

Letter to the Editor

Successful desensitization to rosuvastatin in a patient with a history of anaphylaxis to multiple statins

To the Editor:

Statins (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors) decrease cholesterol levels by inhibiting 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase levels and reduce morbidity and mortality in patients with a previous myocardial infarction (MI).¹ Although the use of statins has been associated with myositis and skin reactions, such as toxic epidermal necrolysis, urticarial vasculitis, drug reaction with eosinophilia and systemic symptoms syndrome, and chronic urticaria,²⁻⁵ anaphylaxis to statins and desensitization to these agents have not been previously reported. We report successful rapid oral desensitization to rosuvastatin in a 37-year-old man with a past medical history of significant premature coronary artery disease caused by familial combined hyperlipidemia and increased lipoprotein A levels who had anaphylaxis to multiple statin agents.

The patient presented with his first MI in ventricular fibrillation arrest at age 30 years. Before hospitalization, he was receiving escitalopram and albuterol, and during resuscitation for ventricular fibrillation, he received lidocaine, succinylcholine, vecuronium, aspirin, clopidogrel, enoxaparin, and intravenous infusion with esmolol, eptifibatide, and propofol without reaction. It was not until 2 days later that a statin was started, without any new medications being administered at that time. Within 30 minutes of starting atorvastatin, he experienced pruritus, entire-body urticaria, lip swelling, and laryngeal edema. The atorvastatin was discontinued, and he had no adverse reactions while being continued on 325 mg of aspirin, 75 mg of clopidogrel, and β -blocker therapy, and thus we do not believe these agents were responsible for his reaction. Two years later, he experienced a second MI and was given simvastatin while in the hospital with a similar systemic reaction consisting of pruritis, urticaria, and laryngeal edema within minutes of drug administration. On both occasions, these systemic reactions were witnessed and documented as anaphylaxis by attending physicians.

The patient was referred to the University of Washington Lipid Clinic for management of his dyslipidemia. Receiving no lipid-lowering medication, he had moderate hypertriglyceridemia with increased non-high-density lipoprotein (HDL) cholesterol levels (178 and 222 mg/dL) and increased apolipoprotein B levels compatible with familial combined hyperlipidemia.⁶ Receiving quadruple drug therapy with fenofibrate, niacin, colesvelam, and ezetimibe, he had very high lipoprotein A levels (391 nm/L), and his non-HDL cholesterol level (156 mg/dL) was still greater than the goal,⁷ indicating a need for addition of a statin drug.

The patient was subsequently referred to the University of Washington Allergy Clinic for evaluation of statin hypersensitivity and consideration for statin desensitization because treatment with quadruple therapy had not sufficiently reduced his cholesterol levels. Given the life-threatening nature of his reaction to 2 different statins that was consistent with an IgE-mediated immediate hypersensitivity mechanism, his significant cardiac history, and the fact that he was experiencing ongoing angina, the patient was not challenged with a full-dose statin agent because of the significant potential associated risks. Rosuvastatin was chosen as

TABLE I. Oral rosuvastatin desensitization protocol*

Time	Dose (mg)	Concentration (mg/mL)	mL
0:00	0.01	0.01	1
0:30	0.02	0.01	2
1:00	0.04	0.01	4
1:30	0.08	0.01	8
2:00	0.1	0.1	1
2:30	0.2	0.1	2
3:00	0.4	0.1	4
3:30	0.8	0.1	8
4:00	1	1	1
4:30	2	1	2
5:00	4	1	4
5:30	8	1	8
6:00	10	10-mg tablet	10-mg tablet

Solutions were made by dissolving a 10-mg tablet of rosuvastatin in 10 mL of saline and subsequently diluting to the 0.1 and 0.01 mg/mL concentrations.

*Doses were given every 30 minutes; if any reaction occurs, the dose can be repeated or decreased based on severity.

the agent for rapid oral desensitization because he had not previously received this statin, and meta-analysis of randomized controlled trials has indicated that rosuvastatin is more potent than atorvastatin and has a similar risk of adverse events.^{8,9} Rosuvastatin contains a sulfonamide group, and the patient had no prior history of adverse reactions to sulfonamides.

Plans for admission to the cardiac intensive care unit at the University of Washington Medical Center were coordinated by the allergy, cardiology, metabolism, and anesthesiology services. His medications before desensitization consisted of niacin, fenofibrate, ezetimibe, colesvelam, metoprolol, isosorbide mononitrate, aspirin, clopidogrel, ranolazine, lisinopril, ranitidine, and lamotrigine. In preparation for the desensitization, metoprolol was held for 72 hours before the procedure should epinephrine need to be administered. He was pretreated with montelukast and zileuton for 48 hours before the procedure, and on the morning of the desensitization, he received aspirin, ranitidine, and ondansetron. H_1 blockers were held before desensitization over concerns that this might mask an early IgE-mediated reaction. He was started on a dose of 0.01 mg of rosuvastatin, which was increased as outlined in Table I. He was monitored closely by using telemetry, and given his compromised cardiac status, he had an arterial line placed to monitor for any signs of hypotension.

After receiving the 0.1-mg dose, he experienced significant pruritus but had no appreciable urticaria, and blood pressure remained stable. He was treated with 50 mg of diphenhydramine and 100 mg of hydrocortisone, the 0.1-mg dose was repeated, and the protocol was continued and successfully completed with a final oral dose of 10 mg without need for epinephrine intervention. During the procedure, he did note chest pain that was consistent with his typical angina symptoms; his vital signs remained normal, no changes were noted on electrocardiography, and he received a bedside echocardiogram that indicated normal left ventricular function. He was monitored overnight in the cardiac intensive care unit, and serial troponin levels were obtained that remained normal. He was discharged home the

TABLE II. Plasma lipid and apolipoprotein levels

Analyte*	November 2010	December 2010	May 2011	November 2011	March 2012	Goal†
Total cholesterol	255	219	194	156	185	<200
Triglyceride	207	186	89	88	191	<150
HDL cholesterol	33	41	38	38	40	>40
LDL cholesterol	181	162	138	100	107	<100
Non-HDL cholesterol	222	178	156	118	145	<130
Apolipoprotein B		143				
Lipoprotein A (nm/L)		391				
Lipid therapy	None	None	‡	‡	‡	
Daily rosuvastatin (mg)				10	20	

LDL, Low-density lipoprotein; Lp(a), lipoprotein A.

*Values are shown as milligrams per deciliter.

†Values are from Grundy et al.⁷

‡Daily medications: 1.5 g of niacin, 10 mg of ezetimibe, 1.25 g of colesvelam, and 160 mg of fenofibrate (stopped November 2011).

next day on 10 mg of rosuvastatin every evening. He was seen in the lipid clinic 7 weeks after desensitization receiving 1.5 g of niacin daily, 10 mg of ezetimibe daily, and 1.25 mg of colesvelam daily; with the addition of 10 mg of rosuvastatin daily, his non-HDL cholesterol level (118 mg/dL) approached the National Cholesterol Education Program goal of 100 mg/dL (Table II).^{6,7} The dose of rosuvastatin has been slowly increased to try and reach the National Cholesterol Education Program goal. He had no pruritus, urticaria, lip swelling, or laryngeal edema at 9 months after desensitization on 20 mg/d rosuvastatin.

We present a patient who experienced anaphylaxis to multiple different statins and required these agents given his combination of 2 familial lipid disorders and severe coronary artery disease. Despite his significant cardiac risk factors, the patient underwent successful desensitization with rosuvastatin. To our knowledge, this is the first published desensitization protocol to statin agents in a patient with a history of anaphylaxis to these agents. We outline a protocol that enabled a high-risk cardiac patient to undergo successful desensitization in a carefully monitored intensive care setting.

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