Indian Health Service
National Pharmacy & Therapeutics Committee
Drug Safety Alert
Statin-Associated Autoimmune Myopathy

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Background:

Statins significantly reduce the incidence of cardiovascular disease and are generally safe. However, over the past 2 years in the Navajo Area Indian Health Service, there has been an increased incidence of a relatively rare condition where an autoimmune myopathy develops in patients treated with statins. While the national incidence of statin-associated autoimmune myopathy (SAAM) is 2-3 in every 100,000 patients treated with a statin drug, the Navajo Area identified 12 cases in the past 2 years[1]. Providers need to maintain a high index of suspicion for those patients on a statin who develop muscle weakness to ensure that the appropriate tests and treatment are initiated.

Discussion:

What is known about Statin-Associated Autoimmune Myopathy?

SAAM is a rare, distinct and serious autoimmune myopathy characterized by muscle weakness, high elevations of serum creatine phosphokinase (CPK), muscle cell necrosis on biopsy, and frequent (but not absolute) presence of antibodies to 3-hydroxyl-3-methylglutaryl coenzyme A reductase (HMGCR), the rate-limiting enzyme in cholesterol production[1-4]. The exact mechanism for developing SAAM is unknown but may include a genetic component (HLA allele DRB1*11:01), increased cellular expression of HMGCR upon statin initiation and/or higher HMGCR protein level expression in regenerating muscle cells. Available evidence on SAAM is scarce and mostly limited to case reports or case series. The SAAM pathway and specific causative agents continue to evolve. Lipophilic statins, like atorvastatin, have greater diffusion into myocytes than hydrophilic statins (e.g., rosuvastatin, pravastatin) and therefore may be more toxic[3]. All statins have however been reported in literature to be associated with cases of SAAM.

What are the clinical signs of Statin-Associated Autoimmune Myopathy?

Healthcare providers should be aware that those patients on a statin who present with proximal upper or lower extremity weakness might have a statin-associated autoimmune myopathy. They may present with muscle pain, difficulty rising from a chair, going upstairs or lifting heavy objects. The weakness can be mild, moderate or severe. Although the onset of myopathy usually occurs soon after initiation of statin, sometimes patients can be on a statin for years before developing symptoms.

How does this differ from the known myopathies/myalgias caused by statin drugs?

Statins, although generally well tolerated, can result in muscular adverse events including myalgias and/or myopathies in 5-20% of patients[5,6]. Typically, these are self-limiting with statin discontinuation. Defined differences of SAAM include progressive weakness and markedly elevated CPK levels (>10-50 times the upper limit of normal), frequently requiring immunosuppressive therapy[1,3,6]. HMGCR antibodies are common with suspected SAAM but are not definitive. Muscle biopsy may be required and is considered the gold standard for diagnosis[3]. Following resolution of SAAM, statin re-challenge has proven unsuccessful and extremely limited in the literature[3,6].

What do Health Care Providers need to do?

If healthcare providers suspect that a patient may have SAAM, they should:

- Stop the statin
- Check a creatine phosphokinase level (CPK)
- If the CPK level is elevated (usually greater than 3,000 IU/L), obtain an HMGCR antibody level
- Submit details of the condition to the FDA MedWatch Voluntary Report (FDA Form 3500)

To make the diagnosis: If a patient presents with proximal muscle weakness, elevated CPK levels and elevated HMGCR antibody levels, the patient most likely has SAAM. Discuss with a neurologist or rheumatologist regarding initiation of immunosuppressive therapy (usually methotrexate, azathioprine or intravenous immunoglobulin (IVIG)).

As with all treatment decisions, providers should balance the risks and benefits of statin medication, discuss treatment recommendations and potential adverse effects with the patient, and monitor therapy. Heart disease and stroke respectively represent the second and seventh leading causes of death in the American Indian and Alaska Native population. Dyslipidemia is a common and important major risk factor for the development of atherosclerotic cardiovascular disease. Complications from statin therapy, including muscular adverse events (and especially SAAM) remain rare, and individual risk is not well understood. Statin therapy continues to be a safe and effective strategy for the primary and secondary prevention of heart disease and stroke in the American Indian and Alaska Native population.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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