

# Botulinum toxin type A and cervical dystonia

## A seven-year follow-up

Carlos Henrique F. Camargo<sup>1</sup>, Hélio Afonso G. Teive<sup>2</sup>,  
Nilson Becker<sup>1</sup>, Renato P. Munhoz<sup>1</sup>, Lineu César Werneck<sup>3</sup>

### ABSTRACT

Most cases of cervical dystonia (CD) are idiopathic, and focal injections of botulinum toxin A (BoNT/A) are the treatment of choice. The objective of our study was to document the effects of long-term BoNT/A treatment in idiopathic CD patients. Fifty-eight patients with idiopathic CD were recruited from March 2001 to May 2002. Twenty-eight of the subjects were available for reassessment after seven years. During this period, all had received regular treatment with BoNT/A injections. Clinical information about patients and the severity of CD (TWSTRS and VAPS) at baseline assessment (2001-2002) and follow-up (2008-2009) was compared. Significant motor improvement was detected based on TWSTRS scale scores, which were used to analyze clinical severity ( $19.6 \pm 6.6$  and  $17.7 \pm 4.8$ ;  $p < 0.05$ ). There was no improvement in the severity of cervical pain ( $p = 0.43$ ). In conclusion, BoNT/A was a safe and effective long-term therapy for CD.

**Key words:** cervical dystonia, botulinum toxin, dysphagia.

### Toxina botulínica A e distonia cervical: avaliação após sete anos

### RESUMO

A maioria dos casos de distonia cervical (DC) são idiopáticos; injeções locais com toxina botulínica A (BoNT/A) são o tratamento de escolha. O objetivo de nosso estudo foi documentar os efeitos do tratamento a longo prazo da BoNT/A em pacientes com DC idiopática. Foram selecionados 58 pacientes com DC idiopática de março de 2001 a maio de 2002. Desses pacientes, 28 estavam disponíveis para re-avaliação após sete anos. Durante esse período, todos foram submetidos a tratamento regular com injeções de BoNT/A. As informações clínicas dos pacientes e a gravidade da DC (TWSTRS e VAS) na primeira avaliação (2001-2002) e na reavaliação (2008-2009) foram comparadas. Houve uma significativa melhora motora detectada pelos resultados da escala TWSTRS, usada para analisar a gravidade clínica ( $19,6 \pm 6,6$  e  $17,7 \pm 4,8$ ;  $p < 0,05$ ). Não houve melhora nos resultados referentes a dor cervical ( $p = 0,43$ ). Em conclusão, BoNT/A foi uma terapêutica de longo prazo efetiva e segura para DC.

**Palavras-Chave:** distonia cervical, toxina botulínica, disfagia.

Dystonia is defined as a syndrome characterized by prolonged muscle contraction causing twisting, repetitive movements or abnormal posture<sup>1</sup>. Most voluntary muscles can be affected, and in the case of the neck muscles the condition is referred to as cervical dystonia (CD). CD is the commonest form of dystonia, and the

majority of cases are focal<sup>2,3</sup>. The etiology of most cases of CD is unknown, but genetic and environmental factors are known to be implicated<sup>3,4</sup>. Injections of botulinum toxin A (BoNT/A), a neurotoxin that has been extensively used to treat a variety of dystonic and non-dystonic movement disorders since the 1980s, is the treatment of

### Correspondence

Carlos Henrique Ferreira Camargo  
Rua Saint Hilaire 86 / apto. 21  
84035-350 Ponta Grossa PR - Brasil  
E-mail: chcarnargo@uol.com.br

Received 16 June 2010  
Received in final form 13 May 2011  
Accepted 20 May 2011

Movement Disorders Unit, Neurology Service, Hospital de Clínicas, Federal University of Paraná, Curitiba PR, Brazil:  
<sup>1</sup>Neurologist; <sup>2</sup>Associate Professor; <sup>3</sup>Full Professor.

choice nowadays for this condition<sup>4,5</sup>. The efficacy and safety of BoNT/A for CD has been proved in various studies<sup>3-7</sup>. Nevertheless, there is conflicting data regarding remission from the disease and long-term reactions to this medication<sup>8,9</sup>. Although spontaneous remission can occur in more than 10% of cases during the natural course of CD and also in patients treated with BoNT/A, most patients face continuous treatment, if not treatment for the rest of their lives<sup>10,11</sup>. Thus, as with most chronic diseases, prolonged follow-up of CD is required, as a patient's clinical response to treatment can vary depending on the natural history of the disease and the patient's immunological and clinical reaction<sup>12</sup>. The aim of this study was therefore to document the effects of prolonged use of BoNT/A in the treatment of CD patients.

## METHOD

### Patient selection

Between March 2001 and May 2002, a total of 85 patients with cervical dystonia who had attended the Botulinum Toxin and Movement Disorders Outpatient Unit in the Neurology Service, Hospital de Clínicas, Federal University of Paraná (HC-UFPR), were selected for clinical assessment and assessment of their response to BoNT/A treatment<sup>3</sup>. Of these patients, 58 were classified as having idiopathic dystonia. Between June 2008 and June 2009, the patients' clinical state and therapy were reassessed. This reassessment was referred to as the "second assessment". The assessment of patients carried out between 2001 and 2002 was referred to as the "first assessment".

The inclusion criteria were: [1] the presence of focal or segmental cervical dystonia; [2] the presence of generalized dystonia, hemidystonia or multifocal dystonia, with BoNT/A treatment indicated only for cervical dystonia; [3] a diagnosis of idiopathic dystonia at the first assessment; [4] attending both the first and second assessment; [5] having had regular follow-up exclusively for CD at HC-UFPR between the first and second assessment; [6] having received regular treatment with BoNT/A between the assessments; and [7] last BoNT/A injections administered not more than four months before the second assessment.

The exclusion criteria were: [1] inability to prove that the patient had been followed up by a physician; [2] inability to retrieve data for the period between assessments; [3] surgical treatment for dystonia between the first and second assessment; and [4] failure to sign the informed consent form.

### Clinical assessment

All the patients were diagnosed with idiopathic cervical dystonia by one or more neurologists, and this was

confirmed by the coordinator for the Movement Disorders Unit (Dr Teive). All the patients were assessed by the author by means of a detailed clinical history and a physical and neurological examination to identify the following: clinical characteristics; an association with other movement disorders and neurological diseases; epidemiological data; the length of time for which the patient had the disease; a history of trauma; the use of medicines; signs and symptoms that might indicate a secondary cause; and a family history of dystonia or other movement disorders.

All the patients were submitted to brain computed tomography and cervical-spine radiography. Additional tests included a complete blood count, TSH, VDRL, blood glucose test, ESR, electrolyte levels and liver and kidney function tests in all the patients. Computed tomography of the cervical spine, magnetic resonance imaging of the brain and other laboratory tests were requested according to the clinical assessment of each patient.

For primary dystonia to be diagnosed, the following conditions had to be met: [1] normal perinatal and developmental history; [2] no history of diseases or medication that could have precipitated the appearance of dystonia; [3] no evidence of pyramidal or cerebellar signs, alterations in sensitivity, or cognitive dysfunction on examination; [4] exclusion of secondary causes by specific tests.

The patients were classified according to the clinical presentation of the cervical dystonia (torticollis, laterocollis, retrocollis, anterocollis or combined forms) and whether they had focal, multifocal or generalized dystonia or hemidystonia.

### Treatment

The treatment patients had been receiving before they were included in the study was continued and adjusted in line with any clinical changes. All the patients were given BoNT/A therapy at regular intervals of between three and six months. BoNT/A injections were administered after the "first assessment" as shown in Table 1 using Botox® (Allergan, Irvine, CA, USA). The lyophilized preparation of the toxin (1 flask=100 U=5 ng) was stored at -20°C and reconstituted with 1 mL of 0.9% saline solution at the time the injection was administered. The 10 U per 0.1 mL solution was administered in a 1cc (1 mL) tuberculin syringe.

On subsequent visits, the commercial formulation available in the Neurology Service at the time was used in a dose adjusted as follows: Dysport® (Beaufour Ipsen Biotech, Paris, France) - 1:3 to 1:5 in relation to Botox®, and Prosigne® (Lanzhou Biological Products Institute, China) - 1:1 in relation to Botox®. The dose was reviewed at each visit and adjusted according to the therapeutic results and adverse effects.

**Follow-up**

The patients were assessed between 2001 and 2002 and between 2008 and 2009 to compare severity, disability and pain using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS - Severity) and a visual analog pain scale (0=absence of pain, 1-3=mild pain, 4-6= moderate pain, 7-9=strong pain, 10=disabling pain).

The adverse effects of the medication and any interference in daily life were measured with a questionnaire. Further information about physician visits in the period between the assessments was sought in the patient’s medical records and the appointment records.

**Statistical analysis**

The distribution pattern for all the data was tested (normal or non-normal). The statistical differences between the means of the groups were measured using the one-tailed Student’s t-test for normal distributions and the Mann-Whitney test for non-normal distributions. The results are given as mean ± SD (standard deviation). Differences were considered significant when p<0.05.

**RESULTS**

Of the expected total of 58 patients, 30 could not be located for follow-up. Twenty-eight patients were therefore included in the study. All attended medical appointments regularly between the first and second assessment and received BoNT/A treatment at varying intervals. The clinical characteristics of the patients included in the study and those not included are shown in Table 2.

Seventeen of the patients (60.7%, i.e., the majority) were female, and the ratio of females to males was 1.54:1. The characteristics of the CD are shown in Table 3. At the first assessment, the most prevalent form of the disease was focal CD (11 patients, or 39.3%). Seven other patients (25%) had segmental dystonia; three of these had cranial dystonia, one had dystonia in the upper limbs and one oromandibular dystonia and dystonia in an upper limb. In the patients with multifocal dystonia, a lower left limb was involved. Hemidystonia was observed in one patient, and eight (28.57%) had generalized dystonia. At the second assessment, the same pattern of dystonia was observed in 26 patients (92.85%). The exception to this was two patients, one of whom initially presented with segmental dystonia with CD and oromandibular dystonia, and the other of whom had hemidystonia. Both patients developed generalized dystonia.

The clinical presentation (torticollis, laterocollis, retrocollis and anterocollis) was as follows: 17 patients (60.7%) had more than one form of CD at the first assessment, and 11 (39.3%) had more than one form at the second (p=0.053). Clinical presentation remained the same throughout the follow-up period in 10 patients (35.7%). In eight patients (28.57%) the number of clinical presentations fell. In five patients (17.85%) the number remained the same, although the side affected by torticollis changed. One patient had an increased number of clinical presentations of CD. More pronounced changes in forms – e.g., a change from torticollis to laterocollis – occurred in four patients (14.3%) (Fig 1).

**Table 1.** Dose and number of botulinum toxin injection points per muscle.

Muscle	Dose	Number of points
Sternocleidomastoid	15-75	2-4
Trapezius	30-100	5-10
Splenius capitis	15-50	2-4
Levator scapulae	15-50	2-4
Paravertebral muscles	15-50	2-4

**Table 3.** Characteristics of cervical dystonia in the study population (n=28).

Characteristic	Mean	Range
Age at onset of CD (years)	28.1	3-63
Total duration of CD (years)	16.43	8-35
Duration of CD at first assessment (years)	9.36	1-28
Duration of CD at the beginning of BoNT/A treatment (years)	7.64	1-22

CD: cervical dystonia; BoNT/A: botulinum toxina.

**Table 2.** Differences between patients included in the study and those not included

	Included (n=28)	Not included (n=30)	p
Age at onset of CD (years)	28.1 ± 16.67	38.9 ± 15.51	0.013
M:F ratio	1:1.54	1:2.33	0.232
TWSTRS	19.6 ± 6.55	18.03 ± 5.56	0.183
Type of dystonia	Focal and segmental – 18 (64.3%) Multifocal and hemidystonia – 2 (7.14%) Generalized – 8 (28.57%)	Focal and segmental – 26 (86.66%) Multifocal and hemidystonia – 2 (6.66%) Generalized – 2 (6.66%)	0.014

M: male; F: female; CD: cervical dystonia; TWSTRS: Toronto Western Spasmodic Torticollis Rating Scale.

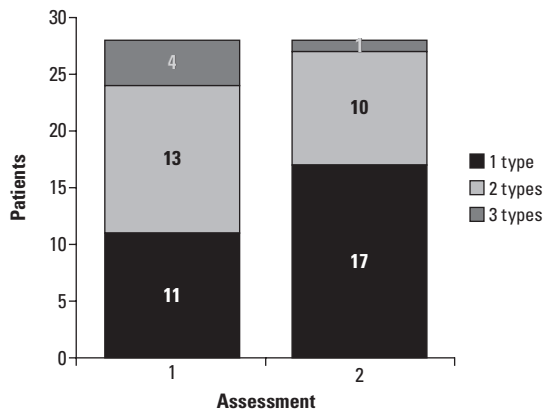


Fig 1. Forms of cervical dystonia.

The severity of abnormal head and neck movements measured on the TWSTRS scale was greater at the first assessment than at the second [ $19.6 \pm 6.6$  and  $17.7 \pm 4.8$ ;  $p=0.033$  (Fig 2)]. Motor symptoms measured on the TWSTRS scale worsened in only three patients: one with focal dystonia, one with segmental dystonia and one with segmental dystonia that evolved to generalized dystonia. Different degrees of pain in the cervical region were reported by 21 patients (75%) at the first assessment and 17 (60.7%) at the second. There was no reduction in the intensity of pain at the second assessment [ $4.3 \pm 2.8$  and  $4.43 \pm 3.7$ ;  $p=0.434$  (Fig 3)]

When questioned, patients did not report any significant adverse effects from the therapy. The one exception was a patient who reported dysphagia and difficulty keeping her neck straight on two occasions when injections were administered; this was subsequently corrected by reducing the dose and changing the commercial formulation used. The data from appointment records and patient medical records supported the patients' impressions.

## DISCUSSION

This study of 28 patients with idiopathic CD treated with BoNT/A showed that the majority experienced an improvement in dystonic motor symptoms over the years of treatment.

Only a small number of patients were included in the study, reflecting the difficulty of adhering to the treatment over the years. Nonetheless, the number of patients assessed after seven years of follow-up (48.27%) is similar to the 35.55% of patients who were still continuing BoNT/A treatment after 12 years of follow-up reported by Haussermann et al.<sup>13</sup>. Patients selected for the study had a different profile from those who were not included, having a lower age at onset and a greater prevalence of generalized dystonia. Many patients may have given up attending the Movement Disorders Unit because of the inefficacy or side effects of the therapy<sup>8,9,13,14</sup>. Another

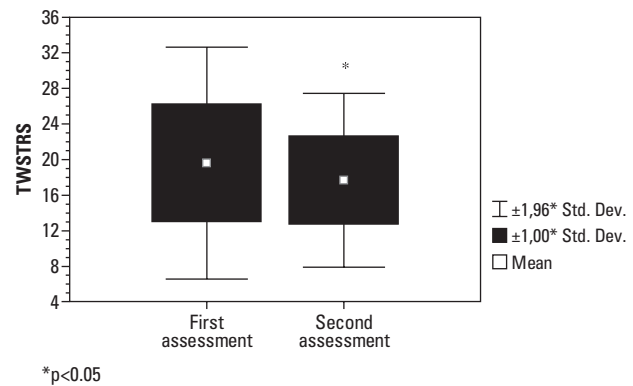


Fig 2. Severity of cervical dystonia on the Toronto Western Spasmodic Torticollis Rating Scale.

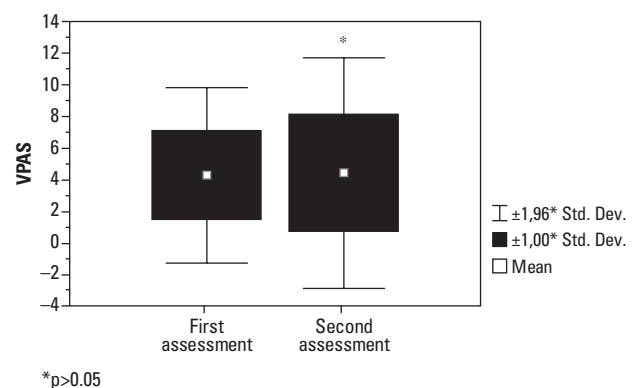


Fig 3. Pain intensity measured on a visual analog pain scale.

possible reason for failure to attend the Unit may have been remission from the disease, very probably as a consequence of BoNT/A treatment. The latter explanation could apply to this series as the number of patients with generalized dystonia (which is both more severe and less likely to lead to remission) who continued until the end of the follow-up was greater than the corresponding number of patients with milder, focal dystonia. However, the initial assessment of severity on the TWSTRS was similar in the patients selected and those who gave up the treatment. In their initial assessment, Brashead et al.<sup>15</sup> also found similarities between the severity of dystonia in patients who continued treatment and those who abandoned it. Of their patients, 21.8% – none of whom had clinical remission – abandoned treatment immediately after the first session of BoNT/A injections. Another important factor associated with patients giving up treatment that should be taken into consideration in our study is that it was carried out in a public hospital, a factor in developing countries that makes it more difficult to obtain suitable treatment regularly because of a range of situations related to patients' socioeconomic conditions. Other possibilities that should be considered

are that patients may have continued the follow-up in different hospitals or died<sup>8,9,13</sup>.

Among patients who underwent regular clinical follow-up, the rate of attendance at medical appointments was similar to that observed in studies in which a high degree of satisfaction with the long-term results of CD treatment with BoNT/A was reported<sup>8,12,15</sup>. BoNT/A is currently the treatment of choice for CD, and the results of long-term follow-up studies have shown the safety and efficacy of this treatment<sup>6,8,9,12,13,15</sup>.

Patient assessment after seven years showed that they had lower severity levels on the TWSTRS and less complex patterns of presentation than at the beginning of the follow-up at the Movement Disorders Unit. The chemical denervation produced by BoNT/A is known to be temporary; however, it is believed that a gradual improvement in CD motor patterns can occur with cumulative doses of BoNT/A administered in a series of visits<sup>16</sup>. Kessler et al.<sup>8</sup> found a progressive, statistically significant motor improvement after the sixth set of BoNT/A injections, and this lasted for at least 15 subsequent injection visits (approximately four years). However, patients whose severity scores were initially higher continued to have higher mean severity scores than those whose severity scores were lower at the first assessment. These findings are in keeping with the data in the present study, which found small differences between the results measured on the TWSTRS at the first and the second assessment for each patient. Another very important factor that should be borne in mind when interpreting the results in terms of the efficacy of the therapy is the possibility of a residual effect of BoNT/A at follow-up assessments simulating a more definitive improvement<sup>8,12</sup>.

The change in the clinical presentation of CD can be measured by means of two parameters: [a] the increase or decrease in the number of types of abnormal postures; [b] the change in the pattern of abnormal postures. Only 10 patients did not have any change, i.e., 62.2% of the patients in this series had a change in their clinical presentation over the years. Maia et al.<sup>17</sup> found that 35.8% of their patients had had changes in their clinical presentation. However, these authors only considered a change in the pattern of abnormal postures and not the side affected by CD to be a change in presentation. Using their methodology, only five patients (17.85%) would have been considered to have had a different presentation at the second assessment. Insofar as the number of presentations of CD is concerned, it is known that the number of abnormal postures is directly related to the severity of the disease<sup>3</sup>. Although it was not statistically significant, the number of patients with more than one abnormal CD posture fell from 60% at the first assessment to 40% at the second. Skogseid and Kerty<sup>12</sup> found that the number

of abnormal postures fell in 19.23% of their patients who considered BoNT/A to have had a beneficial effect. Nevertheless, it is possible that the long-term response to this therapy is not related to the degree of complexity of CD as measured by the number of presentations<sup>8</sup>.

The symptoms were observed to spread to other sites in two patients. This number is much smaller than the 33 to 34.3% of spreading found in other studies<sup>13,18</sup>. However, the difficulties in measuring the spread of symptoms because not all patients were available for the second assessment should also be stressed. This reasoning also applies to analysis of remission from symptoms. The proportion of patients who experience complete remission during the natural course of the disease, usually during the first years, is low (between 4.7 and 30%)<sup>3,10</sup>. Haussermann et al.<sup>13</sup> found six patients with remission in a group of 32 who took part in a complete follow-up. Of these, only one did not need further treatment and was thus considered to have had complete remission. The influence of BoNT/A on the spread of and remission from CD remains to be further elucidated<sup>18</sup>.

The high prevalence of pain (around 70% of patients) distinguishes cervical dystonia from other focal dystonias and contributes significantly to patient disability<sup>19</sup>. BoNT/A is highly effective in controlling pain, and its analgesic effect is sustained for a long time<sup>3</sup>. However, in contrast to the improvements in CD motor symptoms observed with BoNT/A treatment, there was no reduction in pain with cumulative doses. Long-term follow-up studies do not attach particular importance to the pattern of pain observed over the years<sup>8,9,12,13</sup>.

The adverse effects of BoNT/A in our study were reported by very few patients and, with the exception of one patient, were short-lived. It should be remembered that these were the patients who continued to take part in the follow-up and were satisfied with the treatment. As occurred in other studies, the patients who abandoned the follow-up may have included those patients who had more severe adverse effects<sup>8,9,13,15</sup>. The main adverse effects that can make a CD patient abandon follow-up are weakness of the cervical muscles, dysphagia and pain at the injection site<sup>15</sup>.

Most long-term studies demonstrating the efficacy and safety of BoNT/A were carried out in centers where a single commercial formulation was used as the standard throughout the treatment (Botox® or Dysport®)<sup>8,12,13</sup>. Such standardization was not possible in this study because the state government supplied the hospital periodically with the least expensive BoNT/A at the time. For this reason, all the patients received Botox® in the first injections and Dysport® and Prosigne® after that. The change in commercial formulation during the treatment prevented a comparative analysis of the doses and total

amounts of the drug used in the patients. Because they are biological products, the conversion factor between the different commercially available BoNT/A formulations may not be completely accurate and their potencies may not be exactly the same. In an important multicenter study using Dysport® for CD, the efficacy and safety of treatment in patients who had previously received Botox® was similar to that in patients who had not had any previous treatment<sup>20</sup>. In contrast, in another study patients who had received Dysport® showed an improvement when they were treated with Botox®<sup>16</sup>. There was an increase in adverse effects when the Botox® dose was replaced by Dysport® and the doses were automatically changed in the ratio 1:3<sup>21</sup>. Currently, it is known that the relationship between Botox® and Dysport® can vary between 1:3 and 1:5. It is recommended that the BoNT/A dose be adjusted individually for each patient and that an initial Dysport® dose of 500 U be used to minimize side effects<sup>22</sup>. Prosigne® appears to be as effective and safe as Botox® for CD patients. Although a previous study showed that larger doses of Prosigne® were needed to achieve a similar effect to that achieved in CD patients who underwent Botox® treatment, a recent controlled study showed that doses in the proportion 1:1 resulted in the same efficacy and safety<sup>23,24</sup>. Currently available data show that commercially available BoNT/A formulations are safe to use. Nevertheless, the differences in the adverse effects associated with each formulation suggest that each product should be used based on a knowledge of the product, including the product literature, dosage recommendations and methods of administration<sup>25</sup>.

In conclusion, this study has shown that BoNT/A is a safe and effective long-term treatment for controlling CD motor symptoms and leads to a progressive improvement in motor pattern. Further follow-up studies of patients who abandoned therapy during the follow-up period are required to compare the natural history of the disease with the disease in patients who received BoNT/A treatment.

## REFERENCES

1. Fahn S. The varied clinical expressions of dystonia. *Neurol Clin* 1984; 2: 541-554.
2. Nutt JG, Muentner MD, Aronson A, Kurland LT, Melton LJ 3<sup>rd</sup>. Epidemiology of focal and generalized dystonia in Rochester, Minnesota. *Mov Disord* 1988;3:188-194.
3. Camargo CH, Teive HA, Becker N, Baran MH, Scola RH, Werneck LC. Cervical dystonia: clinical and therapeutic features in 85 patients. *Arq Neuropsiquiatr* 2008;66:15-21.
4. Dauer WT, Burke RE, Greene P, Fahn S. Current concepts on the clinical features, aetiology and management of idiopathic cervical dystonia. *Brain* 1998;121:547-560.
5. Tsui JK, Eisen A, Stoessl AJ, Calne S, Calne DB. Double-blind study of botulinum toxin in spasmodic torticollis. *Lancet* 1986;2:245-247.
6. Albanese A, Barnes MP, Bhatia KP, et al. A systematic review on the diagnosis and treatment of primary (idiopathic) dystonia and dystonia plus syndromes: report of an EFNS/MDS-ES Task Force. *Eur J Neurol* 2006; 13:433-444.
7. Jankovic J, Schwartz K. Botulinum toxin injections for cervical dystonia. *Neurology* 1990;40:277-280.
8. Kessler KR, Skutta M, Benecke R. Long-term treatment of cervical dystonia with botulinum toxin A: efficacy, safety, and antibody frequency. *J Neurol* 1999;246:265-274.
9. Hsiung GY, Das SK, Ranawaya R, Lafontaine AL, Suchowersky O. Long-term efficacy of botulinum toxin A in treatment of various movement disorders over a 10-year period. *Mov Disord* 2002;17:1288-1293.
10. Lowenstein DH, Aminoff MJ. The clinical course of spasmodic torticollis. *Neurology* 1988;38:530-532.
11. Jankovic J, Schwartz KS. Longitudinal experience with botulinum toxin injections for treatment of blepharospasm and cervical dystonia. *Neurology* 1993;43:834-836.
12. Skogseid IM, Kerty E. The course of cervical dystonia and patient satisfaction with long-term botulinum toxin A treatment. *Eur J Neurol* 2005;12: 163-170.
13. Haussermann P, Marczych S, Klinger C, Landgrebe M, Conrad B, Ceballos-Baumann A. Long-term follow-up of cervical dystonia patients treated with botulinum toxin A. *Mov Disord* 2004;19:303-308.
14. Erbguth F, Claus D, Jaspert A, Druschky A, Neundorfer B. Which patients discontinue treatment with botulinum toxin in cervical dystonia? *Mov Disord* 1995;10:37.
15. Brashear A, Bergan K, Wojcieszek J, Siemers ER, Ambrosius W. Patients' perception of stopping or continuing treatment of cervical dystonia with botulinum toxin type A. *Mov Disord* 2000;15:150-153.
16. Brans JW, Lindeboom R, Aramideh M, Speelman JD. Long-term effect of botulinum toxin on impairment and functional health in cervical dystonia. *Neurology* 1998;50:1461-1463.
17. Maia FM, Kanashiro AK, Chien HF, Gonçalves LR, Barbosa ER. Clinical changes of cervical dystonia pattern in long-term botulinum toxin treated patients. *Parkinsonism Relat Disord* 2010;16:8-11.
18. Godeiro-Junior C, Felício AC, Aguiar PM, Borges V, Silva SM, Ferraz HB. Retrocollis, anterocollis or head tremor may predict the spreading of dystonic movements in primary cervical dystonia. *Arq Neuropsiquiatr* 2009; 67:402-406.
19. Chan J, Brin MF, Fahn S. Idiopathic cervical dystonia: clinical characteristics. *Mov Disord* 1991;6:119-126.
20. Truong D, Duane DD, Jankovic J, et al. Efficacy and safety of botulinum type A toxin (Dysport) in cervical dystonia: results of the first US randomized, double-blind, placebo-controlled study. *Mov Disord* 2005;20:783-791.
21. Ranoux D, Gury C, Fondarai J, Mas JL, Zuber M. Respective potencies of Botox and Dysport: a double blind, randomised, crossover study in cervical dystonia. *J Neurol Neurosurg Psychiatry* 2002;72:459-462.
22. Poewe W, Deuschl G, Nebe A, et al. What is the optimal dose of botulinum toxin A in the treatment of cervical dystonia? Results of a double blind, placebo controlled, dose ranging study using Dysport. *German Dystonia Study Group. J Neurol Neurosurg Psychiatry* 1998;64:13-17.
23. Wan X, Tang X. Comparison of Botox and a Chinese type A botulinum toxin in cervical dystonia. *Zhonghua Yi Xue Za Zhi* 1998;78:131-134.
24. Quagliato EM, Carelli EF, Viana MA. A prospective, randomized, double-blind study comparing the efficacy and safety of type A botulinum toxins botox and prosigne in the treatment of cervical dystonia. *Clin Neuropharmacol* 2010;33:22-26.
25. Chapman MA, Barron R, Tanis DC, Gill CE, Charles PD. Comparison of botulinum neurotoxin preparations for the treatment of cervical dystonia. *Clin Ther* 2007;29:1325-1337.