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原发性高血压患者 Hcy、hs-CRP 及 IL-6 水平与血压变异性的相关性研究 *

余 谦^{1,2} 卿 秀² 尧逢友² 戴宏勋² 刘 波²

(1 四川大学华西医院心内科 四川 成都 610000; 2 成都市第五人民医院心内科 四川 成都 611130)

摘要 目的:研究原发性高血压患者同型半胱氨酸(Hcy)、超敏 C 反应蛋白(hs-CRP)及白细胞介素-6(IL-6)水平与血压变异性的相关性。**方法:**选取 2016 年 2 月-2017 年 12 月四川大学华西医院收治的 180 例原发性高血压患者为研究对象。将所有患者根据 Hcy 水平的不同分为 I 组 80 例、II 组 61 例、III 组 39 例。根据 hs-CRP 水平的不同分为 A 组 71 例、B 组 68 例、C 组 41 例。根据 IL-6 水平的不同分为 D 组 80 例、E 组 61 例、F 组 39 例。对比不同 Hcy、hs-CRP 以及 IL-6 水平患者的血压变异性及空腹血糖情况,分析 Hcy、hs-CRP 及 IL-6 水平与血压变异性的相关性。**结果:**不同 Hcy 水平患者中 II 组、III 组的 24hSSD、24hDSD 水平高于 I 组,且 III 组高于 II 组($P<0.05$)。不同 hs-CRP 水平患者中 B 组、C 组的 24hSSD、24hDSD 水平高于 A 组,且 C 组高于 B 组($P<0.05$)。不同 IL-6 水平患者中 E 组、F 组的 24hSSD、24hDSD 水平高于 D 组,且 F 组高于 E 组($P<0.05$)。不同 Hcy、hs-CRP 以及 IL-6 水平患者空腹血糖水平比较差异无统计学意义 ($P>0.05$)。经 Pearson 相关性分析显示,Hcy、hs-CRP 及 IL-6 水平与 24hSSD、24hDSD 水平均呈正相关($P<0.05$)。**结论:**原发性高血压患者 Hcy、hs-CRP 及 IL-6 水平与血压变异性存在明显正相关,对空腹血糖无明显影响,值得临床重点关注。

关键词:原发性高血压;血压变异性;同型半胱氨酸;超敏 C 反应蛋白;白细胞介素-6;相关性

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Correlation of Hcy, hs-CRP and IL-6 Levels with Blood Pressure Variability in Patients with Primary Hypertension*

YU Qian^{1,2}, QING Xiu², YAO Feng-you², DAI Hong-xun², LIU Bo²

(1 Department of Cardiology, West China Hospita of Sichuan University, Chengdu, Sichuan, 610000, China;

2 Department of Cardiology, Chengdu Fifth People's Hospital, Chengdu, Sichuan, 611130, China)

ABSTRACT Objective: To study the correlation of Homocysteine (Hcy), Hypersensitive C reactive protein (hs-CRP) and Interleukin-6 (IL-6) levels with blood pressure variability in patients with primary hypertension. **Methods:** A total of 180 patients with primary hypertension, who were admitted to West China Hospita of Sichuan University from February 2016 to December 2017, were selected and were divided into group I (n=80), group II (n=61), group III (n=39) according to the difference of Hcy levels; all the patients were divided into group A (n=71), group B (n=61), group C (n=41) according to the difference of hs-CRP level; all the patients were divided into group D (n=80), group E (n=61), group F (n=39) according to the difference of IL-6 level. Blood pressure variability and fasting blood glucose in the patients with different Hcy, hs-CRP and IL-6 levels were compared; the correlation between Hcy, hs-CRP and IL-6 levels and blood pressure variability were analyzed. **Results:** The levels of 24hSSD and 24hDSD in group II and group III among the patients with different Hcy levels were higher than those in group I, and group III was higher than group II ($P<0.05$). The levels of 24hSSD and 24hDSD in group B and group C among the patients with different hs-CRP levels were higher than those in group A, and group C was higher than group B ($P<0.05$). The levels of 24hSSD and 24hDSD in group E and group F among the patients with different IL-6 levels were higher than group D, and group F was higher than group E ($P<0.05$). There were no significant differences in the level of fasting blood glucose among the patients with different Hcy, hs-CRP and IL-6 levels ($P>0.05$). The Pearson correlation analysis showed that the levels of Hcy, hs-CRP and IL-6 were positively correlated with the levels of 24hSSD and 24hDSD ($P<0.05$). **Conclusion:** The levels of Hcy, hs-CRP and IL-6 in the patients with primary hypertension are positively correlated with blood pressure variability, and there is no obvious effect on fasting blood glucose, which is worthy of clinical focus.

Key words: Primary hypertension; Blood pressure variability; Homocysteine; Hypersensitive c-reactive protein; Interleukin-6; Correlation

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作者简介:余谦(1983-),女,本科,主治医师,从事高血压方面的研究,E-mail:yzgnma@163.com

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前言

原发性高血压属于临床较为常见的心血管疾病之一,且随着近年来人们生活水平的不断提高以及饮食习惯的改变,其发病率呈逐年升高趋势^[1,2]。原发性高血压患者若未给予及时有效的治疗,随着病情的不断恶化,患者的心、脑、肾等脏器会受到不同程度的损害,威胁患者生命健康安全^[3,4]。血压变异性对心血管系统具有重要影响,且越来越多的研究证实血压变异性与高血压患者的靶器官损害以及心血管终点事件密切相关^[5,6]。动态血压不仅可有效反映患者的血压情况,同时能为医生提供较多的血压参数,有利于更准确地分析患者病情严重程度^[7,8]。随着相关研究的逐渐深入,有研究发现原发性高血压患者同型半胱氨酸(Hcy)、超敏C反应蛋白(hs-CRP)及白细胞介素-6(IL-6)水平与血压变异性可能存在一定相关性^[9,10]。鉴于此,本研究通过探讨原发性高血压患者Hcy、hs-CRP及IL-6水平与血压变异性的相关性并予以分析,旨在为临床治疗提供依据,现作以下报道。

1 资料与方法

1.1 一般资料

选取2016年2月-2017年12月四川大学华西医院收治的180例原发性高血压患者为研究对象。纳入标准:(1)所有患者连续3次非同时时间点检测血压值均为收缩压 ≥ 140 mmHg或(和)舒张压 >90 mmHg;(2)所有患者均符合《中国高血压防治指南2010》^[11]中所制定的有关原发性高血压诊断标准;(3)临床病历资料完整者;(4)年龄 >20 岁;(5)所有患者均签署了知情同意书。排除标准:(1)继发性高血压者;(2)血脂水平异常者;(3)合并糖尿病或急、慢性感染者;(4)伴有重度贫血者;(5)合并心、肝、肾等脏器功能严重障碍者。其中男性114例,女性66例,年龄22-88岁,平均 (66.32 ± 10.52) 岁。将所有患者根据Hcy水平的不同分为I组(Hcy <15.0 $\mu\text{mol/L}$)80例,II组(15.0 $\mu\text{mol/L} \leq \text{Hcy} < 20.0$ $\mu\text{mol/L}$)61例,III组(Hcy ≥ 20.0 $\mu\text{mol/L}$)39例。根据hs-CRP水平的不同分为A组(hs-CRP <5.0 mg/L)71

例,B组(5.0 mg/L $\leq$ hs-CRP <10.0 mg/L)68例,C组(hs-CRP ≥ 10.0 mg/L)41例。根据IL-6水平的不同分为D组(IL-6 <25.0 $\mu\text{g/mL}$)80例,E组(25.0 $\mu\text{g/mL} \leq \text{IL-6} < 30.0$ $\mu\text{mol/L}$)61例,F组(IL-6 ≥ 30.0 $\mu\text{mol/L}$)39例。我院伦理委员会已批准本研究。

1.2 研究方法

所有患者于入院次日采集清晨空腹静脉血5 mL,采用日立7060全自动生化分析仪检测空腹血糖水平。采集患者清晨空腹静脉血3 mL,以EDTA抗凝,并进行充分混匀,采用酶循环法检测Hcy水平,具体操作严格按照试剂盒说明书进行,试剂盒购自上海西唐生物科技有限公司。采用患者清晨空腹静脉血5 mL,以3000 r/min离心10 min获取上层血清,待检,分别采用酶联免疫吸附法(相关试剂盒均购自上海酶联科技有限公司)检测血清hs-CRP及IL-6水平,具体操作严格遵循试剂盒说明书进行。采用无创性携带式动态血压检测仪(美国,型号:Spacelabs90207)检测24 h收缩压标准差(24hSSD)、24 h舒张压标准差(24hDSD)水平。

1.3 观察指标

对比不同Hcy、hs-CRP以及IL-6水平患者的血压变异性及空腹血糖情况,分析Hcy、hs-CRP及IL-6水平与血压变异性的相关性。

1.4 统计学方法

本研究数据均采用SPSS20.0软件进行统计分析,Hcy、hs-CRP及IL-6水平等计量资料以 $(\bar{x} \pm s)$ 表示,实施t检验,多组间对比采用单因素方差分析,其与血压变异性的关系予以Pearson相关性分析。检验水准设置为 $\alpha=0.05$ 。

2 结果

2.1 不同Hcy水平患者的血压变异性与空腹血糖情况对比

不同Hcy水平患者的24hSSD、24hDSD水平整体比较差异有统计学意义($P<0.05$),且II组、III组的24hSSD、24hDSD水平高于I组,且III组高于II组($P<0.05$),而空腹血糖水平比较差异无统计学意义($P>0.05$),见表1。

表1 不同Hcy水平患者的血压变异性与空腹血糖情况对比($\bar{x} \pm s$)

Table 1 Comparison of blood pressure and fasting blood glucose in patients with different Hcy levels($\bar{x} \pm s$)

Groups	n	24hSSD(mmHg)	24hDSD(mmHg)	Fasting blood glucose (mmol/L)
I group	80	12.38 $\pm$ 3.17	6.20 $\pm$ 1.80	6.01 $\pm$ 0.93
II group	61	14.31 $\pm$ 4.18 [#]	8.23 $\pm$ 2.07 [#]	6.02 $\pm$ 0.81
III group	39	17.27 $\pm$ 5.28 ^{**}	10.57 $\pm$ 2.51 ^{**}	5.98 $\pm$ 0.96
F	-	11.432	9.587	0.384
P	-	0.000	0.000	0.762

Note: compared with I group, [#] $P<0.05$; compared with II group, ^{*} $P<0.05$.

2.2 不同hs-CRP水平患者的血压变异性与空腹血糖情况对比

不同hs-CRP水平患者的24hSSD、24hDSD水平整体比较差异有统计学意义($P<0.05$),且B组、C组的24hSSD、24hDSD水平高于A组,且C组高于B组($P<0.05$),而空腹血糖水平比较差异无统计学意义($P>0.05$),见表2。

2.3 不同IL-6水平患者的血压变异性与空腹血糖情况对比

不同IL-6水平患者的24hSSD、24hDSD水平整体比较差异有统计学意义($P<0.05$),且E组、F组的24hSSD、24hDSD水平高于D组,且F组高于E组($P<0.05$),而空腹血糖水平比较差异无统计学意义($P>0.05$),见表3。

表 2 不同 hs-CRP 水平患者的血压变异性与空腹血糖情况对比($\bar{x} \pm s$)Table 2 Comparison of blood pressure and fasting blood glucose in patients with different hs-CRP levels($\bar{x} \pm s$)

Groups	n	24hSSD(mmHg)	24hDSD(mmHg)	Fasting blood glucose (mmol/L)
A group	71	11.70 $\pm$ 2.11	7.55 $\pm$ 1.44	6.23 $\pm$ 0.87
B group	68	12.48 $\pm$ 3.12 [#]	9.01 $\pm$ 2.11 [#]	6.12 $\pm$ 0.93
C group	41	15.10 $\pm$ 3.29 ^{**}	10.39 $\pm$ 2.59 ^{**}	5.87 $\pm$ 0.82
F	-	7.372	8.052	0.317
P	-	0.000	0.000	0.780

Note: compared with A group, [#]P<0.05; compared with B group, ^{*}P<0.05.

表 3 不同 IL-6 水平患者的血压变异性与空腹血糖情况对比($\bar{x} \pm s$)Table 3 Comparison of blood pressure and fasting blood glucose in patients with different IL-6 levels($\bar{x} \pm s$)

Groups	n	24hSSD(mmHg)	24hDSD(mmHg)	Fasting blood glucose (mmol/L)
D group	80	11.50 $\pm$ 2.04	7.15 $\pm$ 1.32	6.19 $\pm$ 0.95
E group	61	12.51 $\pm$ 3.02 [#]	9.12 $\pm$ 2.09 [#]	6.21 $\pm$ 0.91
F group	39	14.88 $\pm$ 3.31 ^{**}	10.44 $\pm$ 2.54 ^{**}	5.87 $\pm$ 0.83
F	-	7.384	14.025	0.216
P	-	0.000	0.000	0.833

Note: compared with D group, [#]P<0.05; compared with E group, ^{*}P<0.05.

2.4 Hcy、hs-CRP 及 IL-6 水平与血压变异性的相关性分析

24hSSD、24hDSD 水平均呈正相关(P<0.05),见表 4。

Pearson 相关性分析显示,Hcy、hs-CRP 及 IL-6 水平与

表 4 Hcy、hs-CRP 及 IL-6 水平与血压变异性的相关性分析

Table 4 Correlation analysis of Hcy, hs-crp and il-6 levels and blood pressure variability

Relevant indicators	24hSSD		24hDSD	
	r	P	r	P
Hcy	0.683	0.000	0.623	0.000
hs-CRP	0.587	0.001	0.525	0.010
IL-6	0.605	0.000	0.617	0.000

3 讨论

血压变异性代表着血压波动,主要是指单位时间内患者血压波动的程度,其对心血管系统具有一定的影响^[12,13]。有研究报道显示,血压变异性较大的高血压患者心血管事件的发生风险显著升高^[14]。血压波动会使血流对血管的压力不断变化,进一步导致血管内膜损伤的发生,因此血压变异性与血管重构以及血管内皮损伤密切相关^[15,16]。另有研究报道表明^[17,18],血压变异性较大的高血压患者血管壁损伤更加明显,且血管内皮功能障碍发生的风险更高,容易促使血管收缩以及痉挛,进而降低血管顺应性,最终导致动脉血管粥样硬化斑块的形成。同时,由于血管内皮损伤,诱发了炎症反应,进一步促进动脉硬化的进程^[19]。

本研究结果发现,不同 Hcy 水平患者中 II 组、III 组的 24hSSD、24hDSD 水平高于 I 组,且 III 组高于 II 组(P<0.05),其中 24hSSD、24hDSD 均为 24h 动态血压监测获取到的血压变异指标,说明随着 Hcy 水平的逐渐升高,原发性高血压患者的血压变异性可能随之增加。Hcy 主要是由肝脏合成,属于蛋氨

酸代谢的中间产物,可产生氧自由基,致使血管内皮依赖性的舒张功能失调,同时降低内皮源性一氧化氮活性,导致血管扩张受损以及动脉弹性下降,进一步增加血管疾病发生的风险^[20-22]。此外,不同 hs-CRP 水平患者中 B 组、C 组的 24hSSD、24hDSD 水平高于 A 组,且 C 组高于 B 组(P<0.05),这表明了随着 hs-CRP 水平的不断升高,原发性高血压患者的血压变异性相应升高。究其原因,可能是 hs-CRP 会促使血管内皮表面黏附分子的表达升高,并结合损伤组织、促进白细胞黏附聚集以及激活补体等途径,在动脉粥样硬化以及动脉血栓形成过程中发挥着至关重要的作用^[23-25]。另外,不同 IL-6 水平患者中 E 组、F 组的 24hSSD、24hDSD 水平高于 D 组,且 F 组高于 E 组(P<0.05),提示了炎症因子可能在血压变异性升高过程中起着重要作用。其中主要原因可能在于 IL-6 可直接参与局部与全身炎症反应损伤血管内皮细胞,同时通过增加内皮素-1 的释放以及上调黏附分子与趋化因子,对内皮源性的一氧化氮合成酶产生抑制作用,进一步减少一氧化氮合成对血管舒张性产生的影响^[26-28]。与此同时,炎症因子参与了调控血管平滑肌细胞的凋亡

过程,可能在动脉粥样硬化进程中起着至关重要的作用^[29,30]。不同 Hcy、hs-CRP 以及 IL-6 水平患者空腹血糖水平比较差异无统计学意义($P>0.05$),说明 Hcy、hs-CRP 以及 IL-6 水平对空腹血糖无明显影响。经 Pearson 相关性分析显示,Hcy、hs-CRP 及 IL-6 水平与 24hSSD、24hDSD 水平均呈正相关($P<0.05$),这充分表明了原发性高血压患者的血压变异性随着 Hcy、hs-CRP 以及 IL-6 水平的不断升高而逐渐增大。

综上所述,原发性高血压患者 Hcy、hs-CRP 及 IL-6 水平与血压变异性存在明显正相关,临床工作中可通过对上述指标水平进行有效调控,进一步有效改善血压变异性。

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