

Abstract

Am J Cardiovasc Drugs. 2008;8(6):373-418.

Statin adverse effects : a review of the literature and evidence for a mitochondrial mechanism.

Golomb BA, Evans MA.

Department of Medicine, University of California, San Diego, California 92093-0995, USA.

BACKGROUND: HMG-CoA reductase inhibitors (statins) are a widely used class of drug, and like all medications, have potential for adverse effects (AEs). Here we review the statin AE literature, first focusing on muscle AEs as the most reported problem both in the literature and by patients. Evidence regarding the statin muscle AE mechanism, dose effect, drug interactions, and genetic predisposition is examined.

RESULTS: We hypothesize, and provide evidence, that the demonstrated mitochondrial mechanisms for muscle AEs have implications to other nonmuscle AEs in patients treated with statins. In meta-analyses of randomized controlled trials (RCTs), muscle AEs are more frequent with statins than with placebo. A number of manifestations of muscle AEs have been reported, with rhabdomyolysis the most feared. AEs are dose dependent, and risk is amplified by drug interactions that functionally increase statin potency, often through inhibition of the cytochrome P450 3A4 system. An array of additional risk factors for statin AEs are those that amplify (or reflect) mitochondrial or metabolic vulnerability, such as metabolic syndrome factors, thyroid disease, and genetic mutations linked to mitochondrial dysfunction. Converging evidence supports a mitochondrial foundation for muscle AEs associated with statins, and both theoretical and empirical considerations suggest that mitochondrial dysfunction may also underlie many nonmuscle statin AEs. Evidence from RCTs and studies of other designs indicates existence of additional statin-associated AEs, such as cognitive loss, neuropathy, pancreatic and hepatic dysfunction, and sexual dysfunction.

CONCLUSION: Physician awareness of statin AEs is reportedly low even for the AEs most widely reported by patients. Awareness and vigilance for AEs should be maintained to enable informed treatment decisions, treatment modification if appropriate, improved quality of patient care, and reduced patient morbidity.

PMID: 19159124

