

# BOTULINUM TOXIN TYPE A FOR REFRACTORY POST-STROKE SHOULDER PAIN

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**Abstract** – Botulinum toxin type A (BTX-A) has been used to treat several neurological conditions such as sialorrhea, hyperhydrosis, dystonia, hemifacial spasm, spasticity and pain. Although spasticity has been successfully treated with BTX-A, few are the authors studying the use of BTX-A to treat shoulder pain secondary to stroke. In order to study if BTX-A is effective to treat post-stroke shoulder pain, we followed up during 4 months 16 patients with sustained shoulder pain. Patients received BTX-A according to previous discussion with the rehabilitation group to determine the muscles and dose to be injected and were evaluated by the joint range of motion and analogic pain scale. There was decrease of pain during shoulder motion, mainly during the movements of extension and rotation. We conclude that BTX-A is a safe and efficacious therapy.

**KEY WORDS:** botulinum toxin, spasticity, pain, stroke, hemiplegia.

## Toxina botulínica do tipo A no tratamento do ombro doloroso após AVC

**Resumo** – A toxina botulínica do tipo A (TB-A) tem sido utilizada com sucesso para o tratamento de várias enfermidades neurológicas, tais como sialorréia, hiperidrose, distonia, espasmo hemifacial, espasticidade e dor. Embora espasticidade seja tratada com sucesso após o advento da TB-A, poucos são os autores que utilizaram a TB-A no tratamento da dor no ombro espástico secundária a acidente vascular cerebral (AVC). Com o objetivo de estudar a eficácia da TB-A no tratamento da dor no ombro secundária a AVC, foram acompanhados 16 pacientes com esta enfermidade associada à dor refratária no ombro espástico. Os pacientes receberam TB-A de acordo com dose e pontos de injeção definidos previamente pelo grupo de reabilitação e foram avaliados pelos ângulos de abertura da articulação do ombro e escala de avaliação analógica de dor. Houve melhora da dor à movimentação da articulação do ombro, principalmente nos movimentos de rotação e extensão. Concluímos que a TB-A é uma terapêutica segura e eficaz para o tratamento do ombro doloroso secundário a AVC.

**PALAVRAS-CHAVE:** toxina botulínica, espasticidade, dor, AVC, hemiplegia.

Shoulder pain is a significant problem for 30 to 82% of patients presenting post-stroke hemiparesis<sup>1</sup>. In these patients, shoulder pain is usually associated to bad positioning of the upper limb, fasciites, tendonitis or muscular problems including myofascial pain<sup>2-4</sup>. After 6 months of stroke about 20 to 30% of spastic patients remain with pain and most of them do not relieve with usual treatments such as anti-inflammatory drugs, diazepam, tizanidine or baclofen<sup>4</sup>. Since the beginnings of 1980, botulinum toxin type A (BT-A) has been used to treat several neurologic disorders related to muscle contraction such as hemifacial spasm, hemiparesis and dystonia<sup>5,6</sup>. In this last condition, some authors observed that pain relieved more than the decrease of muscle contraction<sup>6,7</sup>. In 1990, Carruthers et al. observed that patients after treating wrin-

kle with BT-A referred improvement of headache<sup>8</sup>. Also, Aoki et al. observed that BT-A decreased pain in experimental animal models and in vitro decreased neurotransmitters related to pain such as glutamate, substance P and CGRH<sup>9</sup>.

More recently, some authors observed that BTX-A relieves several types of headache, myofascial syndrome and articular pain<sup>10</sup>. In non-published results we have observed that some spastic post-stroke patients relieve their pain after the use of BTX-A in the spastic muscles of the shoulder, which seems independent of the decrease of spasticity.

Thus, in an open label trial, we decided to study the injection of BTX-A in the treatment of shoulder pain associated to post-stroke spasticity.

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## METHOD

This study was approved by the local ethical committee, and was performed according the 1964 Declaration of Helsinki. All patients signed the informed consent form prior to taking part in any procedure of this study. The botulinum toxin was provided by the Health Secretary of the State of Bahia, Brazil to be used in patients with spasticity.

An open, prospective clinical trial was carried out at the Neurosciences Outpatient Clinic, in the Magalhães Neto Pavilion (University Hospital Prof. Edgard Santos) with patients of both genders, older than 18 years, who complained of pain associated to spastic hemiparesis secondary to stroke. Patients with liver, blood or kidney diseases; pregnant or nursing women; or cases of aphasia, dementia or fibrotic retraction of the affected muscles were excluded from the investigation.

To measure the passive amplitude of movement we used monthly goniometry during 4 months. Upper limb spasticity was assessed using the Modified Ashworth Scale for shoulder medial rotators, and elbow, wrist and finger flexors. Assessments were carried out at baseline and weeks 1, 2 and 4. After individualized selection of muscles and doses, BTX-A (Botox®) was applied in the spastic muscles, according to a previous neurological schedule as recently published. All subjects were submitted to rehabilitation therapy.

Demographic variables were presented as means and standard deviation. Data with  $p < 5\%$  were considered significant. Data were entered in databank software, and analyzed through SPSS 9.0; the matched Student t test was used to compare the means.

## RESULTS

From January 2006 to February 2007, 16 patients with hemiparesis and shoulder pain after stroke were evaluated, 1 patient was excluded because referred no improvement with the treatment and one died of respiratory infection. Fifty per cent (50%) of the subjects were male, mean age was 47.8 years, and the mean time from the cerebrovascular event was 4.2 years. Only one patient presented a dominant left side, and the left cerebral hemisphere was affected in 55% of the patients. Characteristics of the patients are shown in Table with summarized mean total dose and doses per muscle.

Pain improvement by Visual Analog Pain Scale appeared as early as Week 1 and remained until the fourth month of follow up when we observed gradual return of pain (Fig 1). However, only the flexion and rotation of shoulder reached statistically significant improvement (Fig 2).

## DISCUSSION

This is the first report of long term effect of BTX-A injection for refractory post-stroke shoulder pain using individualized doses and muscle choice to inject, according previous schedule of rehabilitation group. The degree of pain reduction using the global impression of patient and the range of motion was both statistically and clinically significant lasting more than 4 months. Patients who

Table. Doses of BTX-A (Botox®) in all patients, with summarized mean total dose and doses per muscle.

Patient	Muscle											Total dosage (U)
	PM	GD	B	B-R	FCU	FCR	FDS	FDP	PT	RB	TB	
1	100	100	-	-	-	-	-	-	-	-	-	200
2	50	-	100	50	-	50	-	-	50	50	-	350
3	75	50	100	-	50	50	-	-	50	50	-	425
4	50	50	-	-	50	50	-	-	-	-	50	250
5	75	50	-	-	-	-	50	-	-	50	-	225
6	50	50	-	-	-	50	-	50	-	50	-	250
7	75	75	100	75	-	50	-	50	-	-	-	425
8	75	75	-	-	-	-	-	-	-	-	50	200
9	75	75	100	-	50	50	-	-	-	-	-	350
10	50	50	-	-	-	50	-	50	-	-	-	200
11	75	75	-	-	-	-	-	25	25	50	-	250
12	75	50	100	-	-	-	-	-	-	50	-	275
13	75	75	-	-	-	-	-	-	-	50	-	200
14	75	75	-	-	-	-	-	-	-	50	50	250
15	75	75	100	-	50	50	-	-	-	-	-	350
Mean dose/ muscle & mean total dose	70	66.1	100	62.5	50	55	50	43.75	41.66	50	50	280

PM, pectoralis major; GD, dorsalis major; B, biceps brachii; B-R, brachioradialis; FCU, flexor carpii ulnaris; FCR, flexor carpii radialis; FDS, flexor digitorum superficialis; FDP, flexor digitorum profundus; PT, pronator teres; RB, rhomboid; TB, triceps brachii.

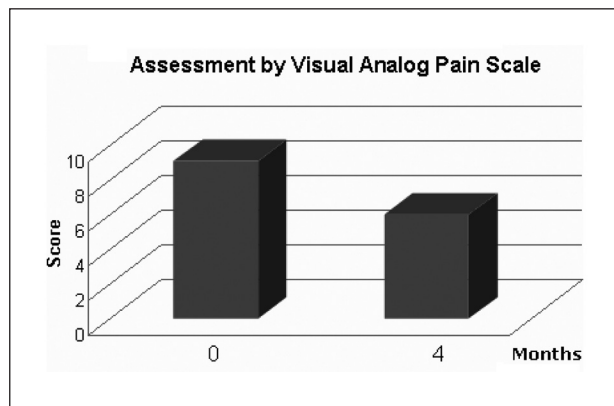


Fig 1. Pain assessment of 15 patients with spastic refractory shoulder pain.

experienced pain reduction were also accompanied by an important improvement in limb function, which could be related to the action of BTX-A in the motor component of spasticity, as has been observed previously<sup>11</sup>. However, it was clear that in some patients relief of pain was more important than the decrease in spasticity.

There are some important limitations to our study that merit comment. This is an open label clinical trial with non-randomized treatment allocation, which favors patient and observer bias. However, the improvement was detected by objective measures, less susceptible to the unblinded bias effect.

Despite some methodological limitations such as absence of blindness and lack of randomized controls, the results of this study show that BTX-A associated to physical therapy should be considered for refractory shoulder pain secondary to stroke. In a previous paper, we have discussed that post-stroke spasticity is a very pleomorphic entity and case series study, where a patient is his self control, is probably better than the randomized studies<sup>11</sup>. Drugs such as tizanide, baclofen, amitriptyline and non-steroid anti-inflammatory are recommended in this group of patients with uncertain results, adverse side-effects, small amount of benefits and short duration of effects. However, BTX-A has been proven safety and efficacious to some types of pain and also to decrease spasticity in post-stroke patient<sup>12</sup>. It could be possible that the observed analgesic effect of BTX-A in our group of patients could be related to decrease of shoulder spasticity. But, it could also be related to improvement of trigger points observed in myofascial syndrome, frequently found in patients with spasticity, or even to BTX-A action over pain neurotransmitters<sup>13</sup>. Despite the described limitations, BTX-A injection seems to be an interesting option to pain associated to post-stroke patient. As has been sufficiently described, the clinical use of BTX-A is expanded, since its initial use centered in the excessive muscular contraction.

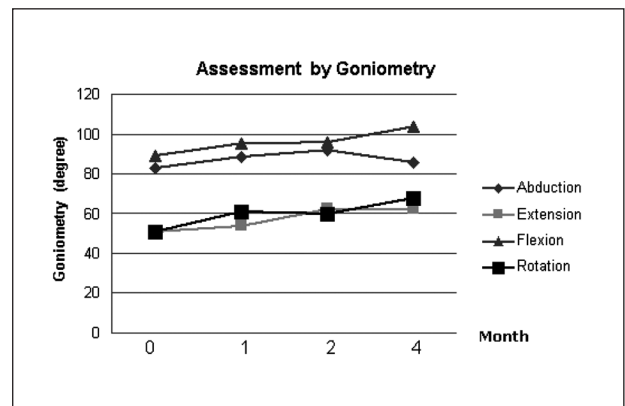


Fig 2. Range of motion assessment of 15 patients with spastic refractory shoulder pain.

Nowadays, BTX-A clinical use include hyperhydrosis, spasmodic dysphonia, detrusor sphincter dysinergia, esophageal sphincter achalasia, papilla of Vater spasm, trigeminal neuralgia, migraine and myofascial pain. Although, in some types of painful syndromes such as chronic tension type headaches there is no evidence of improvement after BTX-A injection, it is possible that some patients with these last conditions have benefits.

Finally, we have to state that despite the limitations of open clinical trials, this study shows that BTX-A is a promising medical strategy to treat shoulder pain in post-stroke patients, however, further controlled studies still are necessary.

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