to-side differences of the therapeutic effect (onset latency, extent, duration) were neither detectable by the patient nor by the physician. Injection site pain was identical and adverse effects did not occur. Xeomin® can be used safely and effectively for the treatment of axillar hyperhidrosis. Size differences between Xeomin® and Botox® do not affect their therapeutic efficacy, tissue diffusion and adverse effect profile. Identical potency labelling allows easy exchange between both products.

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Introduction

Botulinum toxin (BT) has been used for many years with remarkable success to treat hyperhidrosis (Dressler et al. 2002; Naumann et al. 1997; Naumann et al. 2008). So far, several BT type A drugs, such as Botox®, Dysport®, Medy-Tox or Hengli®, and one BT type B drug, NeuroBloc®/Myobloc®, have been used therapeutically. Recently, Xeomin®, a new BT type A drug, became available for therapeutic purposes (Benecke et al. 2005; Roggenkamper et al. 2006). Whilst the BT component of conventional BT drugs contains complexing proteins, Xeomin® is free of these, thus reducing its molecular size from 600 to 900 to 150 kD (Dressler 2006). The purpose of this study was to report Xeomin's first use in autonomic indications and to explore whether the reduced size of the BT component affects tissue diffusion, adverse effect profile and therapeutic properties of this new compound.

Methods

Design

The effects of Xeomin® and Botox® were studied in both the equally affected hyperhidrotic axillae of patients, which had been previously under a stable and successful BT therapy. Patients, injectors, and observers were blinded as to which axilla was treated with which BT drug. The study,

therefore, followed a prospective double blind head-to-head intraindividual comparison design.

Patients

All patients were consecutively selected from our specialised hyperhidrosis clinics. Inclusion criteria consisted of the diagnosis of idiopathic axillar hyperhidrosis, bilateral symmetric skin involvement, regular hyperhidrosis treatment with Botox® with stable positive results and stable injection scheme for at least 2 years, unresponsiveness to conventional hyperhidrosis therapies, subjective severity of 'severe' on a scale of 'mild–moderate–severe', and objective severity with formation of sweat pearls within 1 min. Additional skin areas may have been affected. Exclusion criteria consisted of concomitant antihydrotic treatment, pregnancy, anticoagulation disorders, and infection of the injection area. All patients gave informed consent.

BT therapy

BT therapy was performed with Botox® (Allergan, Irvine, CA, USA) and with Xeomin® (Merz Pharmaceuticals, Frankfurt/M, Germany). Both BT drugs were reconstituted identically, i.e. one vial of each BT drug containing 100 MU was reconstituted with 10.0 ml 0.9% NaCl/H_20 resulting in a BT solution with a concentration of 10 MU/ml. Each axilla received 5.0 ml of this BT solution equalling 50 MU. The total volume assigned to one axilla was divided into 25 subcutaneous 0.2 ml injections of 2 MU each, which were placed with a 5 ml syringe and a 0.4 × 19 mm needle at distances of approximately 2 cm from each over the affected axillar skin. After BT application, the skin was compressed carefully to improve BT tissue penetration and to minimise BT washout. In this study, one treatment session was monitored.

Evaluation

All patients were asked in a structured interview to judge the overall therapeutic effect on a four-item global self assessment scale (0 = no effect, 1 = minor effect, 2 = good effect, 3 = excellent effect). They were then asked to report on the side-to-side differences of the onset, extent, and duration of the therapeutic effect, as well as the occurrence of unresponsive skin areas. Additionally, they were asked to report on any adverse effects including local ones, such as haematoma, dryness of skin, rhagades, and inflammation; motor systemic ones, such as shortness of breath and premature fatique; and autonomic systemic ones, such as dryness of mouth, accommodation difficulties and constipation. Patients were also asked to compare the injection site pain in both axillae. All patients were informed at study entry about the information that would be requested from them as part of this study, so that they were able to take notes during the study if necessary. A clinical examination was performed at the time of BT re-injections to identify side-to-side differences of sweating, including the diffuse sweating pattern and detection of unresponsive skin areas.

The duration of the therapeutic effect was defined as the time between the BT injection and the onset of its decrease as estimated by the patient.

Results

A total of 46 patients (34 females, 12 males, age 32.7 ± 13.2 years) fulfilled the inclusion criteria and were included in this study. Their disease duration was 14.2 ± 12.0 years. None of the patients discontinued the study. All patients continued their BT therapy after the study period.

Subjective outcome

A total of 41 patients (89%) reported the overall therapeutic effect as excellent and 5 (11%) as good. None of the patients reported minor effects or no effect. The duration of the therapeutic effect was 3.2 ± 1.4 months. Figure 1 shows the duration of the therapeutic effect in all patients treated. Most of the patients reported a 2 month duration, while some others reported 3 month and 4 month ones. Longer durations were rarely reported.

When asked in the structured interviews, none of the patients reported side-to-side differences of the therapeutic effect, including its onset latency, extent, and duration. None of the patients reported adverse effects, neither local nor systemic ones, and none reported unresponsive skin areas. The injection site pain was identical on both sides.

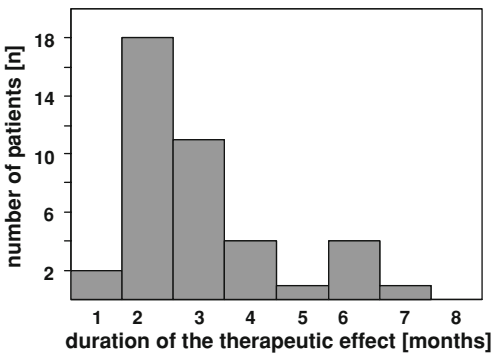

Fig. 1 Duration of the therapeutic effect measured from the botulinum toxin injection until the onset of its decrease as reported by the patient

Objective outcome

The clinical examination at the time of re-injections did not reveal any side-to-side differences in the diffuse sweating pattern and of unresponsive skin areas.

Discussion

When 50 MU of either Xeomin® or Botox® reconstituted with 5 ml of 0.9% NaCl/H_2O is injected into an axilla, 89% of patients with idiopathic axillar hyperhidrosis report an excellent effect and 11% a good therapeutic effect, each lasting approximately 3 months without provoking adverse effects. These features make both, Xeomin® and Botox®, together with Dysport®, another BT type A drug, the treatment of choice for axillar hyperhidrosis.

This study describes the first use of Xeomin® in an autonomic indication, thus adding to our armamentarium a new BT drug with interesting features such as a potentially reduced antigenicity (Dressler 2006). When sometimes longer therapeutic effects are reported in the literature, they are usually measured at the point of re-injection rather than at the onset of the decrease of the therapeutic effect, as in our study. When the point of re-injection is used, it can be affected by multiple factors including treatment availability, patient availability, financial considerations, travel arrangements, etc. all of which usually delay the re-injection and thus produce seemingly longer durations of action. We, therefore, believe the onset of decrease to be a more meaningful parameter despite its subjective character.

When Xeomin® and Botox® were given under the framework of this study, including treatment parameters, treated condition and measurement instruments, neither the patient nor the observer could detect any differences with respect to therapeutic efficacy and adverse effects. This indicates that the substantial size difference of the BT component of Xeomin® and Botox® is therapeutically not relevant. It also indicates that the complexing proteins are neither necessary for BTs therapeutic effect nor relevant for its tissue diffusion. The most likely explanation for this observation is a rapid disintegration of the BT component soon after its injection, leaving botulinum neurotoxin as the only relevant compound (Friday et al. 2002).

Additionally, the data obtained under the framework of this study confirm that the potency labelling of Xeomin® and Botox® seems identical. Although all manufacturers claim potency labelling according to international standards, the potency labelling of Dysport® is clearly different from that of all other BT type A drugs, thus generating an ongoing debate about the comparability of the therapeutic effects and adverse effect profiles. Identical potency labelling of Xeomin® and Botox® was already indicated by two previous studies comparing 463 patients with cervical dystonia (Benecke et al. 2005) and 300 patients with blepharospasm (Roggenkamper et al. 2006). It was also suggested by a head-to-head comparison study based on an LD50 assay (Dressler et al. 2008). Identical potency labelling of Xeomin® and Botox® allows easy drug exchanges without altering individualised and sensitive injection schemes.

Under the framework of this study, we could not detect differences in therapeutic efficacy, adverse effect profiles, potency labelling and tissue diffusion between Botox® and Xeomin®. If these could be detected by more sophisticated methods, they do not seem to matter in the way we currently apply BT therapy for hyperhidrosis. Introducing a BT drug with potentially reduced antigenicity might improve BT therapy of autonomic disorders.

Conflict of interest statement The author does not have competing interests.

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