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血清尿酸水平与老年轻度高血压患者的内皮功能相关性分析*

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摘要 目的:探讨血清尿酸水平与老年轻度高血压患者的内皮功能相关性。**方法:**选取我院2020年1月到2020年12月共收治的200例老年轻度高血压患者作为研究对象,所有患者均为未使用过降压药物治疗,将其分为轻度高血压组。另选取同期收治的200例高血压常规药物治疗患者作为重度高血压组与200名健康者作为对照组,对比三组患者血清尿酸水平与血管内皮功能。对观察组所有患者依照血清尿酸水平进行分组,将血清尿酸水平208-360 $\mu\text{mol/L}$ 的患者分为低尿酸组,共计136例,将血清尿酸水平 $\geq 360 \mu\text{mol/L}$ 的患者分为高尿酸组,共计64例。对比两组患者的一般临床指标、血管内皮功能与氧化应激指标,并分析血清尿酸水平与老年轻度高血压患者的内皮功能相关性。**结果:**重度、轻度高血压组与对照组患者NO、ET-1、SUA水平对比差异显著,具有统计学意义($P<0.05$);高尿酸组与低尿酸组患者TG、TC、DBP、SBP水平对比无明显差异($P>0.05$),高尿酸组患者Cr水平高于低尿酸组,组间对比,差异具有统计学意义($P<0.05$);高尿酸组与低尿酸组患者T-AOC、GSH-Px、LHP、MDA、NO、ET-1水平对比差异显著,高尿酸组患者LHP、MDA和ET-1水平明显高于低尿酸组,高尿酸组患者T-AOC、GSH-Px、NO水平明显低于低尿酸组,组间对比,差异具有统计学意义($P>0.05$);Spearman相关分析结果显示:TG、TC、Cr、DBP、SBP与血尿酸水平无明显相关性($P>0.05$),T-AOC、GSH-Px、NO与血清尿酸水平呈负相关($P<0.05$),LHP、MDA、ET-1与血清尿酸水平呈正相关($P<0.05$)。**结论:**血清尿酸水平与老年轻度高血压患者的内皮功能具有明显相关性,而且证明血尿酸水平的升高可能由患者氧化应激导致,因此氧化应激水平也是引起血管内皮功能障碍的一种潜在机制,希望本研究结果能够为高血压患者的疾病控制提供参考意见。

关键词:高血压;严重程度;血清尿酸;一氧化氮;血管舒张因子

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Correlation between Serum Uric Acid Level and Endothelial Function in Elderly Patients with Mild Hypertension*

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ABSTRACT Objective: To investigate the correlation between serum uric acid level and endothelial function in elderly patients with mild hypertension. **Methods:** 200 cases of elderly patients with mild hypertension in our hospital from January 2020 to December 2020 were selected as the research object, all patients were not treated with antihypertensive drugs, and they were divided into mild hypertension group. In addition, 200 cases of patients with hypertension treated with conventional drugs in the same period were selected as the severe hypertension group and 200 healthy people as the control group. The serum uric acid level and vascular endothelial function of the three groups were compared. All patients in the observation group were grouped according to the serum uric acid level, and the serum uric acid level was $< 420 \mu\text{mol/L}$. The patients were divided into low uric acid group ($n=136$) and low uric acid group ($n=420$) $\mu\text{mol/L}$. The patients were divided into hyperuricemia group ($n=64$). The general clinical indexes, vascular endothelial function and oxidative stress indexes of the two groups were compared, and the correlation between serum uric acid level and endothelial function of elderly patients with mild hypertension was analyzed. **Results:** There were significant differences in the levels of no, ET-1 and SUA between the severe and mild hypertension groups and the control group ($P<0.05$); There was no significant difference in TG, TC, DBP and SBP levels between high uric acid group and low uric acid group ($P>0.05$). CR level in high uric acid group was higher than that in low uric acid group ($P<0.05$); The levels of T-AOC, GSH Px, LHP, MDA, no and ET-1 in high uric acid group were significantly higher than those in low uric acid group, and the levels of T-AOC, GSH PX and no in high uric acid group were significantly lower than those in low uric acid group ($P>0.05$); Spearman correlation analysis showed that TG, TC, Cr, DBP, SBP had no significant correlation with serum uric acid level ($P>0.05$), T-AOC, GSH Px, no were negatively correlated with serum uric acid level ($P<0.05$), LHP, MDA, ET-1 were positively

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correlated with serum uric acid level ($P<0.05$). **Conclusion:** Serum uric acid level is significantly correlated with endothelial function in elderly patients with mild hypertension, and it is proved that the increase of serum uric acid level may be caused by oxidative stress in patients, so oxidative stress level is also a potential mechanism of vascular endothelial dysfunction. It is hoped that the results of this study can provide reference for Disease Control of patients with hypertension.

Key words: Hypertension; Severity; Serum uric acid; Nitric oxide; Vasodilator factor

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前言

高血压是一种常见的慢性疾病,多发生在中老年人身上,现在已经成为了威胁我国人民健康的重大公共卫生问题,随着生活水平的提高,我国高血压的发病率呈现出逐年上升的态势,而且发病患者的年龄趋于年轻化^[1]。目前,血清尿酸水平被认为是心血管疾病和高血压发病率与致死率的相关独立因素^[2]。有研究发现^[3,4],血尿酸水平升高可能会导致血压水平上升。Cicero AF 等^[5]研究进一步印证了此结果,发现血尿酸水平是轻度高血压患者预后的重要指标,但是其具体影响机制尚无明确定论。近期研究发现^[6,7],尿酸水平和高血压相关强度会随着血压增长而降低,因此提示尿酸可能对轻度高血压具有重要作用。在轻度高血压患者中,内皮功能障碍是早期发生事件,但是目前对于轻度高血压患者内皮功能障碍和血清尿酸水平的相关性尚无明确定论^[8,9]。因此,为了进一步分析轻度高血压的疾病发展原理和控制方案,本文选取我院 2020 年 1 月到 2020 年 12 月共收治的 200 例老年轻度高血压患者作为研究对象,探讨血清尿酸水平与老年轻度高血压患者的内皮功能相关性,

具体报告如下。

1 资料与方法

1.1 一般资料

选取我院 2020 年 1 月到 2020 年 12 月共收治的 200 例老年轻度高血压患者作为研究对象,所有患者均为未使用过降压药物治疗,将其分为轻度高血压组。纳入标准:所有患者符合《中国高血压防治指南》中关于原发性高血压的诊断标准,且未使用过降压药物治疗^[10];口服安慰剂 2 周后患者坐位收缩压为 140-180 mmHg,舒张压为 90-109 mmHg^[11];临床资料完整;年龄 ≥ 65 岁;无免疫功能障碍;无凝血功能异常;所有患者对本研究知情并签署同意书。排除标准:对本研究所用药物过敏者;入选前一个月应用免疫抑制剂者;药物依赖者;合并恶性肿瘤者;合并严重肝肾肾功能不全者;合并冠心病、风湿性心脏病、肺心病者。另选取同期收治的 200 例高血压常规药物治疗患者作为重度高血压组与 200 名健康者作为对照组。三组患者一般资料对比无明显差异($P>0.05$),如表 1 所示。

表 1 一般资料

Table 1 General Information

Groups	n	Gender(male / female)	Average age (year)	Hypertension course (year)
Severe hypertension group	200	111/89	71.15 $\pm$ 5.03	5.25 $\pm$ 1.30
Mild hypertension group	200	113/87	71.24 $\pm$ 5.02	5.28 $\pm$ 1.33
Control group	200	109/91	70.25 $\pm$ 5.26	-

1.2 方法

采集所有患者的一般资料,包括性别、年龄、高血压病程等。并应用台式水银柱血压计测量患者的舒张压(diastolic pressure, DBP)和收缩压(systolic pressure, SBP)。取患者清晨空腹静脉血 4 mL,分离血清后,应用 OLYMPUS AU680 全自动生化分析仪检验患者的一氧化氮(nitric oxide, NO)、内皮素-1(Endothelin-1, ET-1)、血尿酸(Serum uric acid, SUA)、甘油三酯(triglyceride, TG)、总胆固醇(total cholesterol, TC)、肌酐(creatinine, Cr)水平。应用酶联免疫吸附法检测两组患者体内的总抗氧化能力(Total antioxidant capacity, T-AOC)、谷胱甘肽过氧化物酶(Glutathione peroxidase, GSH-Px)、脂质过氧化氢(Lipid hydrogen peroxide, LHP)以及丙二醛(malondialdehyde, MDA)的表达水平。

1.3 统计学方法

本研究数据采取统计学软件 SPSS 23.0 进行数据分析,计数资料以例数/百分比(n/%)表示,进行 χ^2 检验;计量资料以符

合正态分布则用均数 $\pm$ 标准差($\bar{x}\pm s$)表示,多组间比较采用 F 检验;采用 Spearman 相关分析方法分析血清尿酸水平与老年轻度高血压患者的内皮功能相关性;以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 三组患者血清尿酸水平与血管内皮功能对比分析

重度、轻度高血压组与对照组患者 NO、ET-1、SUA 水平对比差异显著,具有统计学意义($P<0.05$),如表 2 所示。

2.2 不同血清尿酸水平患者一般临床指标对比分析

高尿酸组与低尿酸组患者 TG、TC、DBP、SBP 水平对比无明显差异($P>0.05$),高尿酸组患者 Cr 水平高于低尿酸组,组间对比,差异具有统计学意义($P<0.05$),如表 3 所示。

2.3 不同血清尿酸水平患者氧化应激指标与血管内皮功能对比分析

高尿酸组与低尿酸组患者 T-AOC、GSH-Px、LHP、MDA、

NO、ET-1 水平对比差异显著,高尿酸组患者 LHP、MDA 和 NO 水平明显低于低尿酸组,组间对比,差异具有统计学意义 ET-1 水平明显高于低尿酸组,高尿酸组患者 T-AOC、GSH-Px、($P>0.05$),如表 4 所示。

表 2 三组患者血清尿酸水平与血管内皮功能对比分析

Table 2 Comparative analysis of serum uric acid level and vascular endothelial function in the three patients

Groups	n	NO($\mu\text{mol/L}$)	ET-1(ng/L)	SUA($\mu\text{mol/L}$)
Severe hypertension group	200	18.59 $\pm$ 4.78	95.24 $\pm$ 6.34	521.23 $\pm$ 105.11
Mild hypertension group	200	25.28 $\pm$ 5.19	86.85 $\pm$ 4.25	442.46 $\pm$ 83.34
Control group	200	31.76 $\pm$ 6.89	75.07 $\pm$ 3.36	357.54 $\pm$ 58.30
F	-	133.767	855.708	187.965
P		0.001	0.001	0.001

表 3 不同血清尿酸水平患者一般临床指标对比分析

Table 3 Comparison and analysis of the general clinical indexes of patients with different serum uric acid levels

Groups	n	TG(mmol/L)	TC(mmol/L)	Cr($\mu\text{mol/L}$)	DBP(mmHg)	SBP(mmHg)
High-level uric acid group	64	1.87 $\pm$ 0.31	4.45 $\pm$ 0.52	78.56 $\pm$ 6.36*	78.36 $\pm$ 6.74	152.56 $\pm$ 4.35
Low-level uric acid group	136	1.83 $\pm$ 0.35	4.54 $\pm$ 0.63	61.25 $\pm$ 5.25	79.47 $\pm$ 5.36	153.57 $\pm$ 3.25

Note: Compared with the low-level uric acid group, * $P<0.05$.

表 4 不同血清尿酸水平患者氧化应激指标与血管内皮功能对比分析

Table 4 Comparative Analysis of Oxidation Stress Index and Vascular Endothelial Function in Patients with Different Serum Acid Level

Groups	n	T-AOC(U/mL)	GSH-Px(pg/mL)	LHP($\mu\text{mol/L}$)	MDA($\mu\text{mol/L}$)	NO($\mu\text{mol/L}$)	ET-1(ng/L)
High-level uric acid group	64	26.70 $\pm$ 3.85*	64.87 $\pm$ 6.70*	30.42 $\pm$ 3.97*	23.53 $\pm$ 3.39*	20.25 $\pm$ 3.45*	88.35 $\pm$ 4.52*
Low-level uric acid group	136	40.62 $\pm$ 4.05	77.76 $\pm$ 7.40	15.85 $\pm$ 1.07	11.59 $\pm$ 3.49	27.52 $\pm$ 3.57	81.25 $\pm$ 5.26

Note: Compared with the low-level uric acid group, * $P<0.05$.

2.4 血清尿酸水平与老年轻度高血压患者的内皮功能相关性

Spearman 相关分析结果显示;TG、TC、Cr、DBP、SBP 与血清尿酸水平无明显相关性 ($P>0.05$),T-AOC、GSH-Px、NO 与血清尿酸水平呈负相关($P<0.05$),LHP、MDA、ET-1 与血清尿酸水平呈正相关($P<0.05$),如表 5 所示。

表 5 血清尿酸水平与老年轻度高血压患者的内皮功能相关性

Table 5 Correlation between serum uric acid levels and endothelial function in elderly patients with mild hypertension

Index	Serum uric acid levels	
	r	P
TG	0.242	0.104
TC	0.231	0.107
Cr	0.127	0.263
DBP	0.245	0.109
SBP	0.184	0.223
T-AOC	-0.325	0.069
GSH-Px	-0.424	0.025
LHP	0.625	0.008
MDA	0.586	0.013
NO	-0.579	0.018
ET-1	0.374	0.009

3 讨论

原发性高血压是心血管疾病发生的重要危险因素,导致患者靶器官损害和多种并发症的发生^[12]。近年来,多项研究发现,炎症反应在高血压的发生发展中起到重要作用,而炎症因子对于内皮细胞所产生的损害,容易造成血管内皮功能障碍,加重高血压,最终导致恶性循环^[13-15]。血管内皮是一个具有调节血管再生、稳态,并预防血栓形成的重要功能,血管内皮功能障碍是许多冠心病、脑卒中、高血压等多种心脑血管疾病发展的重要基础^[16]。研究发现^[17,18],受损的内皮功能具有明显的可逆性,能够通过改善生活方式和药物治疗,使血管内皮功能恢复正常。然而,对于轻度高血压患者来说,由于病情较轻,所以是否应用药物进行治疗还存在一定争议。因此,越来越多学者开始针对高血压的发生机制与日常监测指标展开深入研究。有学者发现^[19],原发性高血压与高尿酸血症具有一定关系。

多项动物实验和人体实验研究发现^[20,21],血尿酸水平是导致轻度高血压的原因,但是具体机制尚无明确定论。而对于血管内皮功能的研究成为了当前血管生物学领域的一个重点研究内容。因此,对于血清尿酸水平与老年轻度高血压患者的内皮功能关系的研究,对临床高血压疾病的控制与预防具有重要价值。本研究结果表明:重度、轻度高血压组与对照组患者 NO、ET-1、SUA 水平对比差异显著,具有统计学意义($P<0.05$),由此证明,高血压的严重程度与一氧化氮、内皮素-1 和血尿酸水平具有一定关系,与 Yu FN 等^[22]研究相似,具体为:应用依那普

利尿酸片联合银杏叶提取物治疗能够提升高血压患者的血管内皮功能,而且患者治疗后血尿酸水平降低。另有研究发现^[23-25],血尿酸水平与血管内皮功能与慢性心衰患者的心功能和高血压具有一定关系,与本研究结果相符;高尿酸组与低尿酸组患者 TG、TC、DBP、SBP 水平对比无明显差异 ($P>0.05$),高尿酸组患者 Cr 水平高于低尿酸组,组间对比,差异具有统计学意义 ($P<0.05$)。虽然人们很早就认识到尿酸具有抗氧化作用,但是随着血尿酸的浓度升高对机体所产生的损伤也会逐渐加大,因此,可发现血尿酸是具有双重作用的^[26]。因此,本研究中,将血尿酸以 $208-360\ \mu\text{mol/L}$ 和 $>360\ \mu\text{mol/L}$ 进行分组,前者为血尿酸水平正常者,后者为血尿酸水平异常者。本研究发现,血尿酸水平与 TG、TC、DBP、SBP 水平无明显关系,可能与 Cr 水平具有一定关系,与 Redon P 等^[27]研究结果相似,即:不同血尿酸水平的单纯收缩期高血压患者的空腹血糖、甘油三酯、总胆固醇、收缩压与舒张压对比无明显差异 ($P>0.05$)。但是与以往研究不同的是本研究在一般指标中加入了肌酐水平研究,发现不同血尿酸水平患者可能存在肌酐水平差异,但具体机制还有待于后续深入研究;高尿酸组与低尿酸组患者 T-AOC、GSH-Px、LHP、MDA、NO、ET-1 水平对比差异显著,高尿酸组患者 LHP、MDA 和 ET-1 水平明显高于低尿酸组,高尿酸组患者 T-AOC、GSH-Px、NO 水平明显低于低尿酸组,组间对比,差异具有统计学意义 ($P>0.05$),由此证明,患者尿酸水平升高,导致机体的抗氧化系统失衡,引发内皮功能障碍。有研究发现^[28,29],高血压本身就有可能引发大血管病变与微血管损害。微血管受损导致组织缺氧,不仅使血中乳酸水平增高导致肾脏清除 UA 减少,而且使 UA 形成过程中的底物,如腺嘌呤、次黄嘌呤以及相关酶增多,与本研究结果相似;Spearman 相关分析结果显示: TG、TC、Cr、DBP、SBP 与血尿酸水平无明显相关性 ($P>0.05$), T-AOC、GSH-Px、NO 与血清尿酸水平呈负相关 ($P<0.05$), LHP、MDA、ET-1 与血清尿酸水平呈正相关 ($P<0.05$)由此证明,血尿酸水平可能与轻度高血压患者的氧化应激指标和内皮功能具有一定关系。Kanbay M Kanbay M 等研究发现^[30],老年高血压患者血尿酸水平和内皮功能障碍具有一定相关性,而高尿酸血症引起的氧化应激和慢性炎症可能是引起内皮功能障碍的潜在机制,与本研究相关性分析结果一致。尽管本研究设计尽量避免其混杂因素的影响,但是可能还存在一定局限性,还需后续加大样本量进行持续研究。

综上所述,血清尿酸水平与老年轻度高血压患者的内皮功能具有明显相关性,而且证明血尿酸水平的升高可能由患者氧化应激导致,因此氧化应激水平也是引起血管内皮功能障碍的一种潜在机制,希望本研究结果能够为高血压患者的疾病控制提供参考意见。

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