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Long term outcome study on botulinum toxin A treatment for primary hemifacial spasm

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Abstract

Hemifacial spasm is usually treated with botulinum toxin A (BTX-A) injections, a proven symptomatic therapy. However, little has been reported on the long-term outcome of patients treated with BTX-A. We reviewed patients with hemifacial spasm treated with BTX-A at the University of Malaya Medical Centre between 1995 and 2003. Of the 82 patients in our BTX-A database, we were able to contact 68 patients to participate in the study, 79% women. They were assessed after a mean duration of disease of 9.5 years and mean duration of 4 years after the first BTX-A injection. Patients were asked the response to BTX-A therapy, to grade their functional severity at baseline prior to BTX-A treatment and at follow up in this study, and asked if they thought their hemifacial spasm had improved since the commencement of treatment. The majority (87%) still reported improvement after their most recent BTX-A injections. At baseline, 50% were mild, not interfering with daily living; 38% were moderate, some interference with daily living and 12% severe, significantly interfered with daily living. At follow up, 35% were mild, 54% moderate and 4% severe. Four (6%) had complete resolution of their spasm. Overall, 19% reported worsening, 57% reported no change, and 24% felt that their condition had improved. Six patients developed permanent facial weakness.
In conclusion, hemifacial spasm is a chronic disorder, with 6% reporting complete remission after 9.5 years of onset of illness. BTX-A injection continues to be effective after 4 years of repeated injections.

INTRODUCTION

Hemifacial spasm is a peripherally induced movement disorder characterised by involuntary, intermittent, tonic or clonic contractions of muscles innervated by the ipsilateral facial nerve. It has been frequently attributed to either hyperexcitability of the facial nerve nucleus[1] or compression of the nerve at the root exit zone (REZ) by an abnormal blood vessel resulting in ectopic excitation and "ephaptic transmission"[2] of the nerve. One of the most common mechanisms of compression is by atherosclerotic, aberrant, or ectatic intracranial arteries near the REZ (usually the inferior cerebellar artery).[3] A few case-control studies show an association between arterial hypertension and hemifacial spasm.[4,5,6] The theory is that hypertension causes elongation and dilation of the arteries, which result in compression of the facial nerve. However, a recent case-control study involving the Asian population shows no greater prevalence of hypertension in patients compared to controls.[7]

Chemodenervation with botulinum toxin A (BTX-A) has proven to be an effective method of treatment for hemifacial spasm with minimal side effects[8-11], and is presently the treatment of choice. Its effects are temporary and patients need to undergo repeated injections. However, little has been reported on the long-term outcome of patients with hemifacial spasm treated with BTX-A, especially with regard to its long-term effect on the condition, adverse reactions and continued efficacy.

In this descriptive study, we reviewed the long-term outcome of a series of patients treated with BTX-A at the University of Malaya Medical Centre (UMMC), Kuala Lumpur.

METHODS

Records of all patients treated with BTX-A at the UMMC were kept in a database at the Neurology unit. From this database, patients with hemifacial spasm were selected and data including sex, ethnic group, age of onset, duration of condition, age at first injection, number of injections, average dose per treatment, associated medical disorders and whether they were still on regular treatment or not, were obtained using a standard questionnaire.

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The patients were then contacted by telephone and were asked further information regarding their hemifacial spasm, including severity of the spasm before commencement of BTX-A therapy and currently, the degree of response to most recent BTX-A injection, the occurrence of any adverse reactions and whether the patients felt that the condition improved or not. Patients, who were no longer on follow up, were asked the reasons for dropping out from treatment.

The severity of hemifacial spasm was evaluated based on the degree in which the spasms interfered with the patient's activities daily living mainly by being socially embarrassed. The severity was graded as: "Mild", no interference with daily living; "Moderate", some interference with daily living; and "Severe", significant interference with daily living.

To evaluate the response to BTX-A injection, patients were asked to rate the effectiveness as follows: No improvement with no change from baseline, moderate improvement with reduction in spasm frequency, and marked improvement with spasms ceased altogether. Patients were also asked to rate subjectively whether over the long-term there was no change, worsening, improvement or complete resolution of their hemifacial spasm.

Statistical analyses were carried out where appropriate.

RESULTS

From 1995 to 2003, there were 82 patients (66 women and 16 men) with hemifacial spasm treated with BTX-A at UMMC. Of these, 12 were lost to follow up and were unable to be contacted for this study and 2 were deceased from other diseases. The remaining 68 patients were recruited for the study. There were 54 women (79%) and 14 men (21%). Fifty-six (82%) were ethnic Chinese, 10 (15%) were Malays and two (3%) were ethnic Indians. Mean age at the onset of hemifacial spasm was 49 ± 13 years (range 16 to 79 years) while the mean duration of the disease prior to BTX-A therapy was 9.5 years (range one to 51 years). Hemifacial spasm was left sided in 43 (63%), right sided in 24 (35%) and bilateral in one patient. Forty-one patients (75%) complained that their spasms were frequently aggravated by emotional factors, such as anxiety, stress and anger; fatigue; and voluntary facial movement. Relaxation was the only relieving factor, identified in 12 patients (18%).

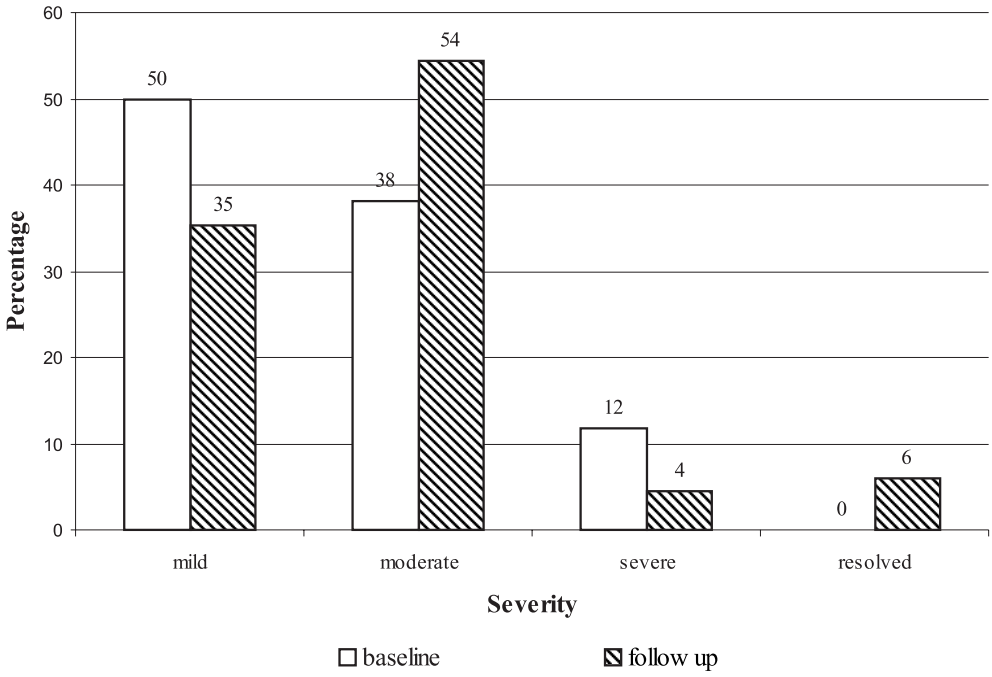
Twenty patients (29%) were hypertensive either preceding or after the onset of symptoms of hemifacial spasm. Other associated diseases were hyperthyroidism and stroke, which were encountered in two patients. Amongst the hypertensive patients, the mean age at onset of symptoms was 51 ± 10 years, older than the non-hypertensive patients (48 ± 14 years). However, the difference between these two groups was not statistically significant.

The mean age at first BTX-A injection was 55 ± 12 years (range 24 to 80 years). The mean number of BTX-A injections per patient was 4.2 (range one to 21) for a mean duration of treatment of 31 ± 27 months. When asked to grade response to their most recent BTX-A injection, 59 patients (87%) reported good response. In 20 patients (29%), there was marked improvement, 39 patients (57%) had moderate improvement, and 9 patients (13%) had no improvement. For the 59 patients reported improvement, the latency period to the onset of effect was 6.0 ± 4.3 (range one to 14) days and the total duration of benefit effect of each injection averaged 10.9 ± 7.2 weeks (range 4 to 52 weeks). Adverse effects after BTX-A injections were noted in 18 patients (27%); 9 (13%) with drooping of the side of the mouth, 6 (9%) with ptosis, 2 (3%) with both ptosis and drooping of mouth. These were temporary.

Patients were assessed after a mean duration 4.0 years (range 0 to 8), since starting BTX-A treatment. The functional severity of the patients at baseline prior to therapy was as follows: Mild in 34 patients (50%), moderate in 26 patients (38%), and severe in 8 patients (12%). As for the current severity of their spasms, 24 (35%) were mild, 37 (54%) were moderate, and 3 (4%) were severe (Figure 1). Complete remission was observed in four patients (6%). One of the patients in remission had hyperthyroidism and the hemifacial spasm ceased spontaneously after thyroidectomy. None the 4 patients underwent any other treatment, such as microvascular surgery or oral medication. In terms of severity, there was no significant difference between status at follow up and at baseline (Wilcoxon's signed-rank test, p=0.807).

A total of 35 patients (52%) had stopped BTX-A therapy for a period of more than one year. The reasons for discontinuation were the temporary nature of its beneficial effect (18 patients, 51%), cost of medication (10 patients, 29%), side effects (2 patients, 6%), complete resolution of the spasm (4 patients, 11%), and other reasons, such as getting used to the spasm (3 patients, 9%). In 16

Figure 1: Functional severity of hemifacial spasm at baseline and at follow up



patients (46%), the current functional status was moderate, while 15 patients (43%) were mild. As a comparison, patients who were continuing therapy had significantly more severe functional status, 3 patients (9%) were severe, 21 patients (64%) were moderate, and 9 patients (27%) were mild, P=0.021.

The patients' overall impression of the status of their hemifacial spasm as compared to before BTX-A treatment, after a mean duration of 4 years were: worsened in 13 (19%), unchanged in 39 (57%), improved in 12 (18%), resolved completely in 4 (6%).

Permanent mild facial weakness was seen in 6 patients (9%). They had significantly greater number of injections, mean 7.3 ± 6.7 injections, compared to those without facial weakness, p=0.02, but not significantly longer duration of disease, p=0.732.

In addition to BTX-A treatment, 20 patients had received other forms of treatment. They included microvascular decompression surgery (3), acupuncture (11), traditional medicine (4), both of traditional medicine and microvascular decompression surgery (2).

DISCUSSION

This study shows that BTX-A continues to be an effective symptomatic therapy for Malaysian patients with hemifacial spasm, 4 years after first BTX-A injection. The majority (87%) still reported improvement after their most recent BTX-A injection. The result is comparable to 76 to 95 per cent reported in other studies.[9,11-13] This is better than those achieved by oral medication[14,15], but slightly lower than those who underwent surgical decompression.[16-18] The interval of benefit of 10.9 ± 7.2 weeks was comparable to the 12 to 20 week benefit duration reported in other studies.[9,11,19] Although the adverse event rate was high (27%) over a mean duration of treatment of 31 months, the adverse effects were mild and temporary. Previous studies reported ptosis was the most frequent adverse effect of BTX-A.[13,16] However, the most common adverse effect in our patients was drooping of the side of mouth, followed by ptosis. Other side effects, such as dry eye and diplopia, were not reported. These were probably related to dose of BTX-A used in each injection site.

However, BTX-A appears to have little long-term effect on the spasms, the majority of our patients stating that their condition remained unchanged since the onset of treatment. Despite this, 4 of our patients (6%) reported complete remission of their spasms after receiving one or two BTX-A injections, and could not be explained by other forms of treatment. This has been noted in other studies.[11,13,19] It appears that in a small

number of patients, the condition remits spontaneously. One of our patients achieved resolution after thyroidectomy for hyperthyroidism. The association between hemifacial spasm and hyperthyroidism is uncertain and has not been previously reported, although hyperthyroidism has been associated with chorea.

Permanent facial weakness is rarely reported in hemifacial spasm and this has often been thought to be due to nerve damage after prolonged compression by the blood vessel.[12] However, the six patients we found with mild permanent facial weakness had significantly greater number of BTX-A injections compared to the others, while their mean duration of the disorder was not significantly longer, suggesting that repeated BTX-A injections may contribute to the permanent facial weakness.

At the University of Malaya Medical Centre, there were more Chinese and Malay patients with hemifacial spasm compared to Indians. Although overall about one third of patients in the hospital were ethnic Indians, it only accounts for 3% of the patients with hemifacial spasm. While these differences could be accounted for partly by the cultural and socio-economic background of the different ethnic groups, the possibility of lower prevalence in hemifacial spasm among Indians versus Chinese and Malays cannot be excluded.

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