PharmaNutrition 5 (2017) 47–51

Contents lists available at ScienceDirect

PharmaNutrition

journal homepage: www.elsevier.com/locate/phanu

Vitamin C supplementation and serum uric acid: A reaction to hyperuricemia and gout disease

Firas S. Azzeh[a,*], Abrar H. Al-Hebshi[a], Haya D. Al-Essimii[a], Mohammed A. Alarjah[b]

[a] Department of Clinical Nutrition, Collage of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia
[b] Pharmaceutical Chemistry, College of Pharmacy, Umm Al-Qura University, Makkah, Saudi Arabia

ARTICLE INFO

Article history:
Received 21 November 2016
Received in revised form 4 February 2017
Accepted 7 February 2017
Available online 11 February 2017

Keywords:
Vitamin C
Hyperuricemia
Gout
Glomerular filtration rate

ABSTRACT

Hyperuricemia and gout are commonly diagnosed in subjects with abnormal purine metabolism. Hyperuricemia is the earliest stage of the gout disease, which is the most common cause of inflammatory arthritis in males over 40 years and females over 60 years old. This work was design to investigate the effect of vitamin C supplements on the serum level of uric acid (UA) in patients suffering from either hyperuricemia or gout disease. The serum creatinine (Cr) level and glomerular filtration rate (GFR) were measured before and after the treatment with vitamin C to study if this treatment would improve the functionality of the renal system of such patients. Thirty males and females' patient were divided into two groups based on their disease condition; hyperuricemia group and gout group 15 patients each, and patients were given 500 mg vitamin C chewable tablet daily for two consecutive months. By the end of the treatment period, the UA level decreased ($P < 0.05$) in the blood of the hyperuricemic individuals, while no significant change was seen on the serum UA concentration in the gouty patients. Additionally, there was no significant effect on the serum creatinine level or on the GFR in both study groups. In conclusion, 500 mg vitamin C oral daily dosing might be of the therapeutic value in lowering UA levels in hyperuricemic patients.

1. Introduction

Hyperuricemia is the precursor of gout disease and it is characterised by a chronic elevation of serum uric acid (UA) [1]. A recent systematic review of population-based epidemiological studies showed a high prevalence of hyperuricemia throughout all regions of the world [2], and Saudi Arabia alone has a hyperuricemia prevalence of 8% [3]. In a 5-year follow-up, 18.8% of the patients with hyperuricemia developed gout [4]. Gout is a disease in which deposits monosodium urate crystal occurs in peripheral joints causing episodes of acute pain [2]. The global burden of gout disease has increased in many parts of the world over the past decade, which is the most common cause of inflammatory arthritis in males over 40 years and females over 60 years old [5].

The uricosuric effect of vitamin C may increase the attention of its therapeutic use in hyperuricemic individuals. Recently, findings of a prospective cohort study suggested that vitamin C supplementation has a reduction effect on serum UA concentrations that might be beneficial in the prevention of gout [6]. The results of a meta-analysis of 13 randomized controlled trials support the potential evidence for the inverse association between increased vitamin C intake and the risk of hyperuricemia [7]. Where both vitamin C and UA have similar antioxidant properties, it has been reported that supplementation with the former reduces the serum level of the latter [8]. This antagonistic relationship could decrease the antioxidant capacity of UA in the body, but vitamin C has the ability to recompense this attenuation [8]. Underlying mechanisms have been proposed to the uricosuric effect of vitamin C are explained by either increase the glomerular filtration rate (GFR) or competition for renal reabsorption of UA [9].

The purpose of this study is to determine the effect of vitamin C supplements on the level of serum UA, serum creatinine (Cr) level and GFR in different phases of gout disease include asymptomatic hyperuricemia and gouty arthritis. To the best of our knowledge, this is the first comparison study which investigates this effect through hyperuricemic subjects and gouty patients among Saudi population.

Abbreviations: Cr, creatinine; GFR, glomerular filtration rate; GG, gout group; HUG, hyperuricemia group; UA, uric acid.

* Corresponding author at: Department of Clinical Nutrition, Faculty of Applied Medical Sciences, Umm Al-Qura University, P.O. Box: 7067, Makkah (21955), Saudi Arabia.
E-mail address: fsazzeh@uqu.edu.sa (F.S. Azzeh).

http://dx.doi.org/10.1016/j.phanu.2017.02.002
2213-4344/

2. Materials and methods

2.1. Subjects

Thirty adults from both genders aged 24–75 years old with hyperuricemia (serum UA >6 mg/dl for females and >7 mg/dl for males) or diagnosed with gout before at least one year were recruited from Doctor Abdulrahman Taha Bakhsh Hospital in Jeddah (Saudi Arabia). Exclusion criteria were patients less than 20 years, history of dialysis, alcohol consumption, pregnant or lactating women, muti-vitamins supplements during the last three months, and diuretic drug and/or any uricosuric agent (such as Allopurinol drug) usage. This study was permitted by the Ethical Committee of Umm Al-Qura University, Mecca, Saudi Arabia, following the rules of the Declaration of Helsinki. All eligible subjects completed the consent form before they participated in the study.

2.2. Study protocol

This experimental trial started in April 2013 and ended in June 2013. Eligible persons were assigned into two study groups; hyperuricemia (HUG; n = 15) and gout (GG; n = 15) groups. Nine and seven males were recruited in GG and HUG, respectively. Groups were matched for their age, gender, BMI, serum UA, and serum Cr level. At the beginning of this work, a basic information questionnaire was filled by each participant, including personal information, medical and drug history information, family history with hyperuricemia, and anthropometric measurements. Nutritional counseling about their disease, the relation between vitamin C and the disease, avoidance of high purine foods, medical conditions that could affect health status and other nutritional recommendations were all explained to the patients by trained dietitians. Each participant supplemented with 500 mg/day vitamin C chewable tablets (Tabuk Pharmaceutical Manufacturing Company, Tabuk, KSA), which were purchased from the local pharmacies. All applicants were followed-up for 8 weeks. Therefore, blood samples were collected two times from each participant; at the beginning and at the end of study period.

2.3. Biochemical analyses

Blood samples were withdrawn after twelve hours fasting, then they were centrifuged at 4500 rpm for 6 min at room temperature by normal centrifuge. Serum specimens were portioned and stored at −30 °C for biochemical tests. Serum UA and Cr concentrations were analyzed using Dimension Vista System instrument (SIEMEMS, Camberley, UK) available in the hospital. Estimated GFR in ml/min/1.73 m^2 was calculated according to the Modification of Diet in Renal Disease equation by Levey et al. [10] as: GFR = 186 × (serum creatinine in mg/dl)$^{-1.154}$ × age$^{-0.203}$ × 0.742 (if female) × 1.21 (if African origin).

2.4. Statistical analysis

Statistical analysis was performed using SPSS software (Statistic Package for Social Sciences) version 20. T-student and chi-square tests were performed to find the significant difference between continuous and categorical data, respectively. Data were presented in tables as mean and standard deviation or as frequency and percent. *P*-value <0.05 was considered statistically significant.

3. Results

All recruited subjects completed the study treatment. The baseline characteristics of participants are shown in Table 1. The mean age for GG was about 53 years and for HUG was 54 years. The mean BMI for GG and HUG were around 31 kg/m^2 and 33 kg/m^2, respectively. Average serum UA in mg/dl for GG was 8.09 and for HUG was 7.94. The mean serum Cr for GG was 1.08 mg/dl and for HUG was 1.06 mg/dl. Estimated GFR (ml/min/1.73 m^2) for GG and HUG were 79.51 and 75.15, respectively. No significant differences were observed in the previous parameters between the two groups. In addition, family history with hyperuricemia was noticed in 26.7% (n = 4) in GG and 13.3% (n = 2) in HUG. Only 3 participants in the GG and 2 in HUG were smokers. The duration of hyperuricemia was significantly ($P < 0.05$) higher in GG (40%; >5years) than HUG (73.3%; <3years), with average values of 4.67 years ± 2.16 and 2.73 years ± 1.33, respectively. No significant difference was perceived in history of kidney stones and the chronic diseases between the groups (diabetes, hypertension, hypertriglyceridemia, cardiovascular diseases, and thyroid disorders; Table 1).

Table 2 demonstrates UA, Cr, and GFR values for the study groups during 2 months study period. The mean serum UA at zero time for GG (8.09 mg/dl) was not significantly different than HUG (7.94 mg/dl). After two months, serum UA for GG increased ($P > 0.05$) and for HUG decreased ($P < 0.05$). Average Cr level slightly decreased for both groups after 8 weeks, with slight increase in GFR, both changes were statistically insignificant.

Table 3 shows the average changes in UA for GG and HUG during the study period. For GG, UA showed insignificant change after 2 months by about +0.3 ± 0.14 mg/dl, while HUG showed a significant ($P < 0.05$) decrease in UA after 2 months of study period by about −0.78 ± 0.3 mg/dl. The reduction of UA was slightly higher for women than men.

4. Discussion

Dietary approaches have long been identified as important factors in management and prevention of hyperuricemia and related diseases. In this study, supplementation with vitamin C at 500 mg/day for 8 weeks significantly ($P < 0.05$) decreased serum UA in hyperuricemic individuals (−0.78 mg/dl) compared to an insignificant increase of serum UA in patients with gout disease (+0.3 mg/dl). These findings are in accordance with Huang et al. [9] who reported an inverse correlation of serum UA with serum ascorbic acid in hyperuricemic individuals after 2 months supplementation of vitamin C (500 mg/day) ($P < 0.001$) compared to placebo group (mean changes −0.5 mg/dl and +0.09 mg/dl, respectively). Additionally, our findings strongly agree with Stamp et al. [11] who found no significant difference in serum UA levels between gout patients group who did or did not take vitamin C supplementation (500 mg/day) after 8 weeks, despite the increase in plasma ascorbate levels. Likewise, many other meta-analysis of randomized controlled trails and cross-sectional studies have reported the urate lowering effects of modest oral dosage of vitamin C supplements in hyperuricemic subjects, as well as the promising role of this vitamin in reduction the risk of gout [1,6,7,12]. Although, these previuos papers have evaluated the efficacy of oral vitamin C supplementaion on UA level, Biniaz et al. [13] found that post-heamodialysis intravenous injection of vitamin C in hyperuricemic chronic kidney disease patients significantly reduced serum UA levels in comparison to control group ($P = 0.09$ and $P = 0.39$). However, no control group was considered in this work, but it is existed in previous research by Kensarah and Azzeh [14] in which they studied the effect of dietary and supplemental vitamin C (500 mg/day) on serum UA at similar conditions and region. At baseline, the mean age and serum UA of the control group (n = 10) were 58 years ± 12 and 8.85 (mg/dl) ± 2.1, respectively. The average increament in serum UA for the control group after 2 months was +0.51 mg/dl. This result