ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2013;94:1473-81

JOURNAL-BASED CME ARTICLE

Meta-Analysis of Botulinum Toxin A Detrusor Injections in the Treatment of Neurogenic Detrusor Overactivity After Spinal Cord Injury

Swati Mehta, MA,[a,b] Denise Hill, MD, FRCPC,[c] Amanda McIntyre, MSc,[a,b] Norine Foley, MSc,[a,b] Jane Hsieh, MSc,[a,b] Karen Ethans, MD, FRCPC,[d] Robert W. Teasell, MD, FRCPC,[a,b,e] Eldon Loh, MD, FRCPC,[a,b,e] Blayne Welk, MD, FRCSC, MSc,[e] Dalton Wolfe, PhD[a,b]

From the [a]Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute, London, ON; [b]St. Joseph's Health Care, Parkwood Hospital, London, ON; [c]Foothills Hospital, Calgary, AB; [d]University of Manitoba, Winnipeg, MB; and [e]Department of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON, Canada.

Statement of Need

Neurogenic detrusor overactivity (NDO) is a common secondary issue after spinal cord injury (SCI). It is caused by spontaneous, involuntary contractions of the bladder wall during urinary filling which can be associated with reduced bladder wall compliance and elevated filling pressures. This can result in vesico-ureteral reflux and even renal failure. Current treatments to facilitate bladder storage typically include anticholinergic drugs. Unfortunately, this method of treatment is not a long-lasting solution since overactivity resumes almost immediately after discontinuing anticholinergic medication. In addition, some patients do not tolerate anticholinergic medication, or do not have an adequate response to the medication.

Need was identified to examine the effectiveness of botulinum toxin A (BTX A) on neurogenic detrusor overactivity (NDO) in individuals with spinal cord injury (SCI). Trials examining the use of BTX-A injections into the detrusor wall in treatment of NDO after SCI were, outcomes of interest were assessed before and after treatment with a single injection of BTX. A meta-analysis of fourteen studies representing data from 734 subjects were included.

This journal-based activity has been planned and developed in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the sponsorship of Professional Education Services Group (PESG).

Accreditation Statement

Professional Education Services Group (PESG) is accredited by the ACCME to provide continuing medical education (CME) for physicians.

Credit Designation Statement

PESG designates this Journal-based CME activity for a maximum of 2.0 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

All other health care professionals completing continuing education credit for this activity will be issued a certificate of participation.

Educational Objectives

To support the attainment of knowledge, competence, and performance, the learner should be able to achieve the following objectives:

1. Identify the effectiveness of botulinum toxin A (BTX A) on neurogenic detrusor overactivity (NDO) in individuals with spinal cord injury (SCI).
2. List the clinical effects of the use of BTX A on neurogenic detrusor overactivity.
3. Compare study results used in the meta analysis.

Planning Committee

Swati Mehta, MA, Denise Hill, MD FRCPC, Amanda McIntyre, MSc, Norine Foley, MSc, Jane Hsieh, MSc, Karen Ethans, MD FRCPC, Robert W. Teasell, MD FRCPC, Eldon Loh, MD FRCPC, Blayne Welk, MD FRCSC, MSc, Dalton Wolfe, PhD, PESG staff, ACRM Editorial Office Staff.

Faculty Profiles & Disclosure Information

As a provider accredited by the ACCME, it is the policy of PESG to require the disclosure of anyone who is in a position to control the content of an educational activity. All relevant financial relationships with any commercial interests and/or manufacturers must be disclosed to participants at the beginning of each activity. The faculty and planners of this educational activity disclose the following:

Swati Mehta
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute and St. Joseph's Health Care, Parkwood Hospital, London ON
No relevant financial relationships to disclose.

Denise Hill
Foothills Hospital, Calgary, AB
No relevant financial relationships to disclose.

Amanda McIntyre
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute; St. Joseph's Health Care, Parkwood Hospital, London ON
No relevant financial relationships to disclose.

Norine Foley
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute; St. Joseph's Health Care, Parkwood Hospital, London ON
No relevant financial relationships to disclose.

Jane Hsieh
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute; St. Joseph's Health Care, Parkwood Hospital, London ON
No relevant financial relationships to disclose.

Karen Ethans
University of Manitoba, Winnipeg, MB
No relevant financial relationships to disclose.

Robert W. Teasell
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute and St. Joseph's Health Care, Parkwood Hospital; Department of Physical Medicine and Rehabilitation St. Joseph's Health Care London, Parkwood Hospital; Department of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON
No relevant financial relationships to disclose.

Eldon Loh
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute; St. Joseph's Health Care, Parkwood Hospital; Department of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON
No relevant financial relationships to disclose.

Blayne Welk
Department of Physical Medicine and Rehabilitation, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON Dr. Welk has received speaker fees from, and has been on advisory boards for Allergan. No compensation was directed towards work on this publication.

Dalton Wolfe
Aging, Rehabilitation and Geriatric Care Program, Lawson Health Research Institute; St. Joseph's Health Care, Parkwood Hospital, London ON
No relevant financial relationships to disclose.

Allen W. Heinemann, Ph.D.
Director, Center for Rehabilitation Outcomes Research Rehabilitation Institute of Chicago Chicago, IL
No relevant financial relationships to disclose.

0003-9993/13/$36 - see front matter
http://dx.doi.org/10.1016/j.apmr.2013.04.011

PESG Staff
No relevant financial relationships to disclose.

ACRM Editorial Office Staff
No relevant financial relationships to disclose.

Resolution of Conflict of Interest
PESG has implemented a process to resolve conflict of interest for each CME activity. In order to help ensure content objectivity, independence, and fair balance, and to ensure that the content is aligned with the interest of the public, PESG has resolved the conflict by external content review.

Unapproved/Off-Label Use Disclosure
PESG requires CME faculty to disclose to the participants:

1. When products or procedures being discussed are off-label, unlabeled, experimental, and/or investigational (not US Food and Drug Administration [FDA] approved); and
2. Any limitations on the information presented, such as data that are preliminary or that represent ongoing research, interim analyses, and/or unsupported opinion. Faculty may discuss information about pharmaceutical agents that is outside of FDA-approved labeling. This information is intended solely for CME and is not intended to promote off-label use of these medications. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.

Intended Audience
This program is intended for physicians and healthcare professionals responsible for the comprehensive care for individuals with chronic illness and disabilities.

Method of Participation

In order to claim credit, participants must complete the following:

1. Pre-activity self-assessment questions.
2. Read the activity.
3. Complete the CME Test and Evaluation. Participants must achieve a score of 70% on the CME Test.

Participants can complete the pre-activity self-assessment and CME Test and Evaluation online by logging on to http://acrm.cds.pesgce.com. Upon successful completion of the online tests and evaluation form, you can instantly download and print your certificate of credit.

To better define and meet the CME needs of health care professionals and enhance future CME activities, PESG will conduct an outcomes-measurement survey following the conclusion of the program. This follow-up survey is designed to measure changes to participants' practice behaviors as a result of their participation in this CME activity. You will be contacted by email 60 days following the conclusion of this activity with an outcomes measurement survey. We would greatly appreciate your participation.

CME Inquiries

For all CME certificate inquiries, please contact us at support@pesgce.com.

This continuing education activity is active starting August 1, 2013 and will expire July 31, 2014.

Estimated time to complete this activity − 2.0 hours

Abstract

Objective: To examine the effectiveness of botulinum toxin type A (BTX-A) on neurogenic detrusor overactivity (NDO) in individuals with spinal cord injury (SCI).

Data Sources: MEDLINE, CINAHL, EMBASE, and PsycINFO databases were searched for all relevant articles published from 1980 to June 2012.

Study Selection: Trials examining the use of BTX-A injections into the detrusor wall in the treatment of NDO after SCI were included if (1) ≥50% of study sample comprised subjects post-SCI; (2) outcomes of interest were assessed before and after treatment with a single injection of BTX-A; and (3) the sample size was ≥3.

Data Extraction: A standardized mean difference ± SE (95% confidence interval) was calculated for at least 1 of the following outcomes in every study: postvoid residual urine volume, reflex detrusor volume, bladder capacity, bladder compliance, catheterization frequency, and maximum flow rate. Results from all studies were then pooled using a random-effects model. Treatment effect sizes were interpreted as small, >0.2; moderate, >0.5; or large, >0.8.

Data Synthesis: Fourteen studies representing data from 734 subjects were included. After BTX-A injection, large treatment effects were observed in postvoid residual urine volume, reflex detrusor volume, bladder capacity, bladder compliance, and catheterization frequency ($P<.01$). Rate of incontinence episodes was reduced from 23% to 1.31% after BTX-A treatment. No significant decrease in max flow rate was observed ($P=.403$).

Conclusions: Results of the meta-analysis indicate BTX-A is effective in treating NDO after SCI. The use of BTX-A was associated with a decrease in incontinence episodes, catheter use, and bladder pressures.

Archives of Physical Medicine and Rehabilitation 2013;94:1473-81

Neurogenic detrusor overactivity (NDO) is a common secondary issue after spinal cord injury (SCI). It is caused by spontaneous, involuntary contractions of the bladder wall during urinary filling that can be associated with reduced bladder wall compliance and elevated filling pressures. This can result in vesicoureteral reflux and even renal failure.[1] Current treatments to facilitate bladder storage typically include anticholinergic drugs.[2] Unfortunately, this method of treatment is not a long-lasting solution because overactivity resumes almost immediately after discontinuing anticholinergic medication. In addition, some patients do not tolerate anticholinergic medication or do not have an adequate response to the medication.

When treatment with anticholinergic drugs fails, alternative bladder management options, such as botulinum toxin type A (BTX-A), are recommended by the Paralyzed Veterans of America clinical practice guidelines for bladder management in individuals with SCI[3] and in the American Urological Association guidelines for diagnosis and treatment of overactivite bladder among non-SCI adults.[4] Botulinum toxin type A is produced by the gram-positive anaerobic bacterium *Clostridium botulinum*. The toxin acts on presynaptic nerve terminals, inhibiting release of acetylcholine and effectively paralyzing neurologic activity,[5] but the effects are not permanent; therefore, repeat injections are required. Nerve terminals develop new acetylcholine releasing sites and become functional over a period of 3 to 9 months, although this regrowth process is both dose and site dependent.[6]

Injections of BTX-A into the detrusor muscle for NDO treatment was first described by Schurch et al[7,8] more than a decade ago. As a treatment for NDO, BTX-A works to relax detrusor muscle tissues, allowing the bladder to expand and fill to greater volumes while maintaining low bladder compliance. Therapeutic benefits include a decrease in the frequency of catheter use,[9] improved bladder

Supported by the Ontario Neurotrauma Foundation (grant no. 2007-SCI-SCIRE-528) and the Rick Hansen Institute (grant no. 2010-01).

No commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a benefit on the authors or on any organization with which the authors are associated (Mehta, Hill, McIntyre, Foley, Hsieh, Ethans, Teasell, Loh, Wolfe).

A commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a financial benefit on the author or one or more of the authors. Welk has received speaker fees from, and has been on advisory boards for Allergan. No compensation was directed toward work on this publication.