

# USE OF BOTULINUM TOXIN IN 55 CHILDREN WITH CEREBRAL PALSY

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**Abstract** - Botulinum toxin A (BTA) inhibits presynaptic release of acetylcholine at the neuromuscular junction and has reportedly been successful in the treatment of spastic disorders.

To evaluate the effect of botulinum toxin on cerebral palsied children with spastic or mixed type of the disease, especially those patients having spasticity as a cardinal symptom without joint contracture, we designed the following study. Ninety-one cases (55 of referred patients to Pediatric Neurology outpatient clinics of Children's Medical Center) were given BTA injections in affected muscles of the lower limb. They were reevaluated 3 to 5 weeks and 3 months later for type of walking and range of affected joints' movement. The study showed a clinically significant gait improvement in 71.2% of patients ( $p < 0.0005$ ) and also an overall increased range of motion in affected limbs after BTA injection ( $p < 0.04$ ). Side effects occurred only in two cases as transient generalized weakness, genu recurvatum and ptosis. Drug effectiveness was time-limited, lasting about 3 months in all patients (a golden time for rehabilitation therapists to improve the patients' condition). Overall, BTA has improved both the type of walking as well as the range of joints motion in our patients. So it's administration is suggested in cerebral palsied children if the spasticity is a major and disabling sign.

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**Key Words:** Botulinum toxin type A, cerebral palsy, child, gait, muscle, neuromuscular agents

## INTRODUCTION

Cerebral palsy (CP) is a static type encephalopathy in children with major motor manifestations occurring almost exclusively in the first years of life. Although it is the most common type of motor disturbance in children but the overall incidence is not very high (1-2/1000) (1,2,3). Despite the low incidence rate, cerebral palsy is a very disabling problem and it is on the top of the list of the handicapping condition in children with major consequences on child health and well being. One of the main symptoms and signs of cerebral palsy is spasticity over the limbs and trunk. There are many recommended treatments, which are mainly directed to reduce the limb spasticity and to increase the range of motion of the affected limbs. Among these modalities, there is growing interest in the therapeutic role of

botulinum toxin A (BTA)(4).

Clostridium Botulinum is an anaerobic bacterium that produces seven immunologically distinct strains of neurotoxin (A to G). The main mechanism of botulinum toxin action is on neuromuscular junction by blocking the synaptic release of acetylcholine from cholinergic nerve terminals. This causes an irreversible loss of motor end-plates. So the muscle is paralyzed until nerve sprouting establishes new junctions (5). BTA has been developed commercially and in Iran it is available as 500 units vials of DYSPORT. Although BTA is more widely used clinically, in adults, particularly in the management of focal dystonias and acquired spasticity (6), but it has also been increasingly used in children with cerebral palsy since the first reports in 1993 (7,8). The largest group of patients reported was 27 cases (9).

To study the effect of BTA in children with cerebral palsy, we designed the following study. The major questions to be answered were:

- 1-How is the effect of BTA on muscle spasticity in children with cerebral palsy?
- 2- How is the effect of BTA on the gait of children with cerebral palsy?
- 3- What are the side effects in the children so treated?

## MATERIALS AND METHODS

During 13 months from July 1998 to August 1999, children with pure spastic cerebral palsy or mixed type of CP with spasticity as a cardinal sign were selected by a simple random sampling method (Fig. 1). These patients were referred to the pediatric neurology outpatient clinic of Children's Medical Center and my office. Parents were well informed about the treatment and possible side effects and those agreed, entered the study (55 patients).

Patients' ages were from 18 months to 12 years with the mean age of 58 months and standard deviation of 24 months. 44.9% of cases were female and 55.1% were male. After being registered in the study, 500 units of BTA (Dysport) were injected in the affected muscles (Fig. 2). Each muscle has been injected through 3 to 4 points. There were 91 injection sessions in 55 patients. Some of them have been injected for

twice or three times (25 patients). In 89.9% of cases injection was done on both sides and in 10.1% on only one side.

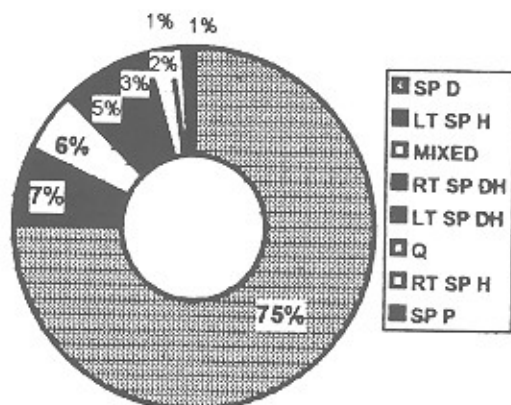


Fig. 1. Relative frequency of patients with different type of cerebral palsy.

SP D = Spastic Diparesis  
 LT SP H = Left sided Spastic Hemiplegia  
 MIXED = Mixed type of cerebral palsy  
 RT SP DH = Right sided Spastic Double Hemiplegia  
 LT SP DH = Left sided Spastic Double Hemiplegia  
 Q = Quadriparesis  
 RT SF H = Right sided Spastic Hemiplegia  
 SP P = Spastic Paraplegia

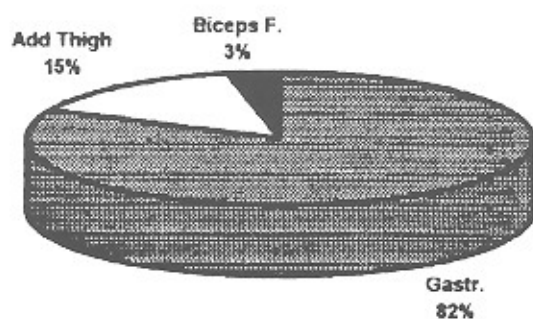


Fig. 2. Injected muscles

Add Thigh = Adductor muscles of thigh  
 Biceps F. = Biceps Femoris  
 Gastr. = Gastrocnemius muscle

At the first visit, before the injection, range of passive motion was determined. There was also an evaluation of the type of walking. After about 3 to 5

weeks there was a reevaluation of the mentioned parameters. Re-evaluation was also done after three months. Range of joints' motion was expressed as degree of flexion on extension and types of walking were evaluated as active vs. passive and improved vs. not improved.

## RESULTS

Six patients (6.85%) had active not-assisted walking before BTA injection and three (3.45%) did not walk at all before but stand to walk after BTA injection. About 78 cases did not walk before and after the injection. Regardless of active or passive walking there was an obvious improvement in the quality of gait in 71.2% of cases (62 patients). The highest improvement rates were seen in hemiplegic patients (92.5%) and the lowest one in quadriparetics (50%). The overall response rate was about 71.2% ( $p < 0.0005$ ) (Fig. 3)

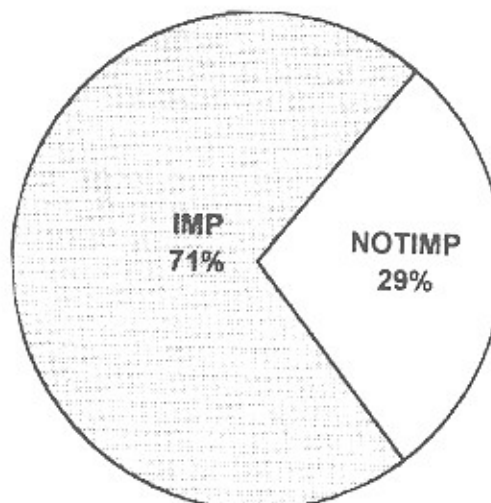


Fig. 3. Gait analysis 3 to 4 weeks after BTA

IMP = Gait improved after BTA injection (relative frequency)

NOTIMP = Gait not improved after BTA injection (relative frequency)

Comparison between passive range of motion before and after BTA injection showed the following results:

1-Right ankle angles showed a mean decrease of 18.87 degree after BTA injection in right gastrocnemius muscles ( $p < 0.003$ ).

2-Left ankle angles showed a mean decrease of 21.61 degree after BTA injection in left gastrocnemius muscles ( $p < 0.04$ ).

3- Thigh angles (angle between the thighs when they are passively flexed and abducted at the hip joint)

showed a mean increase of 37.69 degree ( $p < 0.0005$ ).

4- Right knee angle showed a mean increase of 18 degrees after BTA injection in the right biceps femoris muscles ( $p < 0.69$ ).

5- Left knee angle showed a mean increase of 27.5 degree after BTA injection in left biceps femoris muscles ( $p < 0.52$ ).

6- The effects were all short lasting not more than three months.

Side effects occurred only in two cases as Transient generalized weakness, genu recurvatum and ptosis.

## DISCUSSION

Cerebral palsy is a handicapping condition in children. The most disabling sign and symptom of this entity are spasticity and stiffness. One of the best ways to reduce spasticity is the injection of BTA to the affected muscles (1,9). The largest series of patients so studied in the literature contains 27 patients (9). In our study we review 55 patients (91 cases) with cerebral palsy and spasticity as main symptomatology. So this is the largest series yet reported.

We conclude that BTA injection in these children improved the gait in 71.2% of cases ( $p < 0.0005$ ) and also improved the range of motion in affected joints especially the right and the left ankles ( $p < 0.003$  and  $p < 0.04$  respectively) and thigh ( $p < 0.0005$ ).

The unsuspected results in knee joints are supposed to be due to the little sample size. Although the effects of the drug were short acting, we suggest intramuscular BTA injection in cerebral palsied children if the spasticity is a major disabling problem.

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