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Anti-Inflammatory Effects of Resveratrol in Patients with Ulcerative Colitis: A Randomized, Double-Blind, Placebo-controlled Pilot Study

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Background and Aims. Ulcerative colitis (UC) is a chronic idiopathic inflammatory disease in which reducing pro-inflammatory and/or increasing anti-inflammatory molecules is the mainstay of treatment. The aim of this study was to evaluate the effects of supplementation with resveratrol as an antiinflammatory and antioxidant agent on inflammation and quality of life in patients with active UC.

Methods and Results. In this randomized, double-blind, placebo-controlled study, 50 eligible patients with active mild to moderate UC were supplemented with either a 500-mg resveratrol or placebo capsule for 6 weeks. Serum inflammatory markers, activity of NF-κB in peripheral blood mononuclear cells (PBMC) and quality of life were assessed at baseline and at the end of the study. Resveratrol supplementation led to a significant reduction in plasma levels of TNF-α (19.70 ± 12.80 to 17.20 ± 10.09 pg/mL) and hs-CRP (4764.25 ± 2260.48 to 2584.50 ± 1792.80 ng/mL) and activity of NF-κB in PBMCs (0.19 ± 0.05 to 0.10 ± 0.04 OD) ($p < 0.001$), whereas there were no significant changes of these factors in placebo group. Also, the score of inflammatory bowel disease questionnaire -9 (IBDQ-9) increased, whereas the clinical colitis activity index score decreased significantly in the resveratrol group (32.72 ± 7.52 to 47.64 ± 8.59) ($p < 0.001$) and when compared with the placebo group (35.54 ± 9.50 to 41.08 ± 6.59) ($p < 0.001$).

Conclusion. Our results indicate that 6 weeks supplementation with 500 mg resveratrol can improve quality of life and disease clinical colitis activity at least partially through inflammation reduction in patients with UC. Whether these effects will be continued in longer duration of treatment remains to be determined. © 2015 IMSS. Published by Elsevier Inc.

Key Words: Ulcerative colitis, Resveratrol, Inflammation, Anti-oxidant.

Introduction

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease are chronic intestinal inflammatory disorders in which reducing pro-inflammatory and/or increasing anti-inflammatory molecules is the cornerstone of treatment (1). The etiology of this disease has not yet been well understood. It seems that UC develops by a defect in the regulation of the immune response to intestinal flora in genetically susceptible individuals and influenced by environmental factors (1). Currently, patients undergo some types of drug therapies including amino salicylates, glucocorticosteroids, immune modulators, antibiotics and anti-TNF drugs, which cause severe adverse effects such as increasing anti-antibody reactions, risk of allergy, infection and mutagenesis. Thus, there has always been a big challenge to find a way to decrease the toxicity of these drugs (2,3).

Resveratrol (trans-5,3,4'-trihydroxystilbene) is a polyphenolic phytoalexin natural compound found in plants

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such as grapes, berries and peanuts. A vast range of biological functions are attributed to this molecule, which focuses mainly on modulating oxidation and inflammation (4). It is believed that resveratrol could be one of the possible compounds in preventing and treating chronic inflammation as well as autoimmune abnormalities (5). In experimental models of UC, resveratrol improved the disease activity index and decreased oxidative stress and inflammatory biomarkers, whereas it could increase the activity of tissue antioxidant enzymes (3,5−9). However, there is no study evaluating the effects of resveratrol in patients with UC. Hence, we designed this study to investigate the effects of resveratrol supplementation on inflammatory biomarkers and quality of life in patients with UC.

Materials and Methods

Study Design

This study was conducted as a double-blind placebo-controlled randomized clinical trial. Patients who met the inclusion criteria were invited to take part in the study. At the first visit, the benefits of participation were explained and they were informed of the research goals, method of intervention and duration of the study. Among 165 patients with UC who were interviewed, 50 eligible patients were recruited in the study (Figure 1). All signed an informed consent form, which was approved by the ethics committee of the National Nutrition and Food Technology Research Institute (NNFTRI), Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran. All subjects were informed that they would either be in the supplement group or in the placebo group. At the beginning and at the end of the study, a general information questionnaire, 3-day food record (2 ordinary days and one weekend day), the Simple Clinical Colitis Activity Index Questionnaire (SCCAIQ) (10), and inflammatory bowel disease questionnaire-9 (IBDQ-9) were completed (11,12). It has been shown that the SCCAIQ has a good correlation with existing more complex scoring systems and therefore could be useful in the initial assessment of patients with ulcerative colitis (10,12). IBDQ-9 assesses the patients' quality of life from the four aspects of gastrointestinal, systemic, emotional and social disturbances using nine questions. Responses for each question are scored on a 7-point Likert scale in which 7 corresponds to the highest level of functioning. It has been shown that this questionnaire score is statistically significantly correlated with clinical and colonoscopy scores (11). This questionnaire is linguistically validated in the Iranian population (13). Patients were asked not to change their diet and their physical activities during the study period. They were also asked to inform the researcher of any changes made in the type or dosage of the drugs or of any disease relapse causing hospitalization and prevent taking supplements afterwards.

Ethical Considerations

The study protocol was approved by the medical ethics committee of NNFTRI, SBMU with certificate No 46477. The research has also been registered in the Iranian Center for Clinical Trials (No. IRCT201209154010N10) and is accessible at the following website: www.irct.ir.

Patients

Patients were selected from those who were referred to the Gastroenterology Clinic of Imam Khomeini Hospital, Tehran, Iran, considering underlying inclusion criteria: their tendency to take part in the study, mild to moderate active ulcerative colitis, males and females ≥18 years of age and

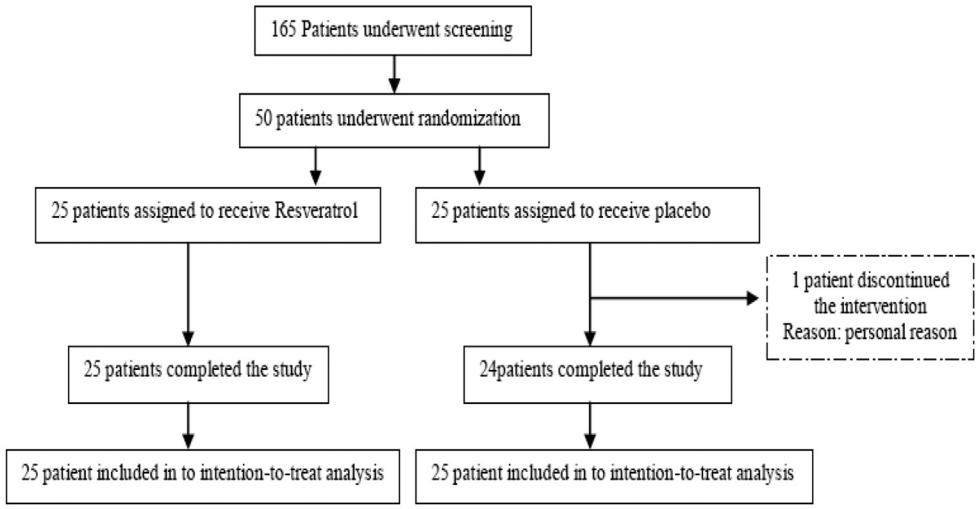

Figure 1. Patient enrollment flow chart.