

Original Scientific Paper

Efficacy of *Monascus purpureus* Went rice on lowering lipid ratios in hypercholesterolemic patients

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Received 13 June 2006 Accepted 30 November 2006

Background Several lipid ratios may be predictors of coronary artery disease risk. We assessed the efficacy of *Monascus purpureus* Went rice (red yeast rice) on lowering lipid ratios.

Method and results We evaluated 79 hypercholesterolemic patients (aged 23–65 years) who received a twice-daily dose of either red yeast rice or a placebo at 600 mg for 8 weeks. The 8-week treatment with red yeast rice showed significantly greater reduction than the placebo treatment in low-density lipoprotein cholesterol levels, total cholesterol/high-density lipoprotein cholesterol, low-density lipoprotein cholesterol/high-density lipoprotein cholesterol and apolipoprotein B/apolipoprotein A-I ratios.

Conclusions Red yeast rice can reduce lipid ratios in hypercholesterolemic patients. *Eur J Cardiovasc Prev Rehabil* 14:438–440 © 2007 The European Society of Cardiology

European Journal of Cardiovascular Prevention and Rehabilitation 2007, 14:438–440

Keywords: hyperlipidemia, lipid ratio, red yeast rice

Introduction

In the report of the fourth working party of the British Hypertension Society [1], total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-C) ratio is counted as a cardiovascular disease risk factor. *Monascus purpureus* Went rice (red yeast rice) has positive effects on plasma lipids [2,3]. Relatively few studies of its effect on lipid ratios, however, have been done; thus we assessed the efficacy of red yeast rice in lowering lipid ratios.

Methods

This was an 8-week, randomized, double-blind, placebo-controlled study. The trial was conducted between December 2001 and January 2003 in the China Medical University Hospital, Taichung, Taiwan. Patients were men and women aged 18–65 years with low-density lipoprotein cholesterol (LDL-C) ≥ 4.14 mmol/l (160 mg/dl).

The exclusion criteria included hypothyroidism, and the use of any drugs known to affect lipid levels, etc. After a 4-week dietary lead-in period with the American Heart Association Step I diet control, patients who had TC ≥ 6.22 mmol/l (240 mg/dl), LDL-C ≥ 4.14 mmol/l and triglycerides ≤ 4.52 mmol/l (400 mg/dl) were randomly separated into two treatment groups: red yeast rice or rice-powder placebo, each administered as capsules at 600 mg twice-daily for a total of 1.2 g/day, 30 min after breakfast and 30 min after dinner for 8 weeks. The composition of red yeast rice has been previously reported [3]. Diet control was continued and all patients received dietary instruction from a registered dietitian. Blood samples were obtained at initial screening, at randomization, and at weeks 4 and 8 of treatment from patients who had fasted for 12 h. Baseline was defined as the measurements taken at randomization. The trial design has been previously published [3]. The protocol was approved by the Institutional Review Board of China Medical University Hospital and by the Department of Health, Taiwan. The protocol number was D-SO-001-01. All the patients gave their informed consent before participation in this trial.

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Statistical methods

Descriptive statistics such as number of observations, means, percentages, and standard deviations were used to summarize the baseline variables. All used tests were two sided and were evaluated at the 0.05 level of significance. The demographic comparability between the two treatment groups was examined by the unpaired *t*-test for continuous variables and χ^2 test for categorical variables. The changes (%) in blood lipids and lipid ratios from baseline to week 4 and week 8 showed a normal distribution. Paired *t*-test and McNemar test were used within groups for the difference from baseline. Efficacy was evaluated on the intention-to-treat participants.

Results

After 4 weeks of diet control, only 79 patients still had a TC ≥ 6.22 mmol/l and LDL-C ≥ 4.14 mmol/l and were randomly assigned to treatments. Demographic characteristics, lipids and lipid ratios at baseline were similar between groups ($P > 0.05$) (Table 1). The 8-week treatment with red yeast rice significantly reduced TC by 20.4%, LDL-C by 26.3%, apolipoprotein (Apo) B by 24.7%, TC/HDL-C ratio by 20.5%, LDL-C/HDL-C ratio by 26.6%, and Apo B/Apo A-I ratio by 26.5% (Table 1). Red yeast rice also significantly decreased the percent of patients with TC/HDL-C ratio > 5 , LDL-C/HDL-C ratio > 5 , and Apo B/Apo A-I ratio ≥ 1 from 64.1 to 33.3%, 33.3 to 7.7%, and 66.7 to 28.2%, respectively (Table 1). In contrast, the 8-week treatment with placebo did not lead to a significant reduction of lipids and lipid ratios.

Actually, after 4 weeks of treatment with red yeast rice, lipid ratios were already significantly reduced (Table 1). The lowering of lipid ratios after 4 and 8 weeks' treatment did not differ between the sexes or with age (data not shown).

Discussion

Lipid parameters can be combined into ratios that reflect the proportion of atherogenic to antiatherogenic lipids and lipoproteins. In this study, red yeast rice reduced the TC/HDL-C ratio by 20.5% and 1.28 units (the mean of TC/HDL ratio from 5.96 to 4.68). Previous study [4] showed that after 1 year of treatment, each 1% decrease in the TC/HDL-C ratio was associated with a 1.3% reduction of coronary artery disease risk, and that each unit difference in the TC/HDL-C ratio was associated with a 17.6% difference in the risk of a coronary event. Furthermore, red yeast rice significantly decreased the percentage of patients with a TC/HDL-C ratio > 5 from 64.1 to 33.3%, and the absolute risk reduction (ARR) was 30.8%. One study [5] showed that patients with 'low-risk' LDL-C levels (≤ 3.37 mmol/l) and high TC/HDL-C ratios (> 5) had a 2.5-fold higher incidence of coronary

Table 1 Change from baseline in serum lipid variables, by week and treatment group

	Red yeast rice (n=39)	Percentage change	Placebo (n=40)	Percentage change
Age (year)	46.3 (10.1)		46.5 (9.5)	
Sex, male, n (%)	23 (59)		22 (55)	
BMI, kg/m ²	24.3 (3.3)		23.4 (2.7)	
TC mmol/l ^a				
Baseline	7.28 (0.84)		7.40 (1.09)	
4 week	5.26 (1.44) ^b	-22.5 (8.8) ^b	6.97 (1.97)	-0.5 (10.7)
8 week	5.78 (0.89) ^b	-20.4 (10.3) ^b	7.36 (1.16)	-0.4 (9.3)
LDL-C, mmol/l ^a				
Baseline	5.20 (0.84)		5.35 (1.12)	
4 week	3.43 (1.14) ^b	-29.1 (12.0) ^b	5.01 (1.61)	-0.5 (13.7)
8 week	3.83 (0.89) ^b	-26.3 (13.4) ^b	5.22 (0.99)	-1.4 (15.6)
Apo B g/l ^c				
Baseline	1.55 (0.26)		1.56 (0.30)	
4 week	1.05 (0.35) ^b	-27.4 (10.8) ^b	1.43 (0.44)	-3.1 (12.4)
8 week	1.16 (0.28) ^b	-24.7 (15.1) ^b	1.50 (0.32)	-3.7 (11.9)
TC/HDL-C				
Baseline	5.96 (1.76)		5.85 (1.50)	
4 week	4.56 (1.40) ^b	-23.5 (8.4) ^b	5.80 (1.50)	-0.5 (9.9)
8 week	4.68 (1.39) ^b	-20.5 (11.7) ^b	5.79 (1.50)	-0.8 (10.2)
LDL-C/HDL-C				
Baseline	4.30 (1.44)		4.25 (1.29)	
4 week	3.03 (1.28) ^b	-30.6 (10.9) ^b	4.18 (1.31)	-0.8 (11.9)
8 week	3.15 (1.20) ^b	-26.6 (13.3) ^b	4.13 (1.23)	-2 (14.4)
Apo B/Apo A-I				
Baseline	1.19 (0.36)		1.22 (0.36)	
4 week	0.85 (0.28) ^b	-29.1 (9.0) ^b	1.18 (0.34)	-2.2 (11.3)
8 week	0.87 (0.29) ^b	-26.5 (14.5) ^b	1.16 (0.35)	-4.6 (15.2)
TC/HDL-C > 5 , n (%)				
Baseline	25 (64.1)		26 (65.0)	
4 week	13 (33.3) ^b	-48.0 ^b	25 (62.5)	-3.8
8 week	13 (33.3) ^b	-48.0 ^b	27 (67.5)	3.8
LDL-C/HDL-C > 5 , n (%)				
Baseline	13 (33.3)		8 (20.0)	
4 week	3 (7.7) ^b	-76.9 ^b	9 (22.5)	12.5
8 week	3 (7.7) ^b	-76.9 ^b	7 (17.5)	-12.5
Apo B/Apo A-I ≥ 1 , n (%)				
Baseline	26 (66.7)		28 (70.0)	
4 week	11 (28.2) ^b	-57.7 ^b	25 (62.5)	-10.7
8 week	11 (28.2) ^b	-57.7 ^b	27 (67.5)	-3.6

Apo A-I, apolipoprotein A-I; Apo B, apolipoprotein B; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides. ^aTo convert total cholesterol and LDL-C to mg/dl, divide values by 0.0259. ^bSignificantly different from baseline, $P < 0.001$. ^cTo convert Apo B to mg/dl, divide values by 0.01.

heart disease than those with similar LDL-C levels but low TC/HDL-C ratios.

We also found that red yeast rice reduced the LDL-C/HDL-C ratio by 1.15 units. Another study [6] showed that the highest hazard ratios were for LDL-C/HDL-C, with each 1-unit increment being associated with a 1.2-fold increase in coronary artery disease risk. Our study showed that red yeast rice decreased the percentage of patients with LDL-C/HDL-C ratio > 5 from 33.3 to 7.7%, and that the ARR was 25.6%. The Helsinki Heart Study [7] revealed that a LDL-C/HDL-C ratio > 5 was associated with increased coronary risk.

In this study, red yeast rice reduced the mean of the Apo B/Apo A-I ratio by 26.5% and decreased the

percentage of patients with Apo B/Apo A-I ratio ≥ 1 from 66.7 to 28.2%, and the ARR was 38.5%. The Apo B/Apo A-I is an indicator of non-HDL particle size divided by HDL particle size. One study [8] revealed that, after adjustment for nonlipid risk factors, the Apo B/Apo A-I ratio was the best discriminator of baseline risk, and that a value of ≥ 1.0 was associated with an increased risk of 38% for a first major coronary event.

The principal finding in this trial was that after 8 weeks of treatment, red yeast rice had significantly greater efficacy than the placebo in reducing TC/HDL-C, LDL-C/HDL-C, and Apo B/Apo A-I ratios. Red yeast rice also significantly reduced the percentage of patients with a lipid ratio above the cutoff point. This study provides, however, only 8 weeks' data, and long-term data on efficacy are now needed.

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