Benign Essential Blepharospasm
CANADIAN RESEARCH FOUNDATION INC.

BENIGN ESSENTIAL BLEPHAROSPASM CANADIAN RESEARCH FOUNDATION INC.

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FOUNDED May 25Th, 1992
by OLGA & SAM MEISTER

Volume 3 08/16

Support Group Meetings

When and Where

Toronto

NORTH YORK CIVIC CENTRE
5100 Yonge Street, Meeting Room #3
Toronto, Ontario

Sunday October 30, 2016

TIME: 1:30 PM TO 4:00 PM

TOPIC: To be determined

Letter From The President

In the coming year, our goal is to augment our Board structure so that we may continue expanding the locations of Support Groups across Canada in order that patients may get more support in their local communities.

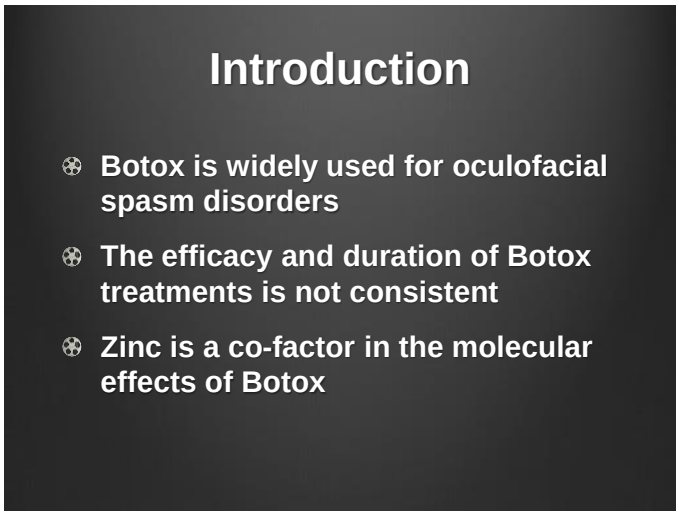
The current Board will maintain their positions, but we would like to add some new people for a designated time frame to help to expand our organization. Because our membership is very spread out across Canada, we are looking into updating our Executive connections so that it can all be done virtually from the comfort of your home.

Our organization is active between September until May, with most of the summer months somewhat inactive. Should you be able to set aside 1 - 2 hours per month volunteer time for BEBCRF, please contact us for further details.

I want to thank everyone for your continued support and look forward to meeting you at the next **Fall Support Group Meeting on Sunday October 30, 2016 in Toronto.** If anyone has a suggested topic for a future Support Group Meeting, please contact us

Dr. Seif's Presentation - A Synopsis

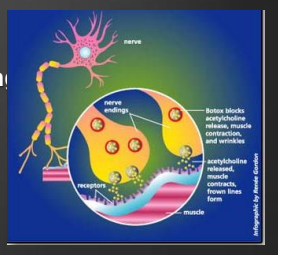
This study examined the use of zinc supplementation for patients who are being treated with botulinum toxin for either benign essential blepharospasm (BEB) or hemifacial spasm (HFS). Botulinum toxin has been used for many years to treat BEB and HFS with variable results. This study aims to assess if this variability is due to the variability of zinc within individual patients.



We know that zinc, as an element, is a 'cofactor', which means that it is something that botulinum toxin needs in order to work effectively. They have done a good deal of basic research where they stripped the zinc off the botulinum toxin and they noted that the toxin did not work as well without the zinc.

Background Information

- Botox cleaves polypeptides that are essential for exocytosis of Neurotransmitter vacuoles in the presynaptic vesicles
- In vitro studies show that stripping Zinc from its bindin site on Botox prevents this catalytic activity[1]



Our hypothesis has been that perhaps the variability in the response that patients have to the toxin maybe related to the amount of zinc that they actually have corporeally.

Hypothesis

The variability in Botox response may be due to the level of zinc available within our patients

- Patients that respond poorly may be zinc deficient
- Zinc supplementation may improve treatment response in these patients

There was an industry sponsored study out of Houston, Texas, that used a drug called Zytaze. Zytaze is a combination of zinc and phytase, an enzyme that breaks down phytate. Phytate is a product that comes in leafy vegetables and things that have a lot of fibre, which are known to reduce the absorption of zinc in the GI tract, in the stomach, and in the intestines. They did show positive results, however, the drug is not available in Canada.

Zytase

J Drugs Dermatol. 2012 Apr;11(4):507-12.

Effect of dietary zinc and phytase supplementation on botulinum toxin treatments.

Koshy JC[1], Sharabi SE, Feldman EM, Hollier LH Jr, Patrinely JR, Soparkar CN.

Author information

Abstract

PURPOSE: To determine whether oral zinc supplementation might affect the efficacy and duration of botulinum toxin treatments.

METHODS: In a double-blind, placebo-controlled, crossover pilot study, we examined the efficacy of three botulinum toxin preparations (onabotulinumtoxinA, abobotulinumtoxinA, and rimabotulinumtoxinB) following oral supplementation with zinc citrate 50 mg and phytase 3,000 PU, zinc gluconate 10 mg, or lactulose placebo in individuals treated for cosmetic facial rhytids, benign essential blepharospasm, and hemifacial spasm.

RESULTS: In seventy-seven patients, 92% of subjects supplemented with zinc 50 mg and phytase experienced an average increase in toxin effect duration of nearly 30%, and 84% of participants reported a subjective increase in toxin effect, whereas no significant increase in duration or effect was reported by patients following supplementation with lactulose placebo or 10 mg of zinc gluconate. The dramatic impact of the zinc/phytase supplementation on some patients' lives clinically unmasked the study and prompted an early termination.

CONCLUSIONS: This study suggests a potentially meaningful role for zinc and/or phytase supplementation in increasing the degree and duration of botulinum toxin effect in the treatment of cosmetic facial rhytids, benign essential blepharospasm, and hemifacial spasm.

Also, the outcome measure that was used has not been validated in the literature. We wanted to do a randomized control trial utilizing over the counter Zinc, which would be much easier for Canadian patients.

Purpose

Randomized control trial to prospectively examine the effect of over the counter (OTC) zinc supplementation on patients with blepharospasm and hemi-facial spasm

Study Design

- Inclusion Criteria
  - Patients greater than 18 y/o
  - Hemifacial spasm or blepharospasm
- Exclusion Criteria
  - Have received Botox treatments within 3 months
  - Prone to malabsorption (i.e. Celiac disease, IBD, liver dx, laxative used)
  - Cannot tolerate zinc supplementation (i.e. severe kidney disease, pregnancy, AIDS, anemia, immunocompromised)

The study design will include patients who are currently being treated by Dr. Harvey and Dr. Khan in their offices and, that are at least eighteen years of age, so they can give their own consent, and, who either have hemifacial spasm or blepharospasm.

Methods

- Experimental group = Zinc (50mg)
- Control group = placebo pill

Both groups took pills 5 days before and 5 days after your regularly scheduled Botox injection

Recruited patient where randomized to receive either 50mg of Zinc or a placebo. The study is being powered to show positive results; meaning we know how many patients we need in order to power the study appropriately. This will not be a pilot study but rather a proper fully functioning randomized control trial.

Participants

	Placebo	Zinc	P value
Patients recruited	19	19	
Male	9	9	
Female	10	10	
BEB	15	16	
HFS	4	3	
Age	66.4 y/o	68.6 y/o	0.38
Units	44.8	57	0.06576
Cycle (pre-study)	126 d	109 days	0.131
Cycle (study)	124 d	107 days	0.74896
Symptom duration	10.4 y	9.0 y	0.63836

Jankovic Rating Scale

Jankovic Rating Scale (please circle)

	Pre-injection	1 wk	1.5 mo	3 mo	Last	Description
Severity		0	0	0	0	None
		1	1	1	1	Increase in blinking present only with external stimuli (e.g. bright light, wind, reading, driving, etc)
		2	2	2	2	Mild but spontaneous eyelid fluttering (without actual spasm), definitely noticeable, possibly embarrassing, but not functionally disabling
		3	3	3	3	Moderate, very noticeable spasm of eyelids only, mildly incapacitating
		4	4	4	4	Severe, incapacitating spasm of eyelids and possibly other facial muscles
Frequency		0	0	0	0	None
		1	1	1	1	Slightly increased frequency of blinking
		2	2	2	2	Eyelid fluttering lasting less than 1 second in duration
		3	3	3	3	Eyelid spasm lasting more than 1 second, but eyes open more than 50% of waking time
		4	4	4	4	Functionally "blind" due to persistent eye closure (blepharospasm) more than 50% of waking time.
Total						

The rating scale was developed by Dr. Jankovic to gage the frequency and severity of the blepharospasm. Dr. Jankovic developed two scales: one to determine the frequency of spasms, and, the second, the severity of the spasms

Blepharospasm Disability Index

Blepharospasm disability index (please rank items in right column using rating sca

Ratings		Items	1 wk	1.5 mo	3 mo
0	No impairment	Reading			
1	Mild impairment	Driving a vehicle			
2	Moderate impairment	Watching television			
3	Severe Impairment	Shopping			
4	Not possible due to disease	Doing everyday activities			
5	Not applicable	Walking			

The main outcome measure was the Jankovic rating score and blepharospasm disability index, which are well-known validated scales that have been used in the literature quite frequently when looking at botulinum toxin and blepharospasm.

Time Points

- **Baseline**
- **1 week post injection**
- **1.5 months post injection**
- **3 months post injection**

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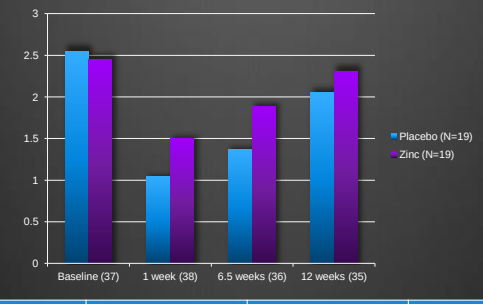
Patients were followed over a period of three months. Each patient was interviewed one week after the botulinum injection, one month and a half after the botulinum injection and, three months post botulinum toxin injections .

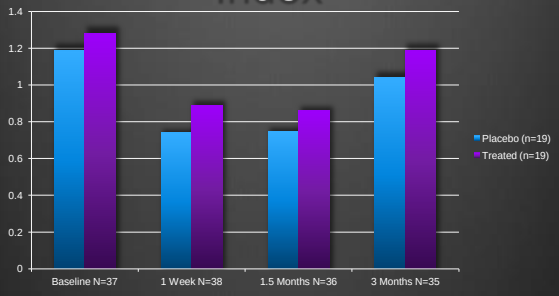
Jankovic Rating Scale



	Placebo N=19	Treated N=19	P-Value
Baseline N=37	2.55 (0.89)	2.45 (0.83)	0.607
1 Week N=38	1.05 (0.86)	1.50 (0.91)	0.158
1.5 Months N=36	1.37 (0.93)	1.88 (0.76)	0.089
3 Months N=35	2.05 (1.07)	2.31 (0.96)	0.496

The Jankovic Rating scale and Blepharospasm disability index did not show any significant difference between the treatment group and control group at all time points.

Blepharospasm Disability Index



	Placebo N=19	Treated N=19	P-Value
Baseline N=37	1.19 (0.84)	1.28 (0.85)	0.736
1 Week N=38	0.74 (0.75)	0.89 (0.87)	0.670
1.5 Months N=36	0.75 (0.91)	0.86 (0.75)	0.305
3 Months N=35	1.04 (1.10)	1.19 (0.86)	0.367

The study's conclusion was that over-the-counter zinc supplementation does not improve the efficacy of botulinum toxin injections for either blepharospasm or hemi-facial spasms.

Conclusion

- **OTC Zinc Supplementation does not improve Botox efficacy for BEB and hemi-facial spasm.**
- **Adds credence for Zytase**

Limitations

- **Population potential not the same between treatment in control groups**
- **Subjective outcome measures**
- **Small sample size**

Although the study did not show any improvement of Zinc in our patient population, there are several limitations such as subjective measurements - the evaluation is made by the patient, and, the size of the group in the sample was small.

The focus of future studies will be to assess whether or not zinc supplementation maybe more useful in specific populations with proven low levels of zinc as measured in their blood stream.

Future analysis

- **Direct head to head comparison between Zytase and OTC Zinc.**
- **Measurement of Serum Zinc levels**
- **Assess for particular patient populations that might have extra benefit from zinc supplementation**

Team Members

- **Funding**
  - **Benign Essential Spasm Canadian Research Foundation(BEBCRF)**
- **Co principal Investigators:**
  - **Dr. John Harvey (Division of Ophthalmology, McMaster University)**
  - **Dr. Yasser Khan (Division of Ophthalmology, McMaster University)**
- **Resident Investigator:**
  - **Dr. Gamal Seif (PGY4, Division of Ophthalmology, McMaster University)**
- **Statistician:**
  - **Dr. Forough Farrokhyar (Department of Surgery, McMaster University)**
- **Research Pharmacist:**
  - **Ms. Christine Wallace (St Joseph's Hospital, Hamilton)**
- **Ancillary Staff:**
  - **Ms. Joanne Verboom (Office of Dr. John Harvey)**
  - **Ms. Abbey Wood (Office of Dr. Yasser Khan)**

Our thanks go out to all those who participated in the study as well as those who helped facilitate the study.

This study was presented at the American Society of Ophthalmic and Reconstructive Surgery annual meeting in November 2015

BEB - A Synopsis

Blepharospasm isn't really very different from other sight problems, apart from the fact that sometimes you can see fine - and then at others you're blind. The big problem is with getting it diagnosed in the first place.

Yet in some ways blepharospasm is, in fact, quite different from most other vision disorders: because it affects the sight without actually damaging the vision. The entire structure of the eye - including the optic nerves, and the areas of the brain connected with sight - remain undamaged; and at the same time quite a lot of people with the condition are *'functionally blind'* because they literally cannot keep their eyes open for long.

Blepharospasm is a form of "dystonia" - a movement disorder that results in uncontrollable (and sometimes painful) muscle spasms. It is a neurological (brain-based) disorder, because the brain is sending the muscles faulty messages.

Some dystonias affect multiple areas, especially the back and the torso, causing the person to jerk and twist uncontrollably. These usually start in childhood, and spread across the rest of the body. Adult dystonias tend to be confined to a "focal" area like the neck, the hand or the mouth. Blepharospasm, the type that affects the muscles around the eyes, usually starts relatively late in life, after the age of 50. It is more common in women than men.

Typically, it may begin with an uncomfortable gritty feeling in the eye and then moves on to excessive blinking; and from there, it can get to the point where the person cannot open their eyes much at all. In most people, it doesn't do anything else and it doesn't spread, although about 20 per cent of people who develop it in this way will also, over time, develop some other muscle spasms to affect the jaw or the head and neck. Many people also find that their symptoms - including their discomfort - gets a lot worse in bright and/or flickering lights.

There's good reason to think that dystonia arises from a problem in the basal ganglia, in the centre of the brain. All messages pass through this part of the brain; it's like a relay or integration unit for sensory information, motor information, motivational information and so on, and it plays a very important role in integrating this information and getting the correct messages out to the nerves. There is a very fundamental process in the brain called 'brain plasticity', which is effectively the mechanism whereby we learn in how to respond to stimuli. It is thought that in dystonia this process is overactive (perhaps triggered by a malfunction in the basal ganglia) and this can lead to *'learning'* errors in some of the programs that control movement. So that sore gritty feeling in the eyes might set off over-active blinking and this triggers an abnormal learned pattern of movement in the muscles around the eyes which is produced all the time.

There appears to be a genetic link as well. BEB often runs in families, and researchers have been investigating the gene connections. So far one gene responsible for early-onset dystonia has been established since 1997.

Personal Giving

Gifts That Count

Individual Giving:

To make your donation by mail please complete and send the enclosed envelope with your cheque. If you wish to donate using a credit card you may do so via Canada Helps at www.canadahelps.org. You will be asked to enter the Foundation's name or keyword.

Planned Giving:

A planned gift is a special gift for the future. It is arranged now, usually within an individual estate or financial plan, but actualized at a later date,

Tributes:

Tributes honour or pay tribute to someone on a special occasion or say thank you. Make your contribution and we will send out a personalized Tribute Card to the recipient. Send a Tribute Card:

To mark any special occasion or milestone be it a birthday, wedding, bar/bat mitzvah, anniversary, graduation, or moving to a new home.

In Memoriam:

You may choose to honour a loved one with a donation in their memory. A personalized card may be sent to a designated family member with a message of your choice.

For further information on any of these Personal Giving Options, please contact us via mail, email or call our toll-free number and someone will be glad to assist you.