International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Botulinum toxin injection in Post-stroke patients with spasticity

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Abstract

Spasticity is a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes 'muscle tone' with exaggerated tendon jerks resulting from hyperexcitability of stretch reflex. Among the established therapeutic interventions for spasticity, focal injection of otulinum toxin type A (BoNT-A) into the spastic muscle has been proved to be beneficial, there are 3 goals of using BTX-A in spasticity, improving active function, improving passive function and reducing impairments. Adverse effects are generally mild and transient. When spasticity is measured objectively, it is better to relate spasticity to function. BTX is the most widely used treatment for focal spasticity.

Keywords: Botox, Spasticity, Stroke.

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1. Introduction

Spasticity is a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes 'muscle tone' with exaggerated tendon jerks resulting from hyperexcitability of stretch reflex, as one component of upper motor neuron syndrome. (1)

Among the established therapeutic interventions for spasticity, focal injection of botulinum toxin type A (BTX-A) into the spastic muscle has been proved to be beneficial. BTX-A inhibits the release of acetylcholine (ACh) at the neuromuscular junction (NMJ) and reduces spasticity of the muscle. (2)

The term "botulism" owes its origins from latin word *botulus* which means "sausage". Van Ermengem, in 1895, discovered Clostridium botulinum, a gram-negative anaerobic bacterium, and its potent neurotoxin during food poisoning outbreak in Ellezelles, Later on, the pathogen was renamed "Clostridium botulinum". (3)

Justinus Kerner first recognized the potential for a therapeutic use for BTX in 1917 and proposed that it could be used as a therapeutic agent**.** In 1960s, Dr. Alan Scott began to use BTX by injecting rhesus monkey extraocular muscles to correct strabismus. Das and Park, in 1989, first reported the use of BTX in the treatment of spasticity in six patients with stroke. (4)

Spasticity can range from mild muscle stiffness to severe, painful, and uncontrollable muscle spasm, if left untreated, it gives rise to many problems, e.g. pain, spasms, limb contracture, and deformity resulting in loss of mobility and dexterity, hygiene/self-care, and an inability to wear, orthoses occur which decreases functioning. The overall prevalence of post stroke spasticity ranges from 4% to 42.6%, whereas disabling symptoms are reported to be present in 2% - 13% of survivors. (5)

- **Pathophysiology of Spasticity:**

It varies depending on the site of the lesion but commonly develops in the antigravity muscles. For instance, excessive muscle tone in the upper-extremity flexor muscles is prominent in spasticity following stroke. (6)

The most basic neural circuit contributing to spastic hypertonia is the segmental reflex arc, within this arc, the alpha motor neuron may be influenced by numerous excitatory and inhibitory modulatory synaptic influences, including:

1. Excitatory post synaptic potentials from group Ia and II muscle spindle afferents and inhibitory postsynaptic potentials from interneuronal connections from antagonistic muscles (mainly corticospinal tracts)**.** (6)

2. Recurrent Renshaw cell mediated inhibition is an inhibitory feedback of the alpha motor neuron cell body (comprise the final Common pathway in the expression of motor functions) by the inhibitory interneuron.

The imbalance in these influences results in hyperexcitability of the stretch reflex arc, which is thought to be the basis for spasticity as shown in figure (1). (7)

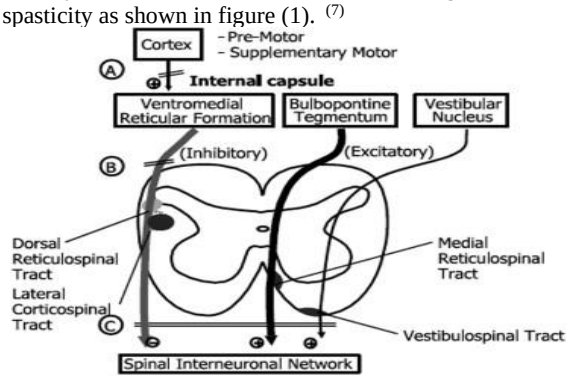

Fig. (1): The major descending pathways controlling spinal re-excitability (The inhibitory fibers are shown in grey). (7)

BTX is currently the most widely used treatment for focal spasticity and avoids the generalized weakness and sedation accompanying oral medications. (3)

Mechanism of action of botulinum toxin:

The BTX molecule consists of a heavy chain (H with molecular weight of 100 kDa) and a light chain (L with a molecular weight of 50 kDa), they are interconnected by a single disulfide bridge. (4)

BTX-A binds to the receptors in the presynaptic, cholinergic motor nerve terminal and is taken up by the nerve cells where the light chain of toxin cleaves a synaptosome-associated protein (SNAP-25) to inhibit acetylcholine release (chemodenervation) from the nerve terminal. [8]

The acidic pH within the endocytotic vesicle cleaves the disulfide bond freeing the light chain and enabling it to traverse into the neuronal cytosol where it disrupts one or more SNARE (soluble N-ethyl maleimi sensitive factor attachment protein receptor) proteins on the presynaptic vesicle as shown in figure (2). [4,8]

The recovery of neuronal activity has been attributed to axonal sprout development in response to growth factor secretion from denervated muscle and vesicular neurotransmitter release that returned in the original nerve terminal. [4,8]

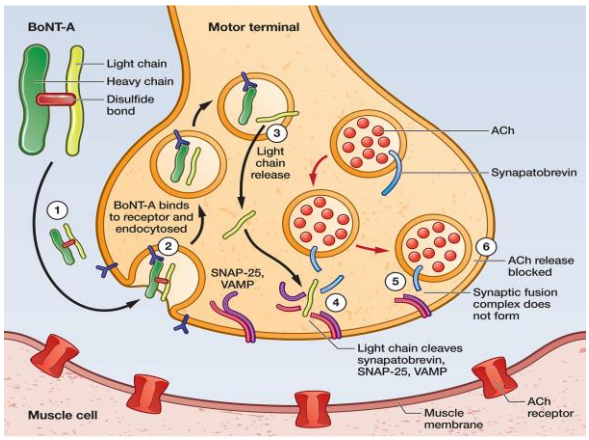

Fig. (2): Mechanism of action of botulinum toxin A. [8]

Benefits of BTX-A injection:

It was reported that there are 3 goals of using BTX-A in the management of spasticity**:** to improve active function (voluntary limb movements e.g. normalizing gait pattern, handling objects with the upper limb and activities of daily living (ADL)). Also improving passive function by making it easier for caregivers to position and perform tasks for patients who are unable to care for themselves. And reducing impairements by prevention of contracture, pain reduction and pressure sore reduction. [9]

Treatment Recommendations:

Adverse effects are generally mild and transient. Local reactions such as erythema, rash and oedema have been reported at the injection site. Systemic effects such as fatigue and flu-like symptoms are reported. [9]

Maneuver of BTX injection:

Each patient's treatment must be individualized. Chronicity, severity, distribution, locus of injury, co-morbidities, availability of care and treatment goals are important decision-making factors in managing spasticity. Increased range of motion, reduction in spasm frequency and pain are the main goals leading to improvement in function. [10]

Injection technique:

- **Planning and siting of injections:**

Larger superficial muscles may be identified with knowledge of surface anatomy. Smaller, less accessible muscles may require EMG to confirm placement within the muscle and to presence of muscle activity. [11]

- **Precaution:**

To prevent pressure injury in the following circumstances:

allergy to splint materials, pressure areas and oedema, other limb pathologies (e.g. rheumatoid arthritis), vascular disorders, sensory and perceptual deficits. [11]

- **Post-injection management:**

The effect of BTX and the duration vary between individuals. The effect is expected to last between 2:6 months, and then gradually wears off. [11]

Assessment of function improvement:

Disabling UMNS affects patient quality of life; significant reductions in manual dexterity, mobility, walking/falling, and performance of activities of daily living (ADL) have been reported by using scales e.g. (WMFT, MAS, Barthel Index). [12]

Many researches provide evidence that BTX injections are able to reduce spasticity, while maintaining motor performance of the weakened spastic muscles in chronic stroke especially if combined with high degree of repetitive volitional movement induced by the facilitative technique might increase efficiency of motor learning with continuous movement of the affected upper-limb. [3-12]

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