

Red Yeast Rice for Dyslipidemia in Statin-Intolerant Patients

William B. Borden

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Rating

- Of importance.

Introduction

Statin-associated myalgias represent a significant health concern as they often limit the ability of patients to receive the mortality benefits associated with statin therapy. Randomized controlled trials show rates of statin-associated myalgias ranging between 1% and 5%, with some rates as high as 15%, although not significantly different from placebo-treated patients [1, 2]. Although not often associated with creatinine phosphokinase (CPK) level elevations or progression to rhabdomyolysis, the symptoms can be disconcerting to patients and are a frequent cause of statin discontinuation. A variety of strategies have been attempted to manage this challenge, including decreasing the statin dose, trying

alternative statins or other lipid-lowering agents, and intensifying therapeutic lifestyle changes [3]. An additional tool used by many patients and physicians has been red yeast rice (*Monascus purpureus*). The mechanism of action is not completely understood, although the active agent is thought to be monacolin K, a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor produced as the pharmaceutical lovastatin. However, red yeast rice also contains other monacolins that may have similar or different effects, making red yeast rice not a “true” statin medication. Thus far, widespread use of red yeast has been limited by the variety of preparations (as it is a dietary supplement rather than a pharmaceutical) and the relative paucity of data on its safety and efficacy relative to statin drugs. Many clinicians do use red yeast rice as an alternative for their statin-intolerant patients; however, no randomized controlled trial has examined using red yeast rice to treat patients with statin-associated myalgias.

Aims

In order to assess the lipid-lowering effects of red yeast rice and intensive therapeutic lifestyle changes in patients intolerant to statins, this study recruited individuals with indications for lipid lowering who had previously tried statins and discontinued them due to myalgias. The study investigated the effect of a formal therapeutic lifestyle education program alone or in combination with a standardized dosing of red yeast rice on laboratory values and on symptoms. Thus, the study sought to determine the additional benefit of red yeast rice to a program of therapeutic lifestyle changes.

W. B. Borden (✉)
Division of Cardiology,
Weill Medical College of Cornell University,
1305 York Avenue, 8th Floor,
New York, NY 10021, USA
e-mail: wbb2001@med.cornell.edu

Methods

This study recruited patients between the ages of 21 and 80 years from a suburban cardiology practice who had hypercholesterolemia, had tried at least one statin, and had discontinued the medication due to myalgias. All patients had to have had relief of their symptoms with discontinuation of the statin to identify the medication as the cause of the myalgias. Patients were excluded if they had abnormal baseline laboratory values; a history of myositis, myopathy, or chronic pain; recent coronary procedures; or were taking other medications or supplements that could impact symptoms or lipid levels. The patients were randomized to either 1,800 mg of red yeast rice twice a day or a matching placebo twice a day. All patients were enrolled in a formal 12-week therapeutic lifestyle change program that included information about cardiovascular disease, heart healthy diets, exercise, and stress reduction.

Laboratory values, weights, and a Brief Pain Inventory Short Form (BPI-sf) were measured at baseline, week 12, and week 24. The BPI-sf is a validated, self-administered assessment of severity of pain and limitations of routine activity meant to measure the possible recurrence of myalgia symptoms. The primary end point of the study was low-density lipoprotein cholesterol (LDL-C) levels at the three time points, with secondary end points of the other laboratory values, weight, and BPI-sf score. The analysis was performed on an intention-to-treat basis.

Results

The placebo and red yeast rice groups were similar in baseline characteristics except that the placebo group had a higher BPI-sf score. On average, the baseline LDL-C was over 160 mg/dL and patients had been previously tried on approximately two statins. Chemical analysis of the red yeast rice detected a variety of monacolins, though monacolin K comprised nearly 50%. For the primary outcome of LDL-C level, both groups improved. The placebo group improved LDL-C by 11 mg/dL and 15 mg/dL at weeks 12 and 24, respectively. The red yeast rice group improved LDL-C by 43 mg/dL at week 12 and by 35 mg/dL at week 24. LDL-C was significantly lower in the red yeast rice group compared with the placebo group at both weeks 12 and 24. In addition, the total cholesterol was also significantly lower in the red yeast rice group than in the placebo group, although triglycerides and high-density lipoprotein cholesterol (HDL-C) were not different. Both groups lost weight over the course of the

study, with the red yeast group losing 3.5 kg and the placebo group losing 3.6 kg by week 24. Side effects were not significantly different between the groups, including no difference in BPI-sf score at 12 and 24 weeks.

Comments

This study provides a careful analysis of a strategy to treat patients with statin-induced myalgias. In hypercholesterolemic patients who had failed an average of two statin medications previously due to side effects, the addition of red yeast rice successfully lowered LDL-C by over 20% by the end of the study. Although the use of red yeast rice alone may not be sufficient to achieve goals for patients at highest risk for cardiovascular events who need to achieve very low LDL-C targets, it is a well-tolerated option for significant LDL-C reduction in addition to other modalities. It is not known why red yeast rice does not cause myalgias to the same degree as pharmaceutical statins, although proposed explanations include that it contains a relatively low dose of statin and that perhaps the LDL-C reduction is obtained through mechanisms other than HMG-CoA reductase inhibition.

A second key point from this trial is that both the red yeast rice and placebo groups improved in the study, which, again, demonstrates the benefit of therapeutic lifestyle changes. The study utilized an intensive therapeutic lifestyle change program involving 3.5-hour weekly meetings. Based on the background of this diet and exercise program, even the placebo group participants lost weight and improved their lipid profiles. Although not all individuals may have access to such supportive lifestyle change programs, this clearly represents a way to make improvements in cardiovascular risk in patients who have been intolerant to statin therapy.

Lastly, this study should be commended for performing a randomized, double-blinded placebo-controlled trial on a nutritional supplement and for assessing the chemical content of the red yeast rice capsules. The two major concerns that many clinicians have about incorporating nutraceuticals into their practice are the lack of strong data and the uncertainty surrounding the composition of the different preparations. This study addressed both of these concerns with scientific rigor in regard to red yeast rice. The main limitation of this study was that it was a small, brief, single-center study that did not evaluate cardiovascular outcomes. Nonetheless, the data suggest that red yeast rice is a safe method of lowering LDL-C and that red

yeast rice appears to be an effective component of a statin-alternative regimen when traditional statins are not an option due to myalgias.

Disclosure Dr. Borden participated in a one-time advisory board meeting for Kowa Company, Ltd.

References

1. Thompson PD, Clarkson P, Karas RH: Statin-associated myopathy. *JAMA* 2003, 289:1681–1690.
2. Kashani A, Phillips CO, Foody JM, et al.: Risks associated with statin therapy: a systematic overview of randomized clinical trials. *Circulation* 2006, 114:2788–2797.
3. Joy TR, Hegele RA: Narrative review: Statin-related myopathy. *Ann Intern Med* 2009, 150:858–868.