ORIGINAL RESEARCH—EPIDEMIOLOGY

Serum Uric Acid as a Risk Predictor for Erectile Dysfunction

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ABSTRACT

Introduction. Serum uric acid (UA) is now beginning to be considered a risk predictor for cardiovascular diseases. However, little is known about the effect of hyperuricemia on the risk of developing other systemic vascular disorders, especially erectile dysfunction (ED).

Aim. To evaluate whether serum UA is a predicting factor for ED while adjusting for other common risk factors.

Methods. Two hundred fifty-one patients aged 45.2 ± 10.1 years with newly diagnosed and documented ED and 252 age-matched participants without ED (aged 45.1 ± 8.4 years) were enrolled in this case–control study. Univariate and multivariate logistic regression analysis were performed to assess the effect of serum UA on ED; odds ratio (OR) and 95% confidence interval (CI) were calculated. Adjustments were made for potential confounding factors, including obesity, hypertension, diabetes, dyslipidemia, serum triglyceride, and smoking.

Main Outcome Measurement. Serum UA concentration and the distribution of potential ED risk factors (age, smoking, lipid profile, hypertension, obesity, and diabetes mellitus) were evaluated. Serum UA levels were organized into tertiles. The five-item International Index of Erectile Function was used to evaluate the presence and the severity of ED.

Results. The mean serum UA levels in ED-positive and ED-negative groups were 6.12 ± 1.55 mg/dL and 4.97 ± 1.09 mg/dL, respectively ($P < 0.001$). On analysis of unadjusted variables, statistically significant differences were found for all variables, including serum UA, between ED-positive and ED-negative groups. After adjustment for major risk factors, a significant trend of increasing risk was found for serum UA concentration (OR 5.95, 95% CI 2.96–11.97; $P < 0.001$, comparing the highest with the lowest tertile). An increase of 1 mg/dL in serum UA level was associated with an approximately twofold increase in risk of ED (OR 2.07; 95% CI 1.63–2.64).

Conclusions. Our findings reveal that serum UA can be considered a risk predictor for ED. Furthermore, hyperuricemia can be regarded as an independent risk factor in addition to the established ones. **Salem S, Mehrsai A, Heydari R, and Pourmand G. Serum uric acid as a risk predictor for erectile dysfunction. J Sex Med 2014;11:1118–1124.**

Key Words. Erectile Dysfunction; Serum Uric Acid; Cardiovascular Disease; Risk Factors; Predicting Marker; Metabolic Syndrome

Introduction

Erectile dysfunction (ED), defined as the persistent inability to reach or maintain penile erection sufficient for a satisfactory sexual performance, is a major health issue with a growing number of cases [1,2]. The estimated prevalence of ED for 2025 will be 322 million men worldwide, and it affects approximately 15% of the male population annually [3]. Nowadays, evidence is being accumulated in favor of a vascular etiology of ED, rather than a psychogenic cause [4,5]. ED not only shares many common risk factors with cardiovascular disease (CVD) but is also recognized as an incremental risk predictor for CVD. Exposure to risk factors including hypertension,

diabetes mellitus, hypercholesterolemia, smoking, obesity, and aging leads to endothelial dysfunction and ultimately vascular obstruction in all vascular beds [2,5–7]. Nevertheless, there might be some undetermined risk factors the effects of which on the development and progression of CVD and ED have yet to be identified.

Serum uric acid (UA) is associated with endothelial dysfunction, oxidative stress, and inflammation and is now beginning to be considered as a risk predictor for CVD [8–12]. However, little is known about the effect of hyperuricemia on the risk of developing other systemic vascular disorders, especially ED.

Considering the probable relation between serum UA and vascular diseases and the ease and cost-effectiveness of therapy to lower serum UA, the potential role of hyperuricemia in ED, and consequently CVD, needs to be investigated to reduce harms and improve the management of vascular events.

This study aims to evaluate the role of serum UA as a potential predicting factor for ED while adjusting for other common risk factors.

Methods

Study Population

This case–control study received ethical committee approval and recruited 251 patients with newly diagnosed and documented ED (cases) and 252 age-matched participants without a clinical history or evidence of ED (controls), all of whom gave their written informed consent to take part in this study conducted at our referral center.

Patients with a previous history of pelvic surgery or trauma, hepatic or renal diseases, psychological conditions, endocrine diseases (except diabetes mellitus), cancer of the prostate or any other organs, terminal cardiac disease, substance abuse, central or peripheral nervous system diseases, or any other morbid and debilitating diseases correlated with the genitourinary system, including Peyronie's disease, were excluded from this study.

All participants were married men with a permanent sexual partner. Furthermore, in order to minimize the possible effects of pharmacological treatments on our participants, we recruited only new patients who had not been previously diagnosed with ED or prescribed any phosphodiesterase-5 inhibitors or exogenous androgen supplementation.

Main Outcome Measurements

Serum UA concentration and the distribution of potential ED risk factors (age, smoking, lipid profile, hypertension, obesity, and diabetes) were evaluated in both groups. All participants underwent a clinical evaluation including taking of a brief medical and psychosexual history, questions as to medication used and smoking habits, and measurement of height, weight, blood pressure (BP), fasting blood sugar (FBS), triglyceride, cholesterol, HDL, and LDL levels using standard protocols. Moreover, ED was documented and quantified via the five-item International Index of Erectile Function (IIEF-5) questionnaire.

Patients were considered to have baseline hypertension if they had systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, used BP medications, or had a documented history of hypertension (stage I or II). Patients were considered to have diabetes mellitus if they had FBS ≥126 mg/dL, used diabetes medications, or had a documented history of diabetes. Hypertriglyceridemia was defined as fasting triglyceride ≥200 mg/dL. Patients were considered to have hypercholesterolemia if they had fasting total cholesterol ≥240 mg/dL, used medication for cholesterol, or had a documented history of fasting total cholesterol ≥240 mg/dL. Patients were considered to have high LDL if they had current fasting plasma LDL ≥160 mg/dL or a documented history of LDL ≥160 mg/dL. Cutoffs for total cholesterol, LDL, HDL, and triglyceride levels are similar to those used for the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines [13]. Obesity was defined as body mass index (BMI) ≥30 kg/m^2. For the purposes of this study, patients were classified into three categories according to serum UA levels, which were defined according to distribution of UA levels in the control group as follows: <4.5, 4.5–5.6, and >5.6 mg/dL.

All participants were asked to complete the IIEF-5 questionnaire. This questionnaire is an abbreviated form of the IIEF, used to diagnose ED, with four items selected from the erectile function domain portion of the IIEF and one addressing sexual satisfaction; it has been validated and correlated with patient reports of ED [14]. The erectile function domain score was calculated as the sum of questions 1 through 5 for men who answered the IIEF-5 completely. The degree of ED was classified according to the erectile function domain score as severe (5–7), moderate