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Botulinum toxin for the management of adult patients with upper motor neuron syndrome

Alberto Esquenazi [a,*], Nathaniel H. Mayer [b], Antonio E. Elia [c], Alberto Albanese [d]

[a] MossRehab Gait & Motion Analysis Laboratory and Department of Rehabilitation Medicine, 60 Township Line Road, Elkins Park, PA 19027, USA
[b] MossRehab Motor Control Analysis Laboratory and Department of PM&R Temple University, Philadelphia, PA, USA
[c] Movement Disorders Unit, Università Cattolica and Istituto Besta, Milano, Italy
[d] Neurological Movement Disorders Unit, Università Cattolica and Istituto Besta, Milano, Italy

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ABSTRACT

The upper motor neuron (UMN) syndrome is a collection of interactive positive signs (associated with spastic hypertonia) and negative signs, such as muscle weakness and loss of voluntary control. In clinical practice, the distinction between active and passive functions allows identifying appropriate treatment objectives. During the last decades, many studies have evaluated the possibility to treat UMN syndromes with botulinum neurotoxin (BoNT). They have shown that BoNT is effective in controlling upper limb spasticity in adults. The clinical improvement is more consistent in the distal joints and the reduction of muscle hypertonia is dose-dependent. The functional efficacy of BoNT for lower limb spasticity has not been documented as well, as some series report efficacy in reducing muscle tone in the lower limb, but not in improving walking.

The functional benefit arising from the reduction of spasticity is often difficult to judge in the context of the complex phenomenology of the UMN syndrome. Certain data indicate that some disabilities related to passive and active function in the upper limb can improve with treatment. However, to date, the functional improvement after BoNT treatment in patients with UMN symptoms remains a point of ambiguity in the literature.

BoNT is overall well tolerated and must be regarded as a safe treatment intervention. Safety data are abundant in the literature for type-A toxin and scant for type-B toxin. There is no clear evidence to suggest the best time to introduce BoNT injections in the management of UMN syndromes. A common sense approach would be to introduce BoNT treatment as early as possible, in order to prevent further complications including contractures.

1. Upper motor neuron syndrome and spasticity

Since the seminal observations of Hughlings Jackson (1875), clinicians have characterized the upper motor neuron (UMN) syndrome as a collection of interactive positive and negative signs. UMN symptoms and signs include loss of selective voluntary movement, dexterity and control, stretch sensitive (spastic) phenomena such as increased phasic and tonic stretch reflexes, spastic co-contraction and spastic dystonia, and non-stretch sensitive phenomena such as released flexor reflex afferent activity, and associated reactions (Sheean, 2002; Mayer and Herman, 2004). In general terms, positive signs are characterized and generated by involuntary muscle overactivity; negative signs such as weakness are related to loss of voluntary control over muscles. In the clinic, these phenomena interact to produce a functional impairment characteristic of the UMN syndrome (Table 1).

* Corresponding author. Tel.: +1 215 663 6676; fax: +1 215 663 6686.
E-mail address: aesquena@einstein.edu (A. Esquenazi).

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Table 1
Upper motor neuron syndrome: positive and negative signs

Positive signs	Negative signs
• Phasic and tonic stretch reflexes (Gracies, 2001; Mayer and Esquenazi, 2003)	• Muscle weakness (Mayer and Esquenazi, 2003)
• Co-contraction (Mayer and Esquenazi, 2003)	• Loss of finger dexterity (Mayer and Esquenazi, 2003)
• Released flexor reflexes (Mayer, 1997; Mayer and Esquenazi, 2003)	• Loss of selective control of limb movement (Mayer and Esquenazi, 2003)
• Associated reactions (synkinesia) (Mayer and Esquenazi, 2003)	
• Spastic dystonia (Mayer and Esquenazi, 2003)	
• Increased muscle stiffness that may contribute to contracture (Mayer, 1997; Mayer and Esquenazi, 2003)	

Table 2
Functional goals of treatment in UMN syndrome

Passive function	Active function
• Increased range of motion*	• Improved upper limb use: reaching, grasping, releasing*
• Improved positioning*	• Improved mobility*
• Increased ease of hygiene*	• Improved gait
• Improved cosmesis*	• Decreased energy expenditure*
• Decreased spasm frequency	
• Improved orthotic fit*	
• Decreased pain*	

Modified from Brin (1997). *, BoNT can help reaching this goal.

Patients with an UMN syndrome may complain of one or more types of problems including symptomatic issues, loss of passive function and loss of active function (Mayer and Esquenazi, 2003). UMN syndrome motor problems can be classified in four types that recognize the main clinical issues (Mayer et al., 2007). In type I, symptomatic issues include such complaints as stiffness, pain, clonus and spasm as some of the presenting problems; in type II, issues of passive function typically refer to the passive manipulation of limbs to achieve functional ends, typically performed by caregivers, though patients may also manipulate their limbs passively with their non-involved limbs; in type III, active functions refer to patient's direct use of the limb to carry out a functional activity. For example, a patient who walks with equinovarus during stance phase may fall because of an unstable base of support. A patient who walks with spastic hip adductor may have difficulty maintaining balance or advancing the uninvolved leg. Type IV is a mixed form, combining two or more of them.

The distinction between active and passive functions allows to identify appropriate treatment objectives (Sheean, 2001). Active function relates to the capacity to move the body or its parts actively and can range from simple active movements at a specified joint to complex movements and even complex actions; it is impaired when spasticity interferes directly with voluntary movement. Passive function relates to the ability to integrate a body part in activities passively (Platz et al., 2005); it is impaired when there is little or no residual voluntary movement due to severe weakness. As far as active function is concerned, the goal of spasticity treatment is to reduce motor overactivity in order to improve movement; for passive function, instead, the main goal is to reduce pain during passive mobilization, painful spasms and attain better hygiene or prevent contractures (Table 2).

In everyday life, bi- or multi-directional joint motion is the rule and fixed positions are not typically maintained for extended periods of time. However, for patients with an UMN lesion, control over individual degrees of freedom of joint motion becomes impaired and, consequently, positive sign activity promotes unidirectional movements that often persist as postures because of the loss of voluntary movement in the return direction. The combined effect of recurring positive and negative signs leads to a net imbalance of muscle torques across individual joints that favor movement stereotypy and postural persistence (Fig. 1). By forcing joints into undesired static positions or into poorly controlled and stereotyped dynamic movements, the combined effects of positive and negative signs lead to limb deformity in patients with UMN syndrome (Fig. 2). Spasticity leads to exaggerated reflexes, posturing (so-called "spastic dystonia"), and flexor or extensor spasms, which are often painful. The terms "muscle hypertonia" and "muscle overactivity" are often used to describe the tone-dependent component of spasticity, which is most apparent in these patients.

Traumatic brain injury, embolic and hemorrhagic stroke, and common types of acquired brain injuries frequently result in motor dysfunction of the UMN type.

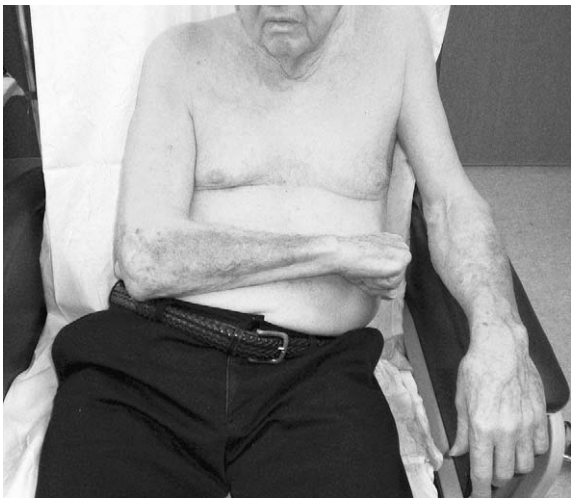

Fig. 1. The adducted, internally rotated shoulder is a common pattern of UMN dysfunction. Patients complain of stiffness, difficulty with passive range of motion especially needed for washing the axilla and dressing the upper limb. Sometimes a passive stretch of adductors is painful. The hyperextended shoulder, especially accompanied by elbow extension, is a problem during gait (e.g., knocking into doorways or furniture) and many patients are uncomfortable with the way they look (Esquenazi et al., 2008).