Published in final edited form as:

N Engl J Med. 2015 October 22; 373(17): 1680–1682. doi:10.1056/NEJMc1506163.

Intravenous Immune Globulin for Statin-Triggered Autoimmune Myopathy

Andrew L. Mammen, M.D., Ph.D. and
National Institutes of Health, Bethesda, MD

Eleni Tiniakou, M.D.
Johns Hopkins University School of Medicine, Baltimore, MD

Andrew L. Mammen: andrew.mammen@nih.gov

To the Editor

Although treatment with statins may cause muscle-related symptoms in 10 to 20% of patients, these symptoms usually resolve within weeks after the medication is stopped. In rare instances, however, the medication causes statin-triggered autoimmune myopathy, a condition characterized by proximal muscle weakness, prominent necrosis of muscle fibers (detected on biopsy), elevated serum levels of creatine kinase, and the presence of autoantibodies that recognize 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the pharmacologic target of statins.[1-3] Moreover, statin-triggered autoimmune myopathy progresses despite the discontinuation of statins and requires control with immunosuppressive therapy.

No clinical trials have been conducted to establish effective treatments for statin-triggered autoimmune myopathy. However, most clinicians use glucocorticoids as first-line therapy. Statin-triggered autoimmune myopathy can be especially difficult to treat; achieving remission frequently requires the addition of not only a second oral agent (e.g., methotrexate) but also intravenous immune globulin (IVIG).[1,3,4]

Among 82 patients with statin-triggered autoimmune myopathy evaluated at the Johns Hopkins Myositis Center, 3 patients with diabetes declined glucocorticoids because of concerns about potential side effects but agreed to try monotherapy with IVIG, administered at a rate of 2 g per kilogram of body weight per month. Detailed clinical characteristics of these patients are shown in Table 1. Immediately before IVIG, the mean (±SD) creatine kinase level for these patients was 4919±3523 IU per liter, and all 3 patients had documented weakness in the proximal arms and legs. No infusion reactions occurred in any of the patients during treatment. After two or three rounds of IVIG, the mean creatine kinase level declined to 1125±1101 IU per liter, quantitative dynamometry showed an increase in the mean strength of arm abduction from 3.5 to 6.2 kg, and hip-flexion strength improved or normalized. These gains persisted without the addition of another agent. Between 9 and 19 months after starting IVIG, 2 patients had no subjective muscle-related symptoms and had

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normal strength on examination. Patient 1 continued to have mild hip-flexor weakness but declined our advice to add another agent.

The mechanisms underlying the effects of IVIG in statin-triggered autoimmune myopathy remain unknown. However, despite partial or full recovery of strength, two patients had persistent creatine kinase elevations and all three continued to have positive titers for HMG-CoA reductase autoantibodies. These findings suggest that IVIG may attenuate statin-treated autoimmune myopathy, allowing muscle regeneration to outpace muscle destruction, but may not completely abolish the pathophysiological processes that cause muscle damage.

The use of IVIG can be associated with serious adverse effects, including anaphylaxis, thromboembolic events, transfusion-associated lung injury, and others. Thus, IVIG therapy must be used cautiously.[5] However, our experience suggests that monotherapy with IVIG may be considered as a first-line treatment for statin-triggered autoimmune myopathy.

Acknowledgments

Supported by the Intramural Research Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health (NIH) and by a grant (T32-AR-048522) from the NIH.

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Table 1

Clinical Characteristics of Patients with Statin-Triggered Autoimmune Myopathy Who Received Intravenous Immune Globulin Monotherapy*

Characteristic	Patient 1	Patient 2	Patient 3†
Age (yr)			
At start of statin	57	53	63
At onset of muscle-related symptoms	57	53	67
At discontinuation of statin	57	65	68
At first IVIG treatment	63	65	69
Evaluation immediately before IVIG			
Creatine kinase (IU/liter)	8916	2323	3517
Strength			
Arm abductors			
Contraction against resistance			
Right	4	4+	4
Left	4	4+	4
Weight resisted (kg)			
Right	2.7	5.0	2.7
Left	2.7	5.0	3.2
Hip flexors			
Contraction against resistance			
Right	2	4	4
Left	2	4	4
Weight resisted (kg)			
Right	NA	13.6	6.4
Left	NA	12.2	6.4
Anti–HMG-CoA reductase antibody titer (NAU)	0.845	0.566	1.650
First evaluation after IVIG			
Time since first IVIG (mo)	3.5	2	1.5
Creatine kinase (IU/liter)	2368	270	738
Strength			
Arm abductors			
Contraction against resistance			
Right	5−	5	5
Left	5−	5	5
Weight resisted (kg)			
Right	4.5	8.6	5.9
Left	4.1	8.6	5.4
Hip flexors			

Characteristic	Patient 1	Patient 2	Patient 3†
Contraction against resistance			
Right	4−	5	4+
Left	4−	5	4+
Weight resisted (kg)			
Right	5.4	NA	10.4
Left	6.8	NA	12.7
Anti–HMG-CoA reductase antibody titer (NAU)	0.654	0.438	1.242
Most recent evaluation			
Time since first IVIG (mo)	9	19	15
Creatine kinase (IU/liter)	1755	64	877
Strength			
Arm abductors			
Contraction against resistance			
Right	5	5	5
Left	5	5	5
Weight resisted (kg)			
Right	6.8	NA	5.9
Left	6.4	NA	8.2
Hip flexors			
Contraction against resistance			
Right	4+	5	5
Left	4+	5	5
Weight resisted (kg)			
Right	13.6	NA	NA
Left	12.7	NA	NA
Anti–HMG-CoA reductase antibody titer (NAU)	0.764	0.471	1.179

*Extent of muscle contraction against resistance was measured with the use of the Medical Research Council scale, in which 0 indicates no movement and 5 indicates normal contraction. Quantitative muscle strength testing was performed with a MicroFet2 handheld dynamometer (Hoggan Scientific). Arm abductors were tested with arms laterally abducted at 90 degrees, and hip flexors were tested with patient supine and leg raised to 30 degrees. Anti–HMG-CoA-receptor titers were determined as previously reported with values greater than 0.367 normalized absorbance units (NAU) considered positive. [5] HMG-CoA denotes 3-hydroxy-3-methylglutaryl coenzyme A, IVIG intravenous immune globulin, and NA not available.

†This patient was treated unsuccessfully with oral glucocorticoids and azathioprine for several months, but these medications were discontinued more than a year before IVIG initiation.