Comparative study Between The Functional Outcomes Of Neuromodulation And Neuroablation Techniques For Treatment Of Secondary Dystonia

Thesis

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By

Mohamed Abd El-Rahman Moustafa Nada
M.B., B.Ch., M.Sc
Neurosurgery Specialist
Dar El-Shifa Hospital, Al-Abbasia

Under Supervision Of

PROF. DR. EMAD MOHAMED GHANEM
Professor of Neurosurgery
Faculty of Medicine
Ain Shams University

PROF. DR. KHALED MOHAMED EL BAHY
Professor of Neurosurgery
Faculty of Medicine
Ain Shams University

ASSIST. PROF. DR. WALID AHMED ABDEL GHANY
Assistant Professor of Neurosurgery
Faculty of Medicine
Ain Shams University

ASSIST. PROF. DR. ZEIAD YOSSRY FAYED
Assistant Professor of Neurosurgery
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
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Abstract

Background:
Secondary dystonia are the syndromes that have dystonic symptoms due to brain insult which can be associated with neonatal encephalopathy syndromes, trauma, vascular injury, infections, demyelinations, or hereditary disorders associated with neurodegenerative process. The disability inflected by dystonia encouraged the development of many neurosurgical procedures in order to improve the quality of life of these patients.
The aim of this study was to compare the outcomes of different Neuroablative and modulation techniques in treatment of secondary dystonia.

Patients and methods
This is a prospective study included 120 patients suffering from intractable secondary dystonia. Ablative techniques included the brain lesioning procedure and combined anterior and posterior lumbar rhizotomy (CAPR). Modulation techniques included deep brain stimulation (DBS) and intrathecal baclofen therapy (ITB). Patients with focal dystonia were included in the Botulinum toxin injection group. Patients with generalized dystonia were included in either of the brain lesioning or the deep brain stimulation, and patients with predominant affection of both lower limbs were included in either of the (CAPR) or the (ITB) groups.
Assessment measures included the evaluation of the muscle tone, range of motion, and the Burke-Fahn-Marsden dystonia rating scale through a follow up period of one year.

Results
Muscle tone was significantly reduced in the ablative techniques and the ITB, but the changes in the DBS group were not significant. The range of motion improved in all groups; the changes were significant in the ablative techniques and the ITB but were not significant in the DBS group. The BFMDRS showed improvement in all groups, the changes were significant in all groups except the DBS group.

Conclusion
Both neuroablative and neuromodulation techniques have the beneficial impact on secondary dystonias especially with stationary neurological pathologies with no significant statistical difference between both techniques.
While the neuromodulation techniques had the advantages of being adjustable, titratable, reversible, and can be performed bilaterally.

Key words: Dystonia; Neuroablation; Neuromodulation

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List of Abbreviations

BADS	Barry Albright dystonia scale
BSDI	Blepharospasm disability index
BoNT	Botulinum neurotoxin
BFMDRS	Burke-Fahn-Marsden dystonia rating scale
CP	Cerebral palsy
CD	Cervical dystonia
CAPR	Combined anterior and posterior rhizotomy
CT	Computed tomography
CBD	Corticobasal degeneration
DBS	Deep brain stimulation
DRD	Dopa responsive dystonia
EMG	Electromyography
GABA	Gamma aminobutyric acid
GPe	Globus pallidus externus
GPi	Globus pallidus internus
IPG	Implantable pulse generator
IQ	Intelligence quotient
ITB	Intrathecal Baclofen
MRI	Magnetic resonance imaging
MRCS	Medical research council scale
MAS	Modified Ashworth scale
MSA	Multiple system atrophy
PKAN	Pantothenate kinase-associated neurodegeneration
PSP	Progressive supranuclear palsy
RF	Radiofrequency
ROM	Range of motion
SEP	Somatosensory evoked potentials
SCS	Spinal cord stimulator
SCM	Sternocleidomastoid muscle
SNc	Substantia nigra pars compacta
SNr	Substantia nigra pars reticulata
STN	Subthalamic nucleus
TWSTRS	Toronto Western spasmodic torticollis rating scale
TMS	Transcranial magnetic stimulation
TENS	Transcutaneous electrical stimulation

UDRS	Unified dystonia rating scale
Vim	Ventralis intermedius nucleus of the thalamus
Voa	Ventralis oralis anterior nucleus of the thalamus
Vop	Ventralis oralis posterior nucleus of the thalamus

Introduction

Dystonia is the syndrome of sustained involuntary muscular contraction, causing twisting or repetitive movements or abnormal postures. Dystonia was first described by Gowers' in 1888, when it was named "tetanoid chorea". Destarac used the term "torticolis spasmodique" for description of cervical dystonia. The word "dystonia" was first used by Oppenheim in 1911 by using the term "dystonia musculorum deformans" **(Kanovsky et al., 2015)**.

David Marsden attributed the syndrome to a disorder of functioning of the basal ganglia **(Marsden and Rothwell, 1987)**, there is a hypothesis that dystonia is the "normal" motor action which is accompanied by abnormal co-contraction of antagonists, and by defective reciprocal inhibition in the other muscle groups. As a result, there is a dystonic pattern or dystonic movement appearing as a result of that abnormal muscle activity **(Albanese et al., 2013[a])**.

Dystonia is observed in different clinical conditions and can be classified according to the etiology to:

- **Primary:** with genetic defects, without gross morphological changes or any other associated symptoms.
- **Dystonia plus syndromes:** appears in association with parkinsonism or myoclonus, due to certain genetic or metabolic defects.

- **Secondary:** with identifiable causes, morphological changes, and\or additional symptoms **(Albanese et al., 2011)**.

Secondary dystonia are the syndromes that have dystonic symptoms due to brain insult associated with: neonatal encephalopathy syndromes, infections, demyelinations, trauma, vascular injury, or hereditary disorders associated with neurodegenerative process **(Jankovic, 2004)**.

Correct diagnosis and categorization of dystonia is critical before deciding the modality of treatment **(Albanese et al., 2006)**.

Dystonia also can be classified according to the body involvement as:

- Focal dystonia: involving a single body region;
- Multifocal dystonia: involving multiple non contiguous body regions;
- Segmental dystonia: involving contiguous body regions;
- Generalized dystonia: involving the whole body.

Some treatments are more effective in certain types of dystonias. For example, pharmacological treatment is usually the first course of action in the early childhood-onset dystonia. The first drug to try in early-onset dystonia is usually levodopa, although; only 5% of early-onset dystonias are dopa-responsive (DRD) **(Khan and Fernandez, 2015)**.

Several medications were used for the treatment of dystonia. These include dopaminergic agents, muscle relaxants, antidopaminergic agents, and anticholinergic drugs.

With the introduction of chemodenervation and the increasing experience of its use in dystonia, botulinum toxin injections are now the treatment of choice for focal and segmental dystonias.

Stereotactic brain lesioning procedures had variable outcomes with respect to the etiology and distribution of dystonia, and with respect to the site of the lesion whether in the thalamus or in the pallidum. By the 1980s, ablative brain surgery for dystonia had widely fallen out of favor and was not widely practiced **(Cersosimo et al., 2008)**.

Deep brain stimulation (DBS) is a viable treatment for patients with primary dystonia and also for a small number of patients with secondary dystonias. Proper patient selection is the key to favorable responses after DBS surgery. Patients who are refractory to conservative measures, including medications and botulinum toxin injections are potential candidates **(Rezai et al., 2008)**.

Intrathecal baclofen (ITB) is a treatment modality which has been used since the mid 1980's. It is titratable, reversible and produces levels higher than the oral dose facilitating the use of smaller doses per day **(Verroti et al., 2006)**.

Peripheral surgical procedures have also been used for focal dystonias. These include: myotomies, rhizotomies, and/or peripheral neurotomies.

Combined anterior and posterior rhizotomy (CAPR) has the potentials to improve severe dystonia affecting the upper or lower extremities in patients with concomitant spasticity. Ventral rhizotomy was expected to help not only secondary dystonia but hereditary degenerative dystonia as well **(Abdel Ghany et al., 2016)** & **(Albright et al., 2001)**.

Ventral rhizotomies appeared to be effective in the treatment of dystonia in the extremities, and could be done either in the lumbar region, the cervical region, or both **(Albright and Kabara, 2007)**.

It becomes obvious that there is a need to assess the treatment we are rendering to the patient. Treatment and assessment of outcomes occurs on four levels: assessing the technical outcome, functional outcome, cost-effectiveness of the treatment, and patient satisfaction.

As we deal with patients with dystonia, the surgeon needs a strong anatomic, physiologic and pharmacologic background, rigorous methods to assess the disorders, and to work in a multidisciplinary team.

This branch of functional neurosurgery has developed extensively, leading to an arsenal of contemporary methods that could improve many disabling situations.

Aim of the study:

1. Compare between the functional outcomes of the neuromodulation and neuroablation techniques for treatment of secondary dystonia.

2. Review the literature about the up-to-date in definitions, etiology, pathophysiological mechanisms and ongoing morbidities of dystonia and the current dystonia rating scales.

3. Outline the standard electrophysiological and physical assessment modalities.

Review of literature

Chapter I:

Anatomical and physiological considerations

Chapter II:

Pathophysiology of dystonia

Chapter III:

Clinical aspects of dystonia

Chapter IV:

Assessment measures and rating scales

Chapter V:

Non surgical treatments of dystonia

Chapter VI:

Surgical treatments of dystonia