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Original article

Efficacy and safety of Monascus purpureus Went rice in children and young adults with secondary hyperlipidemia: A preliminary report

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Abstract

Backgrounds/aims: Nephrotic dyslipidemia is a risk factor for development of systemic atherosclerosis; also it may aggravate glomerulosclerosis and enhance progression of glomerular disease. We aimed to assess the efficacy and safety of Monascus purpureus Went rice vs. fluvastatin therapy in the management of nephrotic dyslipidemia.
Methods: Seventy-two patients with idiopathic persistent nephrotic syndrome with secondary dyslipidemia were included. They were randomly allocated into 3 — age and sex — matched groups. The first group comprised of 20 cases and were given Monascus purpureus Went rice, second group comprised 30 cases were given fluvastatin. The remaining 22 received no anti-dyslipidemic therapy and constituted a control group. All of these patients were subjected to thorough laboratory investigations including renal function tests, lipogram and neurological assessment.
Results: Our results showed that both fluvastatin and Monascus purpureus Went rice were well-tolerated with no significant side effects. Both of them significantly reduced cholesterol after 6 months and 1 year. In comparison to baseline values, fluvastatin achieved a significant and progressive reduction of serum cholesterol by 35%, 38% and 42% at 3 months, 6 months and after 1 year respectively ($p<0.001$). Similar reductions were observed in the Monascus purpureus Went rice group. After one year we observed that serum cholesterol was significantly lower in statin and Monascus purpureus Went rice groups compared to the control group.
Conclusion: Monascus purpureus Went rice is safe, effective cholesterol lowering agent for nephrotic dyslipidemia both in adults and children.

Keywords: Neurotoxicity; Nephrotic; Statin; Glomerulonephritis; Herbal

1. Introduction

Nephrotic hyperlipidemia — multifactorial in origin — is a risk factor for the development of systemic artherosclerosis, and also it may aggravate glomerulosclerosis and enhance the progression of glomerular disease [1].

Diet intervention should be the first-line of treatment, but it partially corrects hypercholesterolemia in such patients [2]. The greatest and the most consistent reductions in LDL-cholesterol were seen with 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase) inhibitors. Many studies have shown that *Monascus purpureus Went rice* contained HMG-CoA reductase inhibitors (statins), large quantities of unsaturated fatty acids, beta-sitosterol, campesterol and stigmasterol [3,4,5]. These components are effective in reducing serum lipid [6].

The lipid-lowering effects of Monascus purpureus — rice food flavor in China and Japan — have been shown in several animal models of hyperlipidemia [7]. Monascus purpureus rice (in Chinese), popularly called red yeast rice, is described as the fermented product of rice on which red yeast (Monascus purpureus) has been grown. This product has been used for centuries in China to make rice wine and to flavor foods.

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Traditional red yeast rice continues to be a dietary staple in many Asian countries with consumption ranging from 14 to 55 g/person per day. One study showed that Monascus purpureus Went rice significantly reduced LDL-C, total cholesterol, triglycerides and apolipoprotein B levels, and was well tolerated in patients with hyperlipidemia [8,9].

In addition red yeast extract significantly reduced cholesterol levels in human hepatic cells HepG2in a dose-dependent manner. They found an association of this reduction with the decreased synthesis and secretion of both unesterified cholesterol and cholesteryl ester (Man RY et al, Cholestin inhibits cholesterol synthesis and secretion in hepatic cells (HepG2). Mol Cell Biochem. 2002 Apr;233(1–2):153–8).

Experience to date suggests that 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors or "statins" offer the most effective therapy and are relatively safe, at least in short term studies.

Newly defined actions of statins, some of which may be unrelated to lipid lowering, are likely to extend the application of these drugs in patients with glomerular disease. However, the long term safety and efficacy of these lipid lowering strategies are lacking in patients with nephrotic syndrome [10]. Treatments of nephrotic dyslipidemia in steroid resistant nephrotic syndrome (NS) have resulted in a considerable benefit not only for the hyperlipidemia but also for the nephrotic state [11].

Prospective controlled studies should evaluate the long-term safety of statins in a large patient population and assess whether reduction in cholesterol decreases the risk for atherosclerosis and inhibits the progression of glomerular disease in patients with NS [12]. Although, statin therapy was considered to be safe in treating nephrotic dyslipidemia on the short-term follow up studies considering EMG [13,14], long-term studies are lacking for this costly regimen.

We aimed to assess the efficacy and safety of Monascus purpureus Went rice vs. fluvastatin therapy in the management of nephrotic dyslipidemia.

2. Patients and methods

2.1. Patient population

Out of 450 patients with idiopathic nephrotic syndrome screened, 72 were — recruited from the nephrology clinic of the Urology and Nephrology Center, Mansoura University for inclusion in this prospective, randomized controlled study for a planned duration of one year.

The patients were recruited with the following inclusion criteria:

(1) Patients with steroid resistant, steroid dependent and frequently relapsing idiopathic nephrotic syndrome. (2) Hypercholesterolaemia with no response to an appropriate diet for at least four weeks and none of them received any lipid lowering agents. (3) Serum creatinine less than 2 mg/dl. (4) Recent renal biopsy with either focal segmental glomerulosclerosis (FSGS) or membranoproliferative glomerulonephritis (MPGN) lesions. We excluded patients with: (1) Hepatic disease, (2) muscle disease, (3) History of familial dyslipidemia, (4) Diabetes mellitus.

This protocol met the requirements of local ethical committee. Upon enrollment, patients were randomly assigned to 1 of the 3 treatment groups. The first group comprised 20 cases and was given Monascus purpureus, the 2nd group comprised 30 cases were given fluvastatin, and the 3rd group comprised 22 cases served as control.

Information regarding the randomized treatment was concealed in sequentially numbered, sealed opaque envelopes. These were opened in the absence of the patients immediately after obtaining informed written consent for participation in the study. The participant physicians were necessarily aware of the randomized treatment in all cases.

2.2. Patients' evaluation

Patients were evaluated at the start of treatment (control values) and monthly for 6 months (test values). The evaluation included:

A) Clinical evaluation: thorough history taking and clinical examination.
B) Laboratory evaluation:
   The following laboratory investigations were carried out:
   ∗Complete urine analysis and 24-hour urinary protein estimation.
   ∗Serum creatinine and creatinine clearance using Cockcroft and Gault formula; Liver function tests; Investigations to exclude secondary causes of glomerulonephritis such as blood sugar, anti-HCV, anti-CMV, anti-HIV, HbsAg, serologic tests for systemic lupus erythematosis rectal mucosal biopsy to exclude schistosomiasis; total serum cholesterol.
C) Neurophysiological evaluation

We used the NIHON KOHDEN-evoked response recorder, model MEP-5200, for electromyography [15] and nerve conduction velocity [16].

1 Electromyography
   The following muscles were tested:
   1 The biceps brachii and the rectus femoris as representative of the proximal muscles of the upper and lower limbs respectively.
   2 The abductor pollicis brevis of the thenar eminence and extensor digitorum brevis as representative of the distal muscles of the upper and lower limbs respectively.

The electrical potentials were recorded by a bipolar EMG needle electrode (NW-120 T). Resting and mild contraction activities were recorded at the interrupted speed and the interference pattern at continuous speed for each muscle.

The mean of at least 20 motor unit action potentials (MUPs), from different sites and depths, gave the duration and amplitude. The reduction in duration and amplitude of motor action potentials will signify myopathic changes.