President’s Message

Quite amazing!
A moderated panel with 4 top MG University Health Network Neurologists at our next MG Support meeting, November 30, 2014
Ask questions. Get answers. Come and meet an MG healthcare professional dream team. See more on page 2 and 3

Passing the torch.

Over the last 40 years MG Ontario benefited from many great volunteers. The last two years Jim Ovens has been Treasurer and helped Joyce Ovens with membership as well. Jim met the challenge with talent and perspiration. As we transitioned to fulfill the dream of a National ‘not for profit’ Association, Jim and Joyce were there to take on the challenge. “Myasthenia Gravis Society of Canada” is a reality.

We have an evolving website www.MGCanada.org with 24/7 information.
Our MG accounting ledger records are current.
Membership data is current.

Thank you Jim for all your MG association time and effort. Your contributions are highly valued and will be missed. Thanks also to Joyce for her volunteer efforts on membership and other ongoing assistance.

Save the Date!

Saturday
October 24, 2015
MG Education Day Conference

See
Information on Page 4 & 5

Continued Page 4
**University Health Network Speak on MG at Nov. 30 Meeting**

**Vera Bril, BSc, FRCPC, MD** | University of Toronto, Toronto, Canada

Vera Bril is a Professor of Medicine (Neurology) at the University of Toronto, Director of Neurology at University Health Network and Mount Sinai Hospital and holds the Krembil Family Chair in Neurology. She is the Interim Director of the Krembil Neuroscience Program at the University Health Network. She has particular expertise in the diagnosis and management of patients with complex neuromuscular disorders. Her research interests have centered on the diagnosis and evidence-based treatment of myasthenia gravis, inflammatory polyneuropathies, and diabetic sensorimotor polyneuropathy. Her work has helped set the standards for electrophysiological investigations in the definition and evaluation of the progression of chronic polyneuropathies. Her research has helped establish the role of intravenous immunoglobulin in the treatment of myasthenia gravis and the Guillain-Barré Syndrome, and the long-term treatment of chronic inflammatory demyelinating polyneuropathy. She has acted in an advisory capacity to Health Canada and the FDA. Dr Bril also serves as the Deputy Physician-in-Chief for Economic Affairs for the Department of Medicine at the University Health Network and Mount Sinai Hospital and Chair of the Economics committee. She is part of the Department of Medicine Executive Committee and helps administer this group of 300 physicians.

**Dr. Carolina Barnett Tapia** is a neuromuscular fellow at the University Health Network / Toronto General Hospital. She obtained her undergraduate and medical degrees at the Pontificia Universidad Catolica de Chile, where she also completed her residency in neurology and was chief resident in 2005-2006. She worked as a general neurologist in Chile before coming to Toronto in 2010 for her Neuromuscular fellowship. She is also a PhD candidate in clinical epidemiology and health care research at the University of Toronto.

In 2012, she was awarded a clinical research fellowship award by the American Academy of Neurology and American Brain foundation. The awarded project is aimed at developing new tools to assess patients with Myasthenia Gravis, and she is focused in incorporating patient reported outcomes. Other research interests include quality of life in MG as well as clinical trials and outcome measures in neuromuscular disease.

**Dr. Hans Katzberg** is a neuromuscular specialist and clinical investigator at the University Health Network / Toronto General Hospital and has been on faculty at the University of Toronto as Assistant Professor of Neurology. He obtained his undergraduate and medical degrees at the University of British Columbia and did his residency in neurology at the University of Toronto where he was chief resident from 2006-7. He later completed fellowships in neuromuscular medicine and neurophysiology (EMG) at Stanford University, where he also obtained a Master’s degree in clinical epidemiology.

He has been on staff at the Helen and Martin Prosserman Center for Neuromuscular Diseases at TGH since 2010, where he runs neuromuscular and EMG clinics, is active in training of neurology and physiatry residents / fellows and conducts clinical research. He is cross-appointed to Sick Kids Hospital where he coordinates a transition clinic for young adults with neuromuscular conditions. In 2014 he took over as fellowship program director at the University of Toronto for the Division of Neurology and is an Associate Editor for the Canadian Journal of Neurological Science. He has a research focus in outcome measures and clinical trials in immune mediated neuromuscular junction disorders such as myasthenia gravis and neuropathies such as CIDP.

**Dr. Ari Breiner:** Information on Dr. Breiner was not available at time of publication.
Myasthenia Gravis Society of Canada

MG Support Meeting
November 30, 2014, 6 - 8 pm

Featuring
Panel and Discussion on Myasthenia Gravis
with University Health Network Neurologists
Dr. Vera Brill, Dr. Carolina Barnett Tapia,
Dr. Ari Breiner, and Dr. Hans Katzberg.

Loblaws Community Meeting Room, Bayview Village Mall
2877 Bayview Village, North York, M2K 2S3.
(The Meeting Room is located upstairs, S/W corner of the store, Elevator access.)

Public Transit Access, subway access at
Bayview Station on the Sheppard Subway.
Free Parking in Bayview Village Mall.

Info at 905 642 2545
For those living with Myasthenia Gravis, caregivers, family, friends & interested others meet to share experiences
All Welcome! Also info at www.MGCanada.org

Smile for Today:
Two men walked into a restaurant. The first one asks for tea. The second also asks for tea. “And make sure the glass is clean,” he tells the waiter. When the waiter returns with the two glasses of tea he asks, “Which one of you asked for the clean glass?”

Joe was referred to an eye specialist. After numerous tests, they find nothing wrong with his eye. He’s offered a cup of tea. As soon as he takes a sip, he feels the pain again. The doctor tells him “Joe, you can’t drink tea anymore.” “No way,” says Joe. “I love tea.” “OK,” says the doc., “But next time remove the spoon from the cup.”
President’s Message Cont. from Page 1

Update on MG Canada Education Day conference, October 24, 2015, Toronto and GTA.

Hosted by MG Canada in collaboration with Dr. Bril’s Neuro Muscular MG team at University of Toronto Health Network

Tentative Speakers and Subjects to date:
Dr. Ari Breiner, Dr. Carolina Barnett Tapia, Dr. Hans Katzberg, Dr. Vera Bril and Vilija Rasutis, RN are confirmed.

It is too early to confirm the final schedule. Some topics we have discussed are:
- Clinical Treatment Trial Updates
- Symptoms of MG: What to look for (for patients) and how to measure them (for clinicians)
- The Landscape of Clinical Care for MG in Canada
- Paediatric MG and Pregnancy Issues in MG
- Nursing Aspects in MG: Nutrition, Sleep and Exercise
- Thymectomy Update 2015
- Common Medications in MG: A Guide for Patients and Clinicians

Jim Ovens and Phil Debruyne have created an MG Canada conference Questionnaire for your consideration. We ask you to fill in a copy and mail by November 25, 2014. Your response will help your MG conference committee plan for this special event next year.

Have any ideas or suggestions that you would like? Here’s a few to get you going.
- Yoga relaxation and meditation
- Exercise Clinic for MG patients
- Dance for fun and relaxation
- A actual food preparation cooking clinic with ideas that are easy for MG patients to digest and swallow
- More of your ideas, please.

MG President’s wish list:
There was one pill to still MG

That every Doctor, Nurse and Healthcare professional knew about MG
That all Emergency rooms took MG seriously with ability for an informed emergency response
All MG patients, families and friends of MG networked and supported each other
All of Canada’s 10 provinces and territories had MG Canada chapters and/or affiliates
That we have...
an MG Canada Facebook coordinator
Secretary for MG Support meetings and to assist with various MG Canada correspondence

www.MGCanada.org Website editor
MG Member support coordinator
MG Education coordinator
MG Canada fundraising team
Public Relations, Publicity person

There is much we need to accomplish. Many volunteers make the load much easier. I hope you’ll consider. Drop me an Email or mail me a note or call me.

And Finally....
Thank you Janie and Becky Shield, your MG Canada librarians, for review and updating all our information brochures; for renewing our friendship and relationship with MGFA, Myasthenia Gravis Foundation of America so that we can publish articles of interest from their newsletters.

Try to see the bright side. Laugh at yourself. Have a little fun. Think of me when I’m on the ice curling. I look ridiculous but I’m having a good time.

Yours truly
Cap Cowan, President
Myasthenia Gravis Society of Canada
Stouffville, Ontario
905 642 2545 Call anytime
www.MGCanada.org
CapCowan@MGCanada.org
Myasthenia Gravis Society of Canada

Questionnaire

MG Canada plans to have an MG Education Day Conference on 24 October 2015

Dr. Vera Bril and others of her neurology team at the University Health Network are committed to support our first MG Education Day. Several presentations will be included on various topics of interest to MG patients, families and caregivers.

Come and hear about:

- The latest information about diagnosis and treatment of MG
- How MG affects you
- Your future as an MG patient
- Caregiver support

Saturday, October 24th, 2015 is the date

The day will start with registration and a continental breakfast at 8 AM

Presentations will commence at 9 am and continue throughout the day to 4 pm

Refreshment breaks will occur in the both morning and afternoon sessions

A light lunch will be provided mid-way through the day

Location is yet to be finalized, but will likely be in the 401 to 407 corridor, convenient to Hwy. 400.

Estimated cost will be approximately $50 - $100/person, dependant on sponsorships

1. Would you plan to attend this event? 
   [ ] Yes  [ ] No

2. Would you be attending alone or with others? 
   How many in your party? [ ]

3. Would you like to have overnight accommodation at the meeting location? 
   (If driving more than 2 hours, then the first night is highly recommended.) 
   [ ] Yes  [ ] No

   Number of nights
   [ ] One  [ ] Two

Name (Please Print) 

MG Patient

Caregiver

Other

MG Canada Education Conference

247 Harold Avenue,

Stouffville, ON,

L4A 1C2  

905 642 2545
My Story: Becky’s Continuing Journey

TRAPPED

By: Becky Shields

Frustration and anger is overcoming me becoming an optimum feeling.

I look in the mirror and hardly recognize the girl staring back at me.

Who is she? I feel bad for her...her face is so chubby, her body scared with stretch upon stretch mark.

I’m glad I’m not her...but I am. I am this girl now. You could say it is what it is, it's the medication, it will go away in no time but how soon is no time?

I’m trapped inside a body I don't recognize as my own. Would I have refused to take this dreaded medication if I had the power to travel back in time?

Probably not... I need it to keep going, to keep the internal part of my body better.

What is the angel among demons? Prednisone.

The pain kicks in late at night leaving tears pouring out of my eyes as I muffle out loud "mom!" Like a little girl experiencing the discomforting strain and she comes to rub the pain away.

As she rubs she feels the clenched muscles in my thighs. The instant relief is a blessing when the pain comes to a halt.

Up a couple sizes in clothes from excessive weight gain, feeling the wrath of the moment when my mom fits into a smaller Jean size than myself. Nothing fits, my kilt tight around my waist blocking my ability to breathe freely and feel comfort.

Picture day comes along, most common worry for a girl is if their hair is set perfectly but not for me, a whole bunch of other stressors surface my mind as I await in line to be rid of that one snapshot, lingering in the yearbook for the whole student body to see.

Dramatic am I being? More like sad, self conscious. I wasn't like this before. Steroids are evil but what choice did I have? Stay how dreadfully weak and tired I was or obtain that extra kick to keep me moving and enjoy some normal activity?

Strong am I? No it's just called living.

Becky Shields, one of our Librarians, is a young teenager. She contacted Myasthenia Gravis last year, and will be undergoing a Thymectomy in November. Please keep her in your thoughts during this difficult time.
### MGSOC Library Literature List

*Information on various MG related subject is available free of charge. To order check boxes below and send your request to: Janie & Becky Librarians c/o 614 Gliddon Avenue, Oshawa, Ontario, L1H 1Z9 or email Janie.Shields12@gmail.com*

- Facts About MG – For Patients & Families (Complied by MGSOC)
- Drugs & MG – Drugs to Avoid
- MG & Swallowing – Angela Colton Hudson MCS Sc - Speech Language Pathologist
- Living with MG – A Caring Partners view (MG Association of Great Britain)
- Human Energy Conservation (Jeanne Rhynsburger, R.N., CCRN, MICN, ACLS)
- Mestinon (MG Foundation of America Inc.)
- Prednisone (MG Foundation of America Inc.)
- Imuran (MG Foundation of America Inc.)
- Plasmapheresis (MG Foundation of America Inc.)
- IVIG (MG Foundation of America Inc.)
- CellCept / Mycophenolate Mofetil (MG Foundation of America Inc.)
- Thymectomy – Form of Treatment (MG Foundation of America Inc.)
- Exercise and MG – Kathleen Wade, EP, RN, BSN
- Dentistry and the Myasthenic – UK MG Foundation.
- MG in the Workplace (various sources)
- Positive Thinking & Positive Actions (Holly Fraser, R.N.)
- Home Injury Prevention (MG Foundation of America Inc.)
- Nutrition & MG (MG Foundation of America Inc.)
- Stress & Myasthenia Gravis – Judith Schiffbauer, M.S.W.
- Emotional Support – Guy R. Corsello MD – Mercy Hospital, Pittsburg PA

### BOOK LIST

To order books, please make cheques payable to MG Canada – Prices includes shipping

- You Me and Myasthenia Gravis $25.00 plus $3.25 HST
- A Guide to Diagnosis & Management of Myasthenia Gravis $25.00 plus $3.25 HST
- Settle It (Karen Vagiste) $15.00 plus $1.95 HST

Name: ____________________________________________________________
Address: _________________________________________________________
Postal Code: _________________________ Phone (optional) ____________________

We would like to know what you are interested in. Please indicate below. It would be a great help to us while building our library.

_____________________________________________________________________
_____________________________________________________________________

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MG Canada—November 2014
A randomized controlled trial

Lorne Zinman, MD, MSc; Eduardo Ng, MD; and Vera Bril, MD

Abstract—Objective: We aimed to determine the effectiveness of IV immunoglobulin (IVIG) in the treatment of patients with myasthenia gravis (MG) and worsening weakness in a randomized, placebo-controlled, masked study. Methods: Fifty-one patients with worsening weakness due to MG were randomized to infusion with 2 g/kg of IVIG or an equivalent volume of IV dextrose 5% in water. The Quantitative Myasthenia Gravis (QMG) Score for Disease Severity, a validated clinical composite scale, was calculated by a masked observer at baseline and days 14 and 28. Results: In IVIG-treated patients, a clinically meaningful improvement in QMG Score for Disease Severity was observed at day 14 and persisted at day 28. The greatest improvement occurred in patients with more severe disease as defined by a QMG Score for Disease Severity greater than 10.5. Conclusion: This study provides level 1 evidence for the effectiveness of IV immunoglobulin in patients with worsening weakness due to myasthenia gravis.

Acquired myasthenia gravis (MG) is mediated by two autoantibodies: acetylcholine receptor antibodies AChRAb) and antibodies to muscle-specific tyrosine kinase (MuSK).[1,2] AChRAb lead to clinical weakness by blocking and accelerating degradation of acetylcholinereceptors, thus impairing neuromuscular transmission,[1,3] but it is unknown if MuSK behave in the same fashion. Successful treatment of MG requires attenuation or elimination of the aberrant immune process using immunosuppressive medications and immunomodulation therapy.[4-8] IV immunoglobulin (IVIG) is an immunomodulatory treatment commonly used in patients with MG with a clinical exacerbation requiring a rapid improvement in strength, who are intolerant of or fail immunosuppressive therapy or who live in centers lacking plasma exchange facilities,[7,9,10] but the efficacy of IVIG in these patients is controversial.[7,9-11] The most recent Cochrane Review concluded that there is insufficient evidence from randomized, controlled trials to determine if IVIG treatment improves functional outcome in patients with chronic MG.[12] Therefore, we sought to determine the effectiveness of IVIG vs placebo in patients with MG in an appropriately powered, double-masked, randomized, controlled clinical trial.

Methods. The study was performed at the University Health Network (UHN) Neuromuscular Clinic from March 2004 to May 2005. Both the UHN Research Ethics Board and the Health Products and Food Branch of Health Canada (Biologics and Genetic Therapies Directorate) approved the study. This study was registered with the US NIH.

Patient population. Patients age 18 or older with a diagnosis of MG and worsening weakness were enrolled in the study after providing written informed consent. Patients were excluded from the study if they had respiratory distress requiring intensive care unit admission, a vital capacity less than 1 L, severe swallowing difficulties with a high risk of aspiration, a change in corticosteroid dosage in the 2 weeks prior to screening, other disorders causing weakness or fatigue, known IgA deficiency, active renal or hepatic insufficiency, clinically significant cardiac disease, known hyperviscosity or hypercoaguable state, or if they were pregnant or breast-feeding. Patients with worsening weakness secondary to concurrent infections or medications (e.g., aminoglycosides) were excluded. No changes in cholinesterase inhibitors or other immunomodulators were made from study initiation to the primary outcome measure on day 14. After day 14, only initiation or changes to cholinesterase medications were allowed. Patients with clinical worsening
Continued from Page 9

requiring initiation of plasma exchange or steroids during the 28 days of the study were considered treatment failures and withdrawn from the study.

The diagnosis of MG was based on the clinical evaluation performed by a neuromuscular expert, abnormal electrodiagnostic studies on single-fiber electromyography (SFEMG) testing, and previous response to treatment. Abnormal repetitive nerve stimulation (RNS) testing supported the diagnosis, and abnormal AChRAb or MuSK levels confirmed the diagnosis, when present. Worsening weakness was defined as increasing diplopia, ptosis, blurring vision, dysarthria, dysphagia, difficulty chewing, or limb weakness severe enough as judged by both the patient and the physician to warrant a change in therapy.

**Study procedures.** Clinical evaluation. Patients with MG attending the UHN Neuromuscular Clinic and who provided informed consent were screened for the study by a neurologist who remained masked throughout the study. Patients had clinical assessments at baseline and 2 and 4 weeks after treatment by the same masked neurologist. The clinical assessments included the Quantitative Myasthenia Gravis (QMG) Score for Disease Severity and the Post-Intervention Status classification.[13-15] The QMG score for Disease Severity is a validated clinical measure of sentinel muscle groups developed by the Myasthenia Gravis Foundation of America and the current clinical gold standard recommended for all prospective studies in MG.[14,16] A change of 3.5 U on the QMG score for Disease Severity is considered clinically meaningful [17] and was the effect size used to determine the sample size for this study. A value of greater or less than 10.5 was used to separate mild from more severe disease.[11] The Post-Intervention Status rates the patient’s clinical status on a five-step scale as improved, unchanged, worse, exacerbation, and died from MG. Adverse events that occurred during the study were assessed by an unmasked neurologist.

Cholinesterase inhibitors were held for a minimum of 12 hours prior to all clinical assessments.

**Electrodiagnostic investigations.** Standardized electrodiagnostic testing (SFEMG and RNS) was performed in all subjects at baseline and at the end of the study by a masked observer and a masked certified technologist. In patients with ocular and bulbar symptoms, the frontalis muscle was used preferentially for SFEMG testing. In patients with limb weakness without ocular or bulbar findings, the extensor digitorum communis muscle was tested. Jitter in at least 20 muscle fiber pairs was measured, and abnormal SFEMG was defined as increased mean jitter for a given muscle, elevated mean consecutive differences value in more than 10% of pairs for a given muscle, or the presence of blocking.[18] RNS was performed by stimulating the facial nerve at a rate of 3 Hz and recording the compound muscle action potential (CMAP) over the frontalis muscle in most patients. Some patients had testing of the musculocutaneous nerve with recordings over the biceps muscle, depending on the clinical presentation. RNS was considered abnormal if the decrement from the first to fifth CMAP was greater than 10%. Cholinesterase inhibitors were held for a minimum of 12 hours prior to testing.

**Laboratory investigations.** All patients had AChRAb levels checked at baseline. If abnormal, then AChRAb titers were rechecked on day 28. In those with normal AChRAb levels, MuSK antibodies were assayed during the study. No other laboratory tests were performed routinely.

**Intervention.** The subjects were randomized in blocks of four to receive either 2 G/kg IVIG (Gamunex; Talecris Biotherapeutics, Toronto, Canada) or the equivalent volume of IV dextrose 5% in water (D5W) divided over 2 days and administered in the Medical Day Unit (MDU). The hospital pharmacist prepared the solutions in opaque bottles indistinguishable to the nursing staff, patients, and treating physicians. All study patients received the MDU standard.

From the Sunnybrook Health Sciences Centre (L.Z.) and University Health Network (E.N., V.B.), University of Toronto, Ontario, Canada. Disclosure: Talecris (formerly Bayer) provided an unrestricted education grant for this study. Bayer/Talecris was not involved in the study design, conduct of the study, collection and management of data, or interpretation of results. A Bayer statistician provided technical support and review of our own analyses of the data. Bayer/Talecris did not play a role in the preparation or approval of the manuscript. Received July 14, 2006. Accepted in final form October 19, 2006.

Address correspondence and reprint requests to Dr. V. Bril, 13N, 1382, Toronto General Hospital, UHN, 585 University Ave., Toronto, Ontario, Canada M5G 2N2; e-mail: vera.bril@utoronto.ca

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treatment protocol for IVIG infusions with the preinfusion administration of acetaminophen tablets and dimenhydramine 50 mg orally.

**Efficacy measures.** The primary outcome measure was the change in the QMG Score for Disease Severity from baseline to day 14. The secondary outcome measures included the changes in the QMG Score for Disease Severity from day 1 to day 28 and from day 14 to day 28, changes in SFEMG and RNS results from baseline to day 14, and the Post-Intervention Status on days 14 and 28.

**Statistical analyses.** Homogeneity of baseline characteristics between treatment groups was assessed by the Student t test for the continuous variables age, baseline QMG Score for Disease Severity, disease duration, percentage decrement on RNS, and SFEMG jitter and by the χ² or Fisher exact test for categorical variables gender, type of MG, baseline disease severity, thymectomy history, thymoma, medications, and presence of AChRAb. Patients with thymoma had either undergone resection or were prethymectomy at the time of the study. An analysis of covariance (ANCOVA) was performed for the primary outcome measure and ANCOVA, χ², or Fisher exact test was performed for secondary outcome measures. p values of <0.05 were considered significant. An exploratory analysis of the IVIG treatment effect was performed stratifying patients by baseline severity of disease using an ANCOVA model. Disease Severity was dichotomized using a QMG Score for Disease Severity greater or less than 10.5 as performed in a previous study.[11] Subsequently, the ANCOVA model was extended to assess the effects of baseline covariates of age, gender, duration of MG, baseline QMG Score, thymoma, presence of AChRAb, SFEMG jitter, and percentage decrement on RNS for the primary outcome measure. For jitter and percentage decrement, the change from baseline to day 14 was used in the model. A change of 3.5 U on the QMG Score for Disease Severity has been demonstrated to be clinically significant in a previous study and requires a sample size of 22 patients per treatment arm.[13,17] We enrolled 52 patients to allow for study withdrawals.

**Results.** Fifty-two patients were recruited for the study. One patient withdrew consent prior to study initiation and was not included in the analysis. The demographic profile for the 51 remaining patients enrolled in the study is shown in table 1. The baseline characteristics were balanced between the IVIG and placebo groups. Cases classified as “ocular” MG by routine clinical history and examination had a mean QMG Score of 10.9 ± 4.9 (range: 5 to 23, 10% at ≤ 6) compared with the mean of 13.0 ± 5.1 for those with “generalized” MG. The maximum QMG Score due to ocular findings alone is 6. At screening, medications included cholinesterase inhibitors in 57%, corticosteroids in 24%, azathioprine in 18%, and cyclophosphamide.

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**Support Meeting in September**

Joyce Ovens thanks Veemi Chouhan for her presentation on helps for daily living through Occupational Therapy. Discussion groups were held to get input on subjects that would be helpful to members of the MG family. Kelly Cowan received thanks from Jim Ovens for moderating the discussion groups.
in 4%. Therapy with cholinesterase inhibitors and immunotherapies was balanced between the treatment groups as shown in table 1. In this MG cohort, 24 patients (47%) were AChRAB positive, and these patients were balanced between treatment groups. In those lacking AChRAB, 14 had elevation of anti-MuSK antibodies, or 52% of those who were AChRAB negative.

Table 2 displays the change in QMG Scores for Disease Severity 14 and 28 days after treatment. A small and significant improvement in QMG Score for Disease Severity was observed for patients treated with IVIG compared with those receiving placebo after 14 days. Treatment with IVIG reduces the QMG Score for Disease Severity by 2.5 U at day 14 (an additional 1.6 U compared with placebo; figure 1). The treatment effect was maintained at 28 days with a 3-U reduction in the QMG score, although it just failed to reach significance ($p = 0.055$).

The Post-Intervention Status measure on day 14 demonstrated that 25% of patients on IVIG improved compared with 6% on placebo ($p < 0.004$, $x^2$ test). None of the patients on IVIG worsened compared with 4% worsening on placebo. Of those on placebo, 42% remained unchanged vs 23% on IVIG ($p < 0.004$, $x^2$ test). No patients required plasma exchange or initiation of steroids during the study. Those patients who had undergone thymectomy had a meaningful improvement in QMG Score at day 14 (-2.8 ± 1.1 on IVIG compared with 1.1 ± 0.9 on placebo; $p = 0.016$) in contrast to patients who had not had thymectomy.

When stratifying patients by baseline MG disease severity (QMG Score for Disease Severity greater or less than 10.5), a significant IVIG treatment effect was observed only in patients with more severe disease (table 3). Patients with moderate to severe MG who were treated with IVIG had a 4.1-U reduction in the QMG score at day 14 (an additional 3.4 U of improvement compared with placebo-treated patients; figure 2). The Post-Intervention Status on day 14 was three times more likely to have improved with IVIG compared with placebo (23%...
improved with IVIG compared with 8% with placebo; \( p < 0.015 \). None of the patients on IVIG worsened, although 6% on placebo worsened. Patients with milder disease (QMG Score for Disease Severity less than 10.5) did not respond to IVIG treatment \( (p = 0.914) \). Additional ANCOVA analyses of QMG Score for Disease Severity change from baseline to day 28 and change from day 14 to 28 showed persistence of the IVIG treatment effect, but no additional improvement. None of the electrophysiologic measures showed a significant improvement with IVIG. When various factors that might influence response to therapy were added to the ANCOVA model, the presence of thymoma predicted a greater response to IVIG.

In this study, no serious adverse events occurred, and headache was the most frequent side effect. In the IVIG group, 18 patients (75%) had headache for a mean duration of 6.9 \( \pm \) 6.2 days (range: 1 to 25 days) compared with 5 patients on placebo (19%; \( p < 0.001, \chi^2 \text{ test} \)). None of the

\begin{table}[h]
\centering
\caption{Mean change in QMG Score for Disease Severity at days 14 and 28} \begin{tabular}{|c|c|c|c|}
\hline
 & IVIG, n = 24 & D5W = 27 & \( p \) Value \\
\hline
Baseline QMG Score (mean) & 12.3 \( \pm \) 4.9 & 12.5 \( \pm \) 5.5 & 0.897 \\
\hline
\( \Delta \text{QMG} \) & & & \\
Day 0–14 & \(-2.54\) & \(-0.89\) & 0.047* \\
Day 0–28 & \(-3.00\) & \(-1.19\) & 0.055 \\
Day 14–28 & \(-0.46\) & \(-0.30\) & 0.823 \\
\hline
\end{tabular}
\end{table}

* Significant by analysis of covariance.

D5W = IV dextrose 5% in water.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{The mean change in Quantitative Myasthenia Gravis (QMG) Score for Disease Severity in all patients treated with IV immunoglobulin (IVIG) and placebo. There is a small decrease in the QMG Score for Disease Severity with IVIG treatment observed at day 14 (2.5 U; \( p < 0.047 \)).}
\end{figure}

\begin{table}[h]
\centering
\caption{Mean change in QMG Score for Disease Severity on day 14 in patients with mild and moderate to severe MG} \begin{tabular}{|c|c|c|c|}
\hline
Baseline severity treatment group & LS means & LS mean difference (95% CI) & \( p \) Value \\
\hline
Mild MG (QMG Score <10.5) & & & \\
IVIG, n = 11 & \(-0.97\) & \(-0.10 (-2.03–1.83)\) & 0.914 \\
Placebo, n = 12 & \(-0.86\) & & \\
Moderate to severe MG (QMG Score >10.5) & & & \\
IVIG, n = 13 & \(-4.10\) & \(-3.39 (-5.88–0.90)\) & 0.010* \\
Placebo, n = 15 & \(-0.71\) & & \\
\hline
\end{tabular}
\end{table}

Stratification for baseline myasthenia gravis (MG) disease severity reveals an IV immunoglobulin (IVIG) treatment effect at day 14 in patients with moderate to severe disease (baseline Quantitative Myasthenia Gravis (QMG) Score for Disease Severity greater than 10.5). There is no treatment difference in patients with milder symptoms of MG (baseline QMG Score for Disease Severity less than 10.5).

* Significant by analysis of covariance.

LS = least squares.
patients required hospitalization and the symptoms resolved with standard nonprescription analgesic therapy.

Discussion. This randomized, double-blind, appropriately powered study provides the first reliable evidence for the effectiveness of IVIG in patients with MG and worsening weakness. A significant benefit of IVIG compared with placebo therapy was demonstrated 14 days after treatment (primary outcome measure), and the treatment effect was maintained 28 days after the infusion. It is of interest that the response to IVIG was rapid compared with the typical response observed with immunosuppressive medications for MG. Therefore, IVIG treatment can be a useful adjunctive therapeutic strategy in symptomatic patients awaiting the characteristically long latent response to immunosuppressive medications.

Despite the significant change, the improvement in motor scores with IVIG vs placebo was relatively small for the entire treatment cohort. Importantly, when subjects were stratified by disease severity, patients with moderate to severe disease demonstrated both a highly statistical and a clinically meaningful improvement with a corresponding improvement in the Post-Intervention Status. It appears that patients with more severe symptoms of MG benefited most from IVIG treatment. These findings are consistent with results from a previous unmasked study showing a comparable benefit of IVIG and plasma exchange at 1 and 4 weeks post treatment in patients with severe symptoms of MG requiring intensive care.7

This study supports therapeutic strategies for the treatment of patients with MG. One course of IVIG treatment given over 2 days produced a clinically meaningful benefit at least 4 weeks post treatment. In patients with more severe disease who cannot tolerate immunosuppressive therapy, IVIG treatments every 4 weeks may be a viable treatment option akin to patients with immune-mediated neuropathies who are maintained on IVIG alone. The low risk of major IVIG side effects observed in this study also supports this therapeutic strategy. Although not addressed in this study, IVIG treatment may be advantageous for patients initiated on steroid treatment to ameliorate the initial paradoxical worsening as the response to IVIG was rapid and effective in patients with moderate to severe disease. However, this steroid-protection hypothesis needs to be evaluated in an appropriately designed trial.

This study also provides data in the context of selecting appropriate patients for IVIG intervention. IVIG treatment did not produce a meaningful improvement in patients with milder symptoms or pure ocular disease, that is, those with abnormalities only on the ocular tests of the QMG Score. Patients with milder disease who do not respond to cholinesterase inhibitors are unlikely to benefit from IVIG treatment, and initiation of immunosuppressive medications should be considered. In this way, IVIG-related side effects and costs may be avoided in patients with milder disease. The results of this study suggest caution in how patients with MG are classified as 90% of patients diagnosed with ocular MG on clinical grounds had QMG Scores placing them in the generalized category. For these patients, denial of IVIG treatment or other therapeutic intervention such as thymectomy may not be the optimal management approach. This finding may also help explain the high sensitivity of SFEMG for patients with a clinical diagnosis of ocular MG.

Although the study was not powered to investigate the association between IVIG and a number of other variables, responsiveness appeared to be independent of patient age, sex, disease duration, and antibody status. The presence of thymoma and thymectomy did appear independently to predict responsiveness, but the number of patients is limited, and this finding needs to be interpreted cautiously. Future studies may further clarify which subgroups of patients with MG are most responsive to IVIG.
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References


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