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Relationship between hyperuricemia and erectile dysfunction on hypertension patients

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ABSTRACT

Hypertension is a major non-communicable disease worldwide including in Indonesia. It can cuase erectile dysfunction through vasculogenic pathway. Uric acid level could be a promising biomarker to predict erectile dysfunction due to it is related to endothelial dysfunction, microvascular disease, and hypertension. The aim of this study was to evaluate the relationship between hyperuricemia and erectile dysfunction on hypertension patients. This was an observational study with cross-sectional design involving 88 male hypertension patients aged more than 18 years who registered as outpatient in the Bethesda Lempuyangwangi Public Hospital, Yogyakarta. Hyperuricemia was measured using uricase method and erectile dysfunction was measured using IIEF-5 form. The results showed that hyperuricemia (OR=3.89; CI 95% 1.08-15.70; p=0.017), blood pressure (OR=6.84; CI 95% 2.35-20.6; p<0.001), and age (p<0.001) are related with erectile dysfunction on the hypertension patients. Furthermore, logistic regression analysis showed that hyperuricemia, age, and blood pressure simultaneously affect the erectile dysfunction occurance, with good calibration (p=0.167) and discriminative level (0.8604). In conclusion, there is significantly relationship between hyperuricemia and erectile dysfunction on hypertension patients.

ABSTRAK

Hipertensi adalah penyakit tidak menular utama di dunia termasuk di Indonesia. Hipertensi dapat menyebabkan disfungsi ereksi melalui jalur vaskulogenik. Kadar asam urat dapat menjadi biomarker yang menjanjikan untuk memperkirakan kejadian disfungsi ereksi Karena berkaitan dengan disgungsi endotel, penyakit mikrovaskular dan hipertensi. Tujuan penelitian ini adalah mengkaji hubungan antara hiperurisemia dan disfungsi ereksi pada penderita hipertensi. Penelitian ini merupakan penelitian observasi dengan rancangan potong lintang yang melibatkan 88 penderita hipertensi pria berumur lebih dari 18 tahun yang terdaftar di Rumah Sakit Bathesda Lempuyangwangi, Yogyakarta. Hiperurisemia ditetapkan dengan metode urikase dan disfungsi ereksi diukur menggunakan form IIEF-5. Hasil penelitian menunjukkan hiperurisemia (OR=3,89; CI 95% 1,08-15,70; p=0,017), tekanan darah (OR=6,84; CI 95% 2,35-20,6; p<0,001), dan usia (p<0,001) berkaitan dengan disfungsi ereksi pada penderita hipertensi. Selanjutnya pada analisis regresi logistik menunjukkan hiperurisemia, usia, dan tekanan darah secara bersama-sama mempengaruhi kejadian disfungsi ereksi dengan nilai kalibrai baik (p=0,167) dan tingkat diskriminatif yang baik (0,8604). Dapat disimpulkan, terdapat hubungan bermakna antara hiperurisemia dengan disfungsi ereksi pada penderita hipertensi.

Keywords:
erectile dysfunction
hyperuricemia
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age

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INTRODUCTION

Hypertension is as major health problem worldwide including in Indonesia.[1] Indonesia's 2013 Basic Health Research (*Riset Kesehatan Dasar* 2013/ *Riskesdas* 2013) reported that prevalence of hypertension on population aged at least 18 years old is 25.8%. Top three provinces with hypertensive population are Bangka Belitung, South Kalimantan, East Kalimantan, respectively.[2]

Uric acid is end-product of purine metabolism in human. High blood uric acid level or hyperuricemia is related to cardiovascular disease, hypertension, stroke, metabolic syndrome and chronic kidney disease.[3] Globally, prevalence of hyperuricemia was reported about 18%.[4] In Banyumas, Central Java, the prevalence of hyperuricemia is 21.15%,[5] whereas in Karangasem, Bali, the prevalence is just 18.8%.[6]

Erectile dysfunction is defined as persistent inability to attain or maintain a penile erection sufficient for satisfying sexual intercourse.[7] This condition can be caused by physical or psychological factors. The physical factors can be further categorized as hormonal, neurogenic, iatrogenic and vasculogenic factors.[8] Hypertensive patients are vulnerable to develop erectile dysfunction, especially through vasculogenic factors. In this setting, serum uric acid level can be used as potential biomarker to predict decline of erectile function as hyperuricemia is related to endothelial dysfunction, microvascular diseases and hypertension.[9] The aimed of this study was to examine the relationship between hyperuricemia and erectile dysfunction on hypertension patients in Bethesda Lempuyangwangi Hospital, Yogyakarta.

MATERIALS AND METHODS

Patients

This was an observational study withcross-sectional design conducted in the Bethesda Lempuyangwangi Hospital, Yogyakarta from May to June 2016. Population of this study was male hypertension patients, aged at least 18 years old and registered as outpatient in the hospital. The sampling technique used was consecutive sampling method. Using particular formula for estimating sample size,[10] with previous prevalence of erectile dysfunction on hypertension patientsis 35.2%,[11] and accuracy level of 0.1. Eighty-eight male hypertension patients were recruited in this study.

All of the subjects must meet these inclusion criteria included married, wife was still alive, sexually active on the last three months, has been diagnosed with hypertension by health officer and giving consent to participate in this study. Exclusion criteria for potential subjects to be screened out were having communication problem, underwent urologic surgery, routinely or occasionally on hemodialysis, previously diagnosed with cancer, chronic kidney disease, diabetes mellitus or stroke.

Protocol of study

Independent variable in this study was hyperuricemia and the dependent variable was erectile dysfunction. Potential confounder fators that being investigated in this study were age, blood pressure categorization, hypercholesterolemia, smoking and purine intake (frequency of food rich in purine consumption).

Hyperuricemia is defined as increased uric acid level above normal level.[12] This study used laboratorium assay with uricase enzymatic method with normal range of 3.5-7.2 mg/dL. Erectile dysfunction was the consistent or recurrentinability of a man to attain and/or maintain apenile erection sufficient for sexual performance, with limitation of "recurrent inability" as being 3 months or greater induration.[13]

The five items International Index of Erectile Function (IIEF-5)[14] questionnaire in *Bahasa Indonesia*[8] (internal validity value of 0.574-0.738 and the Cronbach's alpha is 0.707)[15] used in this study, with normal range of 22-25.[16]

Hypertension is defined by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg measured on someone aged 18 or older.[17] Generally, therapeutic target for hypertension patients is systolic blood pressure <140 mmHg or diastolic blood pressure <90 mmHg. So if a patient could achieve that goal, he/she is categorized as controlled hypertension patient. Otherwise, if the measurement is still showing high blood pressure, he/she is categorized as uncontrolled hypertension patient. On this study, blood pressure measurements were conducted on right arm.

Subjects would be categorized based on the smoking habit, subject who still smoke or having history as smoker was categorized as ever smoking person, otherwise was categorized as never smoking person. Purine intake was frequency of purine-rich food consumption on daily basis, without considering the quantity of the food being consumed. To obtain that data, subjects were being interviewed about frequency of consumption of several items of food in the last 30 days and then deriving the daily frequency from the FFQ form.[18] Protocol of this study has been approved by the Medical and Health Research Ethics Committee, Faculty of Medecine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta (Ref. KE/FK/414/EC/2016).

Statistical analysis

Data were presented as mean ± standard deviation (SD) or median (min-max) and analyzed by Stata® 13. Multivariat analysis was conducted to control the confounders by logistic regression test.

RESULTS

The characteristics of patients are presented on TABLE 1. Mean of patients age were 54.6 ± 12.7 years old. Most of the patients had finished high school (38.64%), only 12.5% of subjects had a diploma or higher education levels. Serum uric acid level of 18.18% patients were categorized as higher than normal and 42.05% patients were detected experience erectile dysfunction by IIEF scoring.

TABLE 1. Characteristics of male hypertension patients

Characteristics	Value
Age (mean ± SD years)	54.6 ± 12.7
Educational level [n (%)]	
• Unfinished elementary school	11 (12.50)
• Elementary school	20 (22.73)
• Junior high school	12 (13.64)
• High school	34 (38.64)
• Diploma or higher	11 (12.50)
Occupation [n (%)]	
• Labor	3 (3.41)
• Private enterprise	16 (18.18)

• Civil servant/police/army	9 (10.23)
• Entrepreneur	22 (25.00)
• Jobless/retired	14 (15.91)
• Other	24 (27.27)
Blood pressure [n (%)]	
• Controlled (<140/90 mmHg)	57 (64.77)
• Uncontrolled (≥140/90 mmHg)	31 (35.23)
High cholesterol level history [n (%)]	
• Yes	19 (21.59)
• No	69 (78.41)
Smoking [n (%)]	
• Ever	74 (84.09)
• Never	14 (15.91)
Purine intake [median (min-max) times/day]	2.67 (0.3-7.259)
Hyperuricemia [n (%)]	
• Yes	16 (18.18)
• No	72 (81.82)
Erectile dysfunction [n (%)]	
• Yes	37 (42.05)
• No	51 (57.95)

The relationship between categorical variables and erectile dysfunction was analyzed using Chi-squared test (TABLE 2), whereas the relationship between numerical variables and erectile dysfunction was analyzed using t-test or Mann-Whitney test (TABLE 3). The blood pressure and age of hypertension patients were related with the erectile dysfunction on hyprtention patients.

TABLE 2. Relationship between categorical variables and erectile dysfunction on hypertension patients

Variables	Erectile dysfunction				p*	OR	95%CI
	Yes		No				
	n	%	n	%			
Hyperuricemia							
• Yes	11	68.7	5	31.3	0.017	3.89	1.08-15.7
• No	26	36.1	46	63.9			
Bloodpressure							
• Uncontrolled	22	71	9	29	<0.001	6.84	2.35-20.6
• Controlled	15	26.3	42	73.7			
Highcholesterol							
• Yes	10	52.6	9	47.4	0.291	1.73	0.55-5.48
• No	27	39.1	42	60.9			
Smoking							
• Ever	32	43.2	42	56.8	0.601	1.37	0.37-5.72
• Never	5	35.7	9	64.3			

*Chi-squared test

TABLE 3. Relationship between categorical variables and erectile dysfunction on hypertension patients

Variables	Erectile dysfunction		p
	Yes (n=37)	No (n=51)	
Age [mean ± SD]	62.4 ± 11.6	49.0 ± 10.3	<0.001*
Purine intake [median (min-max)]	2.52 (0.53-7.26)	2.73 (0.3-6.05)	0.106**

* = independent t-test, ** = Mann-Whitney test

Logistic regression model of the varibales and erectile dysfunction on hypertension patients is presented on TABLE 4. Furthermore, logistic regression analysis showed that hyperuricemia, age, and blood pressure simultaneously affect the erectile dysfunction occurance, with good calibration (p=0.167) and discriminative level (0.8604).

TABLE 4. Logistic regression model of the varibales and erectile dysfunction on hypertension patients

Variables	Coefficient	OR	p	95%CI
Hyperuricemia	1.696	5.45	0.022	1.27-23.40
Age	0.113	1.12	<0.001	1.05-1.19
Bloodpressure	1.335	3.80	0.020	1.24-11.68
Constanta	-7.458	0.00	<0.001	0.00-0.02

DISCUSSION

Prevalence of erectile dysfunction in this study (42.05%) is higher than previous study (35.2%).[11] The Asian people with their culture tend to keep private condition securely, so this finding still can be assumed as an under-reporting finding.

Multivariate analysis showed that hyperuricemia, age and blood pressure were associated with the prevalence of erectile dysfunction (p<0.05). Meanwhile, purine intake, high cholesterol level history, and smoking were not.

Hyperuricemia (OR=3.89; 95% CI 1.08-15.7; p=0.017) showed as significant risk factor of prevalence of erectile dysfunction.

Age as an important factor of erectile dysfunction has been reported previously. Older age are related to higher prevalence of erectile dysfunction.[19] In this study, the patients with erectile dysfunction were 13.4 year older than thos non-erectile dysfunction. It was higher than previous study.[9] Aging male will experience physical and psychological alteration, especially chronic diseases that role as major risk factors of erectile dysfunction.[19]Uncontrolled blood pressure (OR=6.84; 95%CI 2.35-20.6; p<0.001) was also as major risk factor of erectile dysfunction. Endothelial dysfunction and microvascular diseases are underlying mechanisms of this finding. Uncontrolled blood pressure for long time could contribute to kidney impairment, which leads to uremic conditionthat worsen endothelial dysfunction related to further erectile function decline.[20]In this study, there was no difference of purine intake between the patients with erectile dysfunction and they with non-erectile dysfunction. This finding is supported by a theory that considering higher effect of endogenous purine compared to purine from diet. Only one third of total uric acid actually comes from dietary intake of purine nucleotide.[21]Almost 22% of subjects reported having history of high cholesterol level, and this finding was clinically significant (OR=1.73).

But bivariate analysis showed that no statistical difference between groups (p>0.05) was observed. This finding is contrary to previous study that found a relationship between high cholesterol level with erectile dysfunction.[22]Only 16% of the subjects were never smoking, and this finding seemed contrary to other previous studies which mostly because of the different classification used. Bivariate analysis of smoking and erectile dysfunction showed that there was no statistically significant relationship, although there was clinical significancy with OR=1.37. Smoking is a well-known risk factor of erectile dysfunction, mostly by its impact to another cardiovascular risk factors of erectile dysfunction such as hypertension and coronary heart disease.[23]

CONCLUSION

There is significant relationship between hyperuricemia and erectile dysfunction on hypertension patients in Bethesda Lempuyangwangi Hospital Yogyakarta. This relationship is also affected by older age and uncontrolled blood pressure.

Health service provider should not only give medications, but also give counseling about hypertension, hyperuricemia and erectile dysfunction to every man that diagnosed with those conditions. For future research, it is better to use the cohort design to prove the causal relationship between hypertension, hyperuricemia and erectile dysfunction.

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