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Management of statin myopathy

With interest, we read the article by Sahebkar *et al*. about the proposal to treat patients with statin-induced myopathy (SIM) with curcumin in addition to the statin.[1] We have the following comments and concerns.

We do not agree with the statement in the introduction that pharmacotherapy for statin-myopathy is limited. The most effective treatment is discontinuation of the statin and adherence to a strict low-fat diet. However, care has to be taken that patients who are unable to metabolise glucose sufficiently, such as those with a mitochondrial disorder (MID), may depend on serum lipids or proteins, why high serum lipids should not be lowered medicinally in each case. Furthermore, short-chain and medium-chain fatty acids may even increase the respiratory capacity in starved human endothelial cells and monocytes.[2] There is also a need to consider that withdrawal of a statin may not resolve muscle manifestations immediately but with a delay of up to 14 months.[3]

If low-fat diet is ineffective in patients who discontinued a statin because of SIM, lipid-lowering drugs other than statins should be tried. These include fibrates, ezetimibe, niacin, cholestyramine, lomitapide, phytosterols, orlistat, or PCSK9 inhibitors (e.g. alirocumab). However, all these alternatives have their side effects as well and may or may not be tolerated by those to whom they were prescribed.

Most likely, SIM is a secondary mitochondrial myopathy,[4] since statins exhibit their side effects mainly by interaction with mitochondria. For example, in C2C121 myoblasts, it has been shown that statins reduce the capacity of the respiratory chain by inhibition of complex III of the respiratory chain.[5] There are also indications that statins lead to a reduction of serum coenzyme-Q levels.[6] Other studies have shown that statins may activate muscle atrophy genes, may increase muscle-specific NO-synthetase and NO production, and may decrease fatty acid oxidation.[7] When retrospectively evaluating muscle biopsies of SIM patients for the mtDNA content, it has been shown that the mtDNA content is reduced in SIM patients, either due to an adverse effect of the statin or due to an underlying inherent metabolic defect.[8]

In case a patient with SIM does not want to switch from the statin to an alternative compound, several options are available to manage the clinical manifestations of SIM. These include exercise,[9] polyprenols,[10] coenzyme Q,[11] vitamin D,[4] or inhibition of xanthine oxidase via co-administration of allopurinol to reduce the generation of reactive oxygen species (ROS).[12] Dietary changes may additionally contribute to alleviate clinical manifestations of SIM.[4] Particularly, reduction of simple carbohydrates, eating whole foods, and adherence to a high-fiber diet have been shown to resolve manifestations of SIM.[4]

Concerning the muscle biopsy findings in SIM, various different results have been reported. Biopsy in SIM may be normal,[13] may show specific or non-specific changes like in a MID,[14] and may show inflammatory myopathy,[15] or necrotizing myopathy.[16] Statin therapy may even induce dermatomyositis in patients with collagenoses.[17]

Overall, this interesting review should be supplemented by considerations as outlined above. Patients with SIM should be investigated for an underlying subclinical myopathy, in particular myopathy within an MID. Patients with SIM should no longer receive statins, which can be replaced by various alternatives. If treating physicians together with the patient decide for continuation of statin treatment despite SIM, supportive compounds, including curcumin, can be offered.

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The manuscript complies with the ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2015.[18]

Conflict of interest

The authors declare that no conflict of interest relevant to this article exists.

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