

Red yeast rice

Dear bpac

In your recent article "An update on statins" (BPJ 30, Aug 2010), you state that the general consensus is that the use of red yeast rice should be avoided. There is evidence to suggest that this view would lead to an excess of cardiac events in patients intolerant of statins.

The New Zealand Guidelines Group recommends that simvastatin is the first-line medicine of choice for lipid reduction in high risk individuals.¹ Difficulties occur in those who are intolerant to statins. Some patients disagree with the opinion of your authors that the adverse effects of statin therapy are usually minor. Estimates of myalgia without elevated CK have been described as 10–20% outside of clinical trials vs 1–2% within clinical trials.² Many of your readers will have had the experience of patients reporting a significant increase in their quality of life after they or their doctor withdrew their simvastatin because of myalgia.

If atorvastatin also causes myalgia the GP faces difficulties in how they can best treat the patient. As your authors note, fibrates only weakly lower LDL-cholesterol, there is little evidence of clinical benefit from ezetimibe and nicotinic acid is either poorly tolerated or costs \$100 a month.

Red yeast rice may offer a better alternative for this group of patients. One small study has shown red yeast rice to lower LDL-cholesterol by a mean 30% and to be better tolerated than pravastatin.³ Another has shown that, in combination with fish oil and lifestyle changes, red yeast rice lowers LDL-cholesterol in proportions similar to simvastatin.⁴ A randomised, placebo controlled trial of red yeast rice in secondary prevention in nearly 5000 people in China showed a reduction of cardiovascular mortality of 30% and of total mortality of 33%.⁵

Red yeast rice presents a challenge to GPs. As a fermentation product there is variability in batches and amongst manufacturers in monacolin content.² As your authors note red yeast rice can cause the same adverse effects and have the same interactions as statins. The safest way for statin intolerant patients to navigate the difficulties of red yeast rice therapy is in collaboration with their GP. When red yeast rice is used carefully under medical supervision there is evidence to suggest a benefit for statin intolerant patients. If there truly is a general consensus that red yeast rice should be avoided, then those who subscribe to that consensus should make it clear why the risks described in the article outweigh the benefits of red yeast rice in statin intolerant patients.

References

1. New Zealand Guidelines Group (NZGG). *New Zealand cardiovascular guidelines handbook: A summary resource for primary care practitioners*. 2nd ed. Wellington: NZGG, 2009.
2. *Best evidence interview: Using red yeast rice to lower cholesterol in patients intolerant to statins*; May 28, 2010. Available from: www.medscape.com/viewarticle/722339 (Accessed Oct, 2010).
3. Halbert SC, French B, Gordon RY, et al. Tolerability of red yeast rice (2,400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance. *Am J Cardiol* 2010;105:198-204.
4. Becker DJ, Gordon RY, Morris PB, et al. Simvastatin vs therapeutic lifestyle changes and supplements: randomized primary prevention trial. *Mayo Clin Proc* 2008;83:758-64.
5. Lu Z, Kou W, Du B, et al. Chinese Coronary Secondary Prevention Study Group. Effect of Xuezhikang, an extract from red yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction. *Am J Cardiol* 2008;101:1689-93.

Dr Paul Nola, GP

Auckland

As the popularity of red yeast rice supplements grows, more research is beginning to emerge. There is some evidence that red yeast rice is effective in lowering cholesterol, however it is important to carefully examine these studies.

In the Halbert study, red yeast rice was observed to lower LDL-cholesterol by 30% in a small group of people, however LDL-cholesterol was lowered by 27% in the pravastatin group. There was no significant difference between the number of patients who withdrew due to myalgia (one in the red yeast rice group and two in the pravastatin group), the mean pain severity due to myalgia or muscle strength. The authors concluded that both regimens were tolerated as well as each other and achieved a comparable reduction in LDL-cholesterol. The authors also note that the red yeast rice supplements used in this study were rigorously analysed for consistent composition and the results should not be generalised to commercially available red yeast rice supplements, in which potency differs.¹

In the Becker study, similar reductions in LDL-cholesterol were observed in groups receiving simvastatin and alternative therapy, including red yeast rice. However it is difficult to attribute this result specifically to the use of red yeast rice. Patients in the group receiving simvastatin were provided with pre-printed material regarding diet and exercise, based on American Heart Association recommendations. Patients in the alternative therapy group received red yeast rice (at two different strengths depending on their initial LDL-measurements) and fish oil supplements and were also enrolled in a 12-week multidisciplinary lifestyle programme. This included counselling from a dietitian on following a modified Mediterranean diet, with reduced saturated fat intake and restricted carbohydrates. An exercise physiologist also coached the patients to increase their exercise levels to five to six times per week. It is perhaps unsurprising then, that the alternative therapy group were able to achieve reductions in LDL-cholesterol levels.²

Results are still emerging from the China Coronary Secondary Prevention Study (CCSPS), but it does appear that xuezhikang, an extract from red yeast rice, has a beneficial effect on cardiovascular morbidity and mortality in Chinese people.³ However, it is important to note that conventional statin use reduces cardiovascular mortality by a similar degree. Authors of an objective review of the Lu study conjectured that as it has been shown that the cardio-protective effect of statins in Japanese populations occurs at a lower dose than in Western populations, it is also possible that the low doses of lovastatin found in the red yeast rice supplements is sufficient to produce the reduction of cardiac events in the Chinese population in the CCSPS trial. A similar trial with red yeast rice would need to be conducted in a Caucasian population to resolve these doubts.⁴

The issues with recommending red yeast rice for cholesterol lowering can perhaps be more concisely summarised by Thomas Lee, Editor-in-chief of the Harvard Heart Letter:⁵

- Standardised, quality-controlled preparations of red yeast rice can lower cholesterol, but there is no evidence that this will translate to fewer heart attacks or strokes or increased life expectancy, as has been shown for statins.
- There is no way of knowing what is in the red yeast rice supplement you are buying. Multiple analyses have found that the amount of cholesterol lowering compounds in red yeast rice supplements can vary by as much as 100-fold and some contain the toxic compound citrinin.
- Red yeast rice can cause myalgia, just like statins
- Statins are considerably less expensive for the patient

If statin intolerance is a significant issue and lowering doses, switching types of statins and using other lipid-lowering medicines have been tried and failed, then red yeast rice supplements could be considered on an

individual basis. However, it may be difficult for clinicians to supervise its use, given that so little is known about the effects of this product and exactly what its constituents are. Further compelling evidence and strict regulatory requirements would be needed before red yeast rice could be routinely recommended as a statin alternative.

References

1. Halbert SC, French B, Gordon RY, et al. Tolerability of red yeast rice (2,400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance. *Am J Cardiol* 2010;105:198-204.
2. Becker DJ, Gordon RY, Morris PB, et al. Simvastatin vs therapeutic lifestyle changes and supplements: randomized primary prevention trial. *Mayo Clin Proc* 2008;83: 758-64.
3. Lu Z, Kou W, Du B, et al. Chinese Coronary Secondary Prevention Study Group. Effect of Xuezhikang, an extract from red yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction. *Am J Cardiol* 2008;101:1689-93.
4. Ong H, Cheah J. Statin alternatives or just placebo: an objective review of omega-3, red yeast rice and garlic in cardiovascular therapeutics. *Chin Med J* 2008;121(16):1588-94.
5. Lee, T. Ask the doctor. What is the story on using red yeast rice to lower cholesterol? *Harv Heart Lett* 2009;20(4):8.

Clopidogrel in secondary stroke prevention

Dear bpac,

*If the ProFESS trial shows that clopidogrel is equally as effective as aspirin plus dipyridamole in secondary prevention of stroke/TIA why hasn't bpac made this first choice for secondary stroke prevention? ("Access to clopidogrel now widened", *BPJ* 30, Oct 2010).*

Taking one tablet a day rather than three is going to be better for compliance, simpler and in my experience, patients often struggle with the GI side effects of dipyridamole. Am I missing something? It seems illogical

to suggest a combination of three tablets taken twice daily is a better choice than one.

Dr Andrew Miller, GP

Christchurch

In the list of indications, clopidogrel would have been better described as an alternative first line treatment (as mentioned later in the article) rather than second line to aspirin plus dipyridamole.

Since the publication of the ProFESS trial, international guidelines have been inconsistent in their recommendations. Some guidelines consider aspirin plus dipyridamole as first choice, however a very recent consensus paper considers clopidogrel alone to be a safe and effective first line option for secondary stroke prevention.¹ There is no evidence that clopidogrel alone is clinically superior to aspirin plus dipyridamole, and it is not currently considered an absolute first choice for this indication. Choice of treatment will depend on factors such as tolerance to adverse effects and compliance issues. It is also relevant to mention that the clinical effectiveness of clopidogrel may be reduced in people who are poor metabolisers to the active agent (up to 10% of the population) and in those taking proton pump inhibitors (particularly omeprazole). The clinical significance of these factors in the post stroke/TIA patient population is not currently known.

Reference

1. Furie KL, Kasner S, Adams R, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack. A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2010; [Epub ahead of print].



**We value your feedback. Write to us at:
Correspondence, PO Box 6032, Dunedin
or email: editor@bpac.org.nz**