DIFFERENT MODALITIES IN THE TREATMENT OF DYSTONIA

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INTRODUCTION

The term dystonia refers to twisting movements that are sustained at their peak, frequently repetitive, they often progress to prolonged abnormal postures *(Burghaus et al., 2005; Kanner, 2004).*

Because in some subjects dystonia may progress to a life threatening stage or become a major fixed handicap, and given the limited efficacy of drug regimens in dopa- non responsive dystonia , alternative solutions have been sought since the early 1940s, including surgical treatment *(Herdeen et al, 1988).*

Russel Meyers, during the 1940s, was the first to perform lesioning of the basal ganglia to treat movement disorders. Shortly thereafter, in 1945, Spiegel first used a stereotactic frame in conjunction with pneumoencephalography for human surgery. As stereotactic techniques improved over the next two decades, basal ganglia surgery was performed for a variety of movement disorders including dystonia. Cooper in the year 1976, reported the largest early series using thalamotomy for dystonia, more recently pallidotomy regained popularity as a treatment of dystonia *(Vitek et al, 1998).*

Although many patients benefit from ablative thalamic or pallidal surgical procedures, deep brain stimulation still holds the advantage of avoiding ablating neurochemical pathways and receptors for future interventional pharmacotherapy *(Benabeid et al, 1994).*

Intrathecal baclophen infusion through an implantable pump which has been effective in relieving spastic limbs associated with demyelinating diseases, cerebral or spinal cord trauma, cerebral palsy, transverse myelitis and hereditary spasticity, have been used with both idiopathic and secondary dystonia with sporadic

instances of benefit. *(Dalvi et al, 1998)*

Cervical dystonia is the most frequent form of focal dystonia seen in movement disorders centers. The goals for treatment of cervical dystonia are improving the abnormal neck posture and associated pain and preventing secondary complications such as development of contractures, cervical myelopathy and radiculopathy. These goals may be achieved either by modification of the central mechanisms involved in the generation of dystonia or by weakening of the dystonic muscles. Medical treatment and physiotherapy often have a limited benefit, and the treatment of choice noewadays is the local injection of botulinum toxin type A into the dystonic muscles *(Dauer et al, 1998).*

Surgical treatment options for patients with otherwise intractable cervical dystonia include selective peripheral denervation and posterior ramisectomy in addition to functional stereotactic surgery *(Ford et al, 1998).*

AIM OF THE WORK

1- To review the literature of the up-to-date about Definition, Types, etiology, Pathophysiological mechanisms and ongoing morbidities of dystonia in addition to diagnosis and different modalities of management.

2- To evaluate the current modalities involved in treatment of dystonia in the selected patients, including the techniques, complications, efficacy & outcome.

HISTORY OF DYSTONIA

In 1897, Barraquer-Roviralta described a patient with generalized dystonia under the term of athetosis, (a term previously used primarily by W.A. Hammond). The twisting, sustained character and action exacerbation of both dystonia and athetosis led clinicians and researchers to focus on the structures Hammond had identified as abnormal in athetosis, namely the basal ganglia *(Goetz et al, 2001)*.

In 1908, Schwalbe expanded on the concept of dystonia when he wrote a lengthier thesis on dystonic spasms, under the designation, *Tonic Cramps with Hysterical Symptoms.* Whereas he aptly described the hereditary pattern and progression of generalized torsion dystonia, his terminology introduced a long-lasting ambiguity of dystonia as a neurological or psychiatric condition. Although the deforming postures of dystonia suggested a neurological basis, the bizarre contortions, their exacerbation with voluntary movement, and the *gestes antagonistes* prompted strong adherence to psychiatric hypotheses *(Goetz et al, 2001)*.

The term "*dystonia*" was introduced by Oppenheim in 1911 to reflect his conclusion that the disorder was associated with a generalized abnormality of tone with coexistent hypo- and hypertonia *(Goetz et al, 2006)*.

Dystonia as a nosographic entity was vehemently argued at the Tenth International Neurological Meeting in Paris in 1929 by leading speakers including Van Bogaert, Froment, Marinesco, Barre´, Meige, and Lhermitte. Thereafter, though neurological investigators largely dropped their interest in dystonia for over a

decade, psychiatrists, especially under the strong psychoanalytic influence of the period, avidly offered Freudian hypotheses to explain the contorted and disfiguring posture of focal and generalized dystonia *(Goetz et al, 2001)*.

As a phenomenon and as a disease, dystonia remained a vague and controversial term until E. Herz wrote his seminal article on generalized dystonia in 1944, in his study he captured the characteristic features of dystonia, emphasizing the slow, long-sustained, powerful, and non patterned contortions of axial and appendicular muscles. Further, he documented how dystonic spasms were action-induced or action-exacerbated and how they spread from one body part to another, evolving into generalized spasms *(Goetz et al, 2006)*.

In spite of their extensive study of the basal ganglia, the Vogts (1937) failed to identify specific lesions in generalized dystonia. The frustration of such poor clinico-pathological correlation, the very pillar of neurology since the time of Charcot, was reversed in 1985 when Marsden et al. took a different tack and studied cases of hemidystonia rather than generalized dystonia. They found that the putamen, caudate nucleus, and posterior ventral areas of the thalamus were frequently lesioned contra lateral to the hemidystonia. In the 1980s and1990s, well-established genetic pedigrees, especially among U.S. Jews of Ashkenazi descent, and priority funding from the Dystonia Medical Research Foundation, led to intense genetic studies of generalized dystonia, called DYT1. As an autosomal dominant disorder, DYT1 is based on a three-base pair deletion in a gene on chromosome 9q32-34 *(Goetz et al, 2001)*.

History of botulinum toxin for treatment of dystonia

The district medical officer Justinus Kerner (1786–1862), who was also a well-known German poet, published the first accurate and complete descriptions of the symptoms of food-borne botulism between 1817 and 1822 and attributed the intoxication to a biological poison. Kerner also postulated that the toxin might be used for treatment purposes. In 1870, Muller (another German physician) coined the name botulism. The Latin form is *botulus*, which means sausage. In 1895, an outbreak of botulism in the small Belgian village of Ellezelles led to the discovery of the pathogen "Clostridium botulinum" by Emile Pierre van Ermengem. Modern botulinum toxin treatment was pioneered by Alan B. Scott and Edward J. Schantz in the early 1970s, when the type-A serotype was used in medicine to correct strabismus. Other preparations of the type-A toxin were developed and manufactured in the United Kingdom, Germany, and China, whereas a therapeutic type-B toxin was prepared in the United States. Up to date, the toxin has been used to treat a wide variety of conditions associated with muscular hyperactivity, glandular hypersecretions and pain *(Erbguth, 1999).*

In December 1989, BTX-A was approved by the US Food and Drug Administration (FDA) for the treatment of strabismus, blepharospasm, and hemifacial spasm in patients aged younger than 12 years. BTX-A received FDA approval for treatment of cervical dystonia on December 21, 2000 *(Kedalaya, 2006).*

History of functional stereotactic surgery for the treatment of movement disorders

The early neurosurgical pioneers concentrated on the diagnosis and treatment of nervous system lesions. Significant exceptions were Sir Victor Horsley, who can be considered the father of functional neurosurgery he concentrated on the study and treatment of pain, epilepsy and movement disorders. Horsley dared to remove all or part of the motor cortex for treatment of movement disorders as early as 1890 *(Bakay, 2004).*

Also one of the earliest reports of a systematic approach to movement disorders was that of Bucy and Buchanan. They extirpated the motor cortex for the treatment of athetosis in 1931. Although the patients' initial symptoms improved they were frequently replaced by other major disabilities. *(Bakay, 2004).*

Russell Meyers first attacked the basal ganglia directly in 1939. He developed a number of surgical approaches, including a trasventricular extirpation of the head of the caudate nucleus and adjacent structures in 1939 and sectioning of the ansa lenticularis by a subtemporal, interhemispheric or transventricular approach in 1942. Meyers was forced to admit that the high morbidity and the 15.7% mortality rates were prohibitive; however, this work was seminal in proving that it is possible to abolish involuntary movements without impairing consciousness or imposing weakness *(Lunsford et al, 1990).*

This era was marked by empirical trial and error based on a rudimentary understanding of the neuroanatomy and pathophysiology. Progress was made through successes and failures. This is best exemplified by the work of Irving Cooper. In