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Botulinum toxin type A in the treatment of hemifacial spasm

An 11-year experience

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ABSTRACT

In order to evaluate the long-term effect of botulinum toxin type A (BTX) in the treatment of hemifacial spasm (HFS), a retrospective analysis of patients treated at the Movement Disorders Unit of the Division of Neurology, Clinical Hospital, University of São Paulo, School of Medicine from 1993 to 2004 was made. A total of 808 injections with BTX were administered to 54 patients with HFS. The mean duration of improvement per application was 3.46 months and the mean rate of improvement using subjective judgement by the patient was of 83%. Adverse effects, mostly minor, were observed in 64.8% of patients at least once along the period of follow-up and the most frequent of them was orbicularis oris paralysis (38.8%). There was no decrement in response when compared the first and the last injection recorded.

Key words: botulinum toxin, hemifacial spasm.

Toxina botulínica tipo A no tratamento do espasmo hemifacial: 11 anos de experiência

RESUMO

Para avaliar o efeito em longo prazo da toxina botulínica tipo A (TXB) no tratamento do espasmo hemifacial (EHF), foi feita uma análise retrospectiva de pacientes tratados no Ambulatório de Distúrbios do Movimento da Divisão de Clínica Neurológica - Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo no período de 1993 a 2004. Um total de 808 aplicações de TXB foram administradas a 54 pacientes com EHF. A duração média de melhora foi de 3,46 meses e a taxa média de melhora segundo avaliação subjetiva do paciente foi de 83%. Efeitos adversos, em sua maioria menores, foram observados em 64,8% dos pacientes ao menos uma vez durante o seguimento e o mais freqüente foi paralisia do orbicular da boca (38,3%). Não se observou decremento na resposta quando se comparou a primeira com a última aplicação anotada.

Palavras-chave: toxina botulínica, espasmo hemifacial.

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Hemifacial spasm (HFS), a chronic disorder characterized by involuntary and irregular tonic and clonic contractions of the muscles supplied by the facial nerve[1,2], has been known as a clinical entity for centuries[3]. Until the introduction of botulinum toxin (BTX) as a therapeutic alternative for HFS, treatment options consisted of oral medications with disappointing results, and surgical intervention which carries an inherent risk of complications[1,2]. The use of BTX type A (BTX-A) in HFS was approved by the U.S. Food and Drug Administration in 1989 (in Brazil, the use of BTX for the treatment of movement disorders was licensed in 1992) and since then, in view of growing evidence supporting its efficacy[2,4-8], it has become a standard treatment for HFS.

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Because HFS is a chronic condition that rarely remits spontaneously[2], it is important to gather information concerning the safety and efficacy of the long-term treatment. To this date, only a small number of studies have described the long-term use of BTX in HFS[4-8] and none of them was in Brazil. The aim of this article is to describe our 11-year experience in a tertiary center in Brazil.

METHOD

Patients

Patients with a diagnosis of HFS receiving treatment at the Movement Disorders Clinic of the Division of Neurology, Clinical Hospital, University of São Paulo, School of Medicine, between 1993 and 2004 were identified. Patients with a follow-up of less than one year or who received up to 3 injections were excluded from the study. From a group of 82 patients who received treatment with botulinum neurotoxin type A (Botox®) during this period, 54 were included in this study. This study was approved by the local ethics committee.

Botulinum toxin treatment

The injections were performed according to a modified scheme proposed by Consky[9]: 5 points in the muscle orbicularis oculi, 1 point in the muscle corrugator supercilii, 3 points in the orbicularis oris and 1 point in the muscle mentalis. Sites of injection were sometimes changed depending on the effects of the toxin achieved after each application, either to enhance its efficacy or to decrease collateral effects. The dose at the first application was usually 5 units per point around the eye; 4 units around the mouth and 2 units at the chin. The toxin was used within 4 hours after its reconstitution. A vial of 100 units freeze dried BTX-A (Botox®) was reconstituted with 2 ml of preservative free 0.9% saline solution to yield toxin in a concentration of 5 units per 0.1 ml. The dose for the subsequent injections was sometimes modified according to the therapeutic response and tolerance. General guidelines used in our service include: usage of minimum dose that achieved best efficacy; avoidance of booster injections; longest interval tolerated and not shorter than 3 months. In our department the efficacy of each application is routinely evaluated by the patient based on a scale of subjective degree of functional impairment (Columbia University Rating Scale)[10] ranging from 0 to 100%; 0% indicates a total lack of improvement with the application and 100% indicates complete improvement with return to normal function. Duration of the effect is also routinely recorded as reported by the patient in terms of duration of maximum effect and not including residual effects; because the residual benefit is of much longer and variable duration, many times lasting for longer than the interval between the injections, only the duration of maximum benefit was recorded for this study. The interval between injections is of a minimum of 3 months in our clinic, and it can be longer according to availability of appointments and the duration of effect observed on previous injections; the real duration of the interval was recorded for this research. BTXA injections were performed by six neurologists, either trained or in training, during the period of the study.

Medical records review

A retrospective analysis was conducted using the medical records of the patients. Past medical history of the patients regarding comorbidities and previous use of oral medication or surgical procedures was collected. Data recorded for each application included the dose used (in units), the subjective benefit reported by the patient in the above described scale from 0 to 100%. The interval between each injection was also recorded. Prevalence of collateral effect was recorded in an all-or-none variable that would point to its occurrence at least once during the treatment, as well as a description of any individual collateral effect that occurred.

Statistical analysis

A paired samples t-test was used to compare means. A significance value of 0.05 was used throughout.

RESULTS

From the initial group of 82 patients, 28 were excluded from the study (26 received less than 3 injections and were followed for less than one year; 1 completed less than one year of follow-up; and 1 had incomplete data). Fifty-four patients were then included in the analysis that will henceforth be commented. The age of the patients at the beginning of symptoms ranged from 31 to 79 years and the mean age was 48.3 years (SD 10.8). Most of the patients were female (75.9 %). HFS was present on the left side in 33 patients (61.1%). Before BTX-A treatment, 32 patients had used oral medication for HFS (19 had used carbamazepine and 20, benzodiazepines; other drugs were used by a minority of patients). Only 9 patients (16.6%) reported some response with oral drugs, which was usually mild.

A total of 808 treatments with multiple sites injections of BTX-A were administered to 54 patients with

HFS in this period. The mean time of follow-up of these 54 patients studied was 5.88 (SD 3.64) years (range 2-12 years) with an average of 14.96 (SD 8.99) applications per patient. There was a marginally significant difference between the average response (mean subjectively rated improvement) for the first (83.18%, SD 11.12) and last (78.63%, SD 19.23) injection (p=0.052), but no difference between the duration of effect in the first (3.42 months, SD1.62) and last (3.22 months, SD1.16) injection of BTX (p=0.407). None of the patients presented primary or secondary resistance. Twenty-two patients (40.7%) had a reduction of the dose in order to avoid side effects, and only 6 patients (11.1%) had an increase in the dose. A significant difference was found between the amount (in units) of BTX in the first (34.47, SD7.41) and last (37.61, SD 9.37) injections (p=0.02).

Adverse effects, mostly minor, were observed in 64.8% of patients at least once along the period of follow-up, the most frequent being orbicularis oris paralysis (38.8%), followed by ptosis (31.4%) and lagophthalmos (18.5%).

DISCUSSION

This is the first study performed in Brazil on the long-term use of BTX in HFS, and focuses in our experience with botulinum neurotoxin type A (Botox®). In this patient sample there was a higher number of females than males, and a mean age of 48.8 years at symptom presentation. These results are consistent with the results previously reported by Defazio et al.[5], Hsiung et al.[6], Pérez-Saldaña et al.[8], Thussu et al.[11] and Felicio et al.[12]. As previously reported in the literature by Thussu et al.[11] and Felicio et al.[12], the symptoms were more frequently seen on the left side of the face.

There was a statistically significant increase in the amount of BTX injected from the first to the last injection. Hsiung et al.[6] also encountered a trend for the increment of dose, but it was not significant. Pérez-Saldaña et al.[8] reported a progressive increase of BTX dose in the first years, but with a subsequent stabilization (difference was only found among the first four years and between the seventh and eighth years of follow-up). There was no difference between the duration of effect in the first and last BTX injections in our series, confirming previous findings by Defazio et al.[5], who also showed no difference between treatment response in the first and tenth year of treatment. Hsiung et al.[6] showed maintenance of sustained benefit (defined as a continued benefit of 50% or more from baseline) with repeated application, but the benefit in the second and fifth years of observation was respectively 96% and 88%. In our series the difference in the rate of improvement reported by each patient after the initial and the last injection was marginally significant, suggesting that a larger study could provide significance to this finding. Nevertheless, in our population no cases of primary or secondary resistance were found. This could be explained by the lower rate of resistance found among patients with HFS than other facial dystonias[6].

Local side effects, such as mild facial paresis (lagophthalmos or lower facial paralysis), ptosis, diplopia and ecchymosis were transitory, disappearing after days or weeks. Biglan et al.[13] observed that if the total amount of BTX (Botox) injected around the eye exceeds 50 units (quantity that was not achieved in our patients), there was a considerable raise in the risk of lagophthalmos. The most frequent side effect in our casuistic was orbicularis oris paralysis, which contrasts with the results of other groups (that have found ptosis as the most frequent side effect)[1,5,6,8,14]. This finding could be explained by the orbicular oris BTXA injection scheme. Systemic effects of BTX were not observed in this population. The rate of adverse effects reported here is higher than what is found in preceding reports[5,6,8]. This could be partially explained by the fact that in our casuistic, any side effect that could be related to the injection in any moment during follow-up reported by the patients was accounted. Besides, the injections were sometimes performed by neurologists in training, which could have contributed to the increase in the rate of adverse effects. It must be taken into consideration that, in every case, the adverse effect was temporary. The frequency of side effects tend to decrease over time[5,7,8]. Five out of 54 patients discontinued treatment in our service. However, all of them continued their treatment in other public health services or private practices.

In our series, efficacy was maintained after long periods of treatment with high degree of patient satisfaction. For the treatment of HFS, results indicate that BTX injections provide very good response rate with sustained effects while the use of oral medication was highly unsatisfactory but did not interfere with the response to the BTX treatment. Along with previous studies reporting long-term efficacy of BTX treatment in HFS[5,6,8] and in spite of the need to raise the amount of BTX injected in the period analyzed (which by no means invalidates its efficacy), BTX (and specifically in our case, Botox®) can be considered a treatment with prolonged effectiveness in HFS. Overall, the results indicated that BTX is safe and effective for the treatment of HFS, even in a long-term use scenario.

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