

· 临床研究 ·

老年人高同型半胱氨酸高血压与血尿酸、纤维蛋白原的关系

高银凤, 柳 达*, 罗文利, 王 婧

(石河子大学医学院第一附属医院老年病科, 石河子 832000)

【摘要】目的 探讨老年人高同型半胱氨酸(Hcy)高血压(H型高血压)与血尿酸(UA)、纤维蛋白原(FIB)水平的关系。**方法** 选择2013年1月至2014年1月在石河子大学医学院第一附属医院老年病科门诊及病房收治的老年原发性高血压患者251例,其中Hcy水平 $\geq 15\mu\text{mol/L}$ 为老年H型高血压组121例,Hcy水平 $< 15\mu\text{mol/L}$ 为单纯高血压组130例;另外同期选择老年健康体检患者150例为对照组。同期测定Hcy、UA、FIB水平,比较各组UA、FIB水平的差异。**结果** 老年H型高血压组、单纯高血压组、与对照组3组UA[(320.97 ± 106.61)、(280.74 ± 71.27)与(261.01 ± 71.80) $\mu\text{mol/L}$]及FIB[(3.22 ± 0.52)、(3.05 ± 0.52)与(2.68 ± 0.41) g/L]两两比较差异均有统计学意义($P < 0.01$);logistic回归分析结果示,H型高血压与UA(OR = 3.896)、FIB(OR = 3.100)水平及叶酸降低水平(OR = 2.776)成正比($P < 0.05$)。**结论** 老年H型高血压与UA、FIB密切相关。监测UA及FIB对老年H型高血压的管理具有重要意义。

【关键词】 高血压; 同型半胱氨酸; 尿酸; 纤维蛋白原

【中图分类号】 R544.1; R592

【文献标识码】 A

【DOI】 10.3724/SP.J.1264.2014.000136

Correlation of H-type hypertension with serum uric acid and fibrinogen in the elderly

GAO Yin-Feng, LIU Da*, LUO Wen-Li, WANG Jing

(Department of Geriatrics, the First Affiliated Hospital, Medical College of Shihezi University, Shihezi 832000, China)

【Abstract】Objective To investigate the correlation of high homocysteine (Hcy) hypertension (H-type hypertension) with serum levels of uric acid (UA) and fibrinogen (FIB) in the elderly. **Methods** A total of 251 elderly in- and out-patients with essential hypertension admitted in our department from January 2013 to January 2014 were recruited in this study. They were divided into H-type hypertension group [$n = 121$, serum Hcy level $\geq 15\mu\text{mol/L}$] and primary hypertension group ($n = 130$, serum Hcy level $< 15\mu\text{mol/L}$). Another 150 elderly individuals without hypertension taking physical examination in our hospital during same period served as controls. Serum levels of Hcy, UA and FIB were detected in all the patients, and the results were compared among different groups. **Results** For the H-type hypertension, primary hypertension and control groups, there were statistical differences in the levels of UA [(320.97 ± 106.61), (280.74 ± 71.27) and ($261.01 \pm 71.80\mu\text{mol/L}$)] and FIB [(3.22 ± 0.52), (3.05 ± 0.52) and ($2.68 \pm 0.41\text{g/L}$)] between any of the 2 groups ($P < 0.01$). Logistic regression analysis showed that H-type hypertension was positively correlated with the serum level of UA (OR = 3.896) and FIB (OR = 3.100) and with the reduced level of folic acid (OR = 2.776, all $P < 0.05$). **Conclusion** H-type hypertension is closely associated with UA and FIB. Monitoring their levels is of great significance in the management of H-type hypertension in the elderly.

【Key words】 Hypertension; homocysteine; uric acid; fibrinogen

Corresponding author: LIU Da, E-mail: liuda1964@126.com

流行病学已经证明同型半胱氨酸(homocysteine, Hcy)是心血管疾病的独立危险因素^[1]。有研究提出,尿酸(uric acid, UA)、纤维蛋白原(fibrinogen, FIB)也是心血管疾病的独立危险因素^[2,3]。本文通过联合检测老年患者Hcy、UA及FIB水平,探讨UA、FIB水平与老年人高Hcy高血压(H型高血压)的关系。

1 对象与方法

1.1 对象

2013年1月至2014年1月石河子大学医学院第一附属医院老年病干部保健科门诊及病房收治符合入选标准的老年单纯高血压组130例,其中男53例,女77例,年龄65~91(71.20 ± 4.50)岁;H型高血压组121例,

其中男63例,女58例,年龄65~86(71.65±4.12)岁;对照组150例,其中男61例,女89例,年龄65~86(71.29±3.62)岁。

纳入标准:(1)患者年龄≥65岁;(2)符合2010年修订版中国高血压防治指南中原发性高血压诊断标准^[4];(3)两组高血压患者服用降压药物匹配;(4)另选同一时期在我院老年病干部保健科门诊及体检中心的150名健康老年人(排除高血压、冠心病等心血管疾病)为对照组。所有入选者均满足排除标准:(1)继发性高血压;(2)严重心、肺、肝、甲状腺、肾功能或凝血功能异常者;(3)各种恶性肿瘤、大动脉炎、自身免疫疾病及近期服用抗凝、叶酸、维生素B₁₂及影响尿酸排泄的药物等。

收集研究对象的性别、年龄、身高、体质量、血压、家族史、吸烟饮酒史、是否有冠心病、糖尿病、脑梗死,计算体质量指数(body mass index, BMI)等。

1.2 观察指标

患者均于清晨空腹12h采集静脉血,采用贝克曼Au2700仪器循环酶法测定Hcy;贝克曼全自动血凝分析仪比色法测定FIB;日立全自动生化仪常规检测UA、甘油三酯(triglycerides, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)、脂蛋白a、空腹血糖(fasting blood glucose, FBG)水平;贝克曼DXI800仪器化学发光免疫法测定叶酸(folic acid, FA)水平。

1.3 统计学处理

数据采用SPSS17.0软件进行统计分析。计量

资料用均数±标准差($\bar{x} \pm s$)表示;计数资料比较用 χ^2 检验;多组间比较正态方差齐采用方差分析,非正态或方差不齐采用非参数检验。多因素分析采用logistic回归分析。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 3组患者基线资料的比较

3组患者的性别、年龄、饮酒、BMI、TG、TC、HDL-C比较差异均无统计学意义($P > 0.05$);3组吸烟、LDL-C、FBG、收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)比较差异有统计学意义($P < 0.05$;表1)。

2.2 3组患者UA、FIB的比较

3组患者UA、FIB水平呈递增趋势,且3组UA、FIB两两比较差异均有统计学意义($P < 0.01$;表2)。

2.3 老年H型高血压影响因素的logistic回归分析

在老年高血压人群中,以Hcy为因变量,性别、吸烟、饮酒、冠心病、糖尿病、脑梗死、BMI、TG、TC、LDL-C、HDL-C、UA、FIB、脂蛋白a、FBG、FA、SBP、DBP为自变量,进行logistic回归分析,结果显示,老年H型高血压与UA、FB水平及FA降低水平成正相关($P < 0.05$;表3)。

3 讨论

高血压患者中,有75%的患者伴有Hcy水平升高,其中有约49.1%为老年患者^[5]。大量临床流行病学表明,Hcy是心血管疾病的独立危险因素,可引起动脉粥样硬化、心肌梗死、中风、静脉血栓等^[6]。

表1 3组基线资料比较
Table1 Baseline data of the three groups

Item	Control group (n = 150)	Primary hypertension group (n = 130)	H-type hypertension group (n = 121)	P value
Age(years, $\bar{x} \pm s$)	71.29 ± 3.62	71.20 ± 4.50	71.65 ± 4.12	0.324
Male[n(%)]	61 (40.7)	53 (40.8)	63 (52.1)	0.110
BMI(kg/m ² , $\bar{x} \pm s$)	24.09 ± 3.07	24.43 ± 3.35	24.57 ± 3.38	0.450
Smoking history[n(%)]	20 (13.33)	16 (12.31)	35 (28.93)	< 0.01
Drinking history[n(%)]	15 (10.00)	8 (6.15)	16 (13.22)	0.166
TG(mmol/L, $\bar{x} \pm s$)	1.92 ± 1.63	1.74 ± 0.93	1.76 ± 1.16	0.498
TC(mmol/L, $\bar{x} \pm s$)	4.44 ± 0.91	4.29 ± 1.05	4.35 ± 1.12	0.296
LDL-C(mmol/L, $\bar{x} \pm s$)	2.48 ± 0.75	2.68 ± 0.86	2.52 ± 0.83	0.029
HDL-C(mmol/L, $\bar{x} \pm s$)	1.39 ± 0.38	1.41 ± 0.37	1.32 ± 0.34	0.112
FBG(mmol/L, $\bar{x} \pm s$)	4.85 ± 0.92	5.33 ± 1.41	5.36 ± 1.39	< 0.01
SBP(mmHg, $\bar{x} \pm s$)	122.15 ± 13.51	135.77 ± 17.43	138.50 ± 19.60	< 0.01
DBP(mmHg, $\bar{x} \pm s$)	75.67 ± 9.02	79.52 ± 9.96	79.76 ± 11.13	< 0.01

BMI: body mass index; TG: triglycerides; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FBG: fasting blood glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure. 1mmHg = 0.133kPa

表2 3组患者UA和FIB比较
Table 2 Comparison of UA and FIB among three groups ($\bar{x} \pm s$)

Group	n	UA($\mu\text{mol/L}$)	FIB(g/L)
Control	150	261.01 $\pm$ 71.80	2.68 $\pm$ 0.41
Primary hypertension	130	280.74 $\pm$ 71.27**	3.05 $\pm$ 0.52**
H-type hypertension	121	320.97 $\pm$ 106.61***	3.22 $\pm$ 0.49***

UA: uric acid; FIB: fibrinogen. Compared with control group, ** $P < 0.01$; compared with primary hypertension group, *** $P < 0.01$

表3 老年H型高血压患者影响因素的logistic回归分析
Table 3 The logistic regression analysis of the influence factors of H-type hypertension in the elderly

Factor	B	SE	P	OR	95%CI
UA	1.360	0.406	0.001	3.896	1.757–8.638
FIB	1.131	0.313	0.000	3.100	1.678–5.726
FA	1.021	0.449	0.023	2.776	1.151–6.700

UA: uric acid; FIB: fibrinogen; FA: folic acid

高Hcy与高血压具有协同作用,可加重心血管损害,造成靶器官损坏^[7]。而老年高血压患者具有更高的心血管风险和严重的靶器官损害^[8]。有研究提出,UA及FIB同样是心血管疾病的危险因素。故本研究探讨老年H型高血压与UA、FIB的关系,结果显示对照组、单纯高血压组及H型高血压组的性别、年龄、饮酒、BMI、TG、TC、HDL-C比较差异无统计学意义($P > 0.05$);3组UA、FIB比较差异有统计学意义($P < 0.01$),H型高血压组UA、FIB水平明显高于单纯高血压组及对照组。对老年H型高血压患者影响因素的logistic回归分析显示,UA、FIB是老年H型高血压患者的危险因素($P < 0.05$),提示H型高血压与UA、FIB密切相关,Hcy水平越高,患者UA及FIB水平越高,在导致心血管事件上可能具有协同作用。

高Hcy血症与高血压的靶器官损害有关^[9]。有研究提出Hcy与UA呈正相关^[10,11],UA在动脉硬化的早期认为具有抗氧化作用,但在病理过程的后期却转变为促氧化作用。来自S-腺苷Hcy的代谢产物腺苷是尿酸合成的前体,将Hcy与尿酸的体内合成代谢联系到了一起^[10]。国外研究表明,Hcy代谢酶的活性影响了Hcy和UA水平,Hcy与UA的关系是由肾功能受损引起^[12],Hcy与UA之间的强关联是建立在纯合子型5,10-亚甲基四氢叶酸还原酶基础上,并研究提出,很大一部分5,10-亚甲基四氢叶酸还原酶参与嘌呤的合成,增加UA的排泄^[13]。Hcy可直接降低纤维蛋白溶酶对纤维蛋白原或纤维蛋白的裂解敏感性,可能是通过改变纤维蛋白溶酶裂解位点上的赖氨酸实现的。组织型纤维酶原激活剂(tissue plasminogen activator, tPA)是纤溶系统的重要激活剂,功能是

使纤维酶原变成纤维蛋白溶酶,Hcy对tPA有选择性结合抑制作用,高Hcy使纤溶酶原激活物抑制剂-1降低,血液凝固性增高^[14,15],更易发生栓塞性疾病,因此与高血压靶器官损害密切相关。本研究结果也显示H型高血压与FA降低水平成正相关($P < 0.05$),已有证明提出Hcy的升高与FA的缺乏有关,降低Hcy最安全有效的方法是补充FA^[16]。

综上所述,针对老年高血压患者,控制血压的同时降低Hcy,监测UA及FIB的水平,为老年H型高血压患者的管理提供理论依据,对防止老年高血压患者的心血管事件及靶器官损害具有重要的临床意义。

【参考文献】

- [1] Mangoni AA, Woodman RJ. Homocysteine and cardiovascular risk[J]. Am Coll Cardiol, 2011, 58(10): 1034–1035.
- [2] Palmer TM, Nordestgaard BG, Benn M, *et al.* Association of plasma uric acid with ischaemic heart disease and blood pressure: mendelian randomisation analysis of two large cohorts[J]. BMJ, 2013, 347: f4262.
- [3] Zhang XD, Zheng HJ, Chen YC, *et al.* The detection and significance of high sensitivity C-reactive protein and fibrinogen in patients with essential hypertension[J]. J Int Lab Med, 2013, 34(16): 2167–2168. [章小东, 郑穗瑾, 陈以初, 等. 原发性高血压患者超敏C反应蛋白及纤维蛋白原的测定及意义[J]. 国际检验医学杂志, 2013, 34(16): 2167–2168.]
- [4] Liu LS. The 2010 Chinese Guidelines for the Management of Hypertension[J]. Chin J Hypertens, 2011, 19(8): 701–708. [刘力生. 中国高血压防治指南2010[J]. 中华高血压杂志, 2011, 19(8): 701–708.]
- [5] Hu DY, Xu XP. Effective control of H-type hypertension—new ideas for stroke prevention[J]. Chin J Intern Med, 2008, 47(12): 976–977. [胡大一, 徐希平. 有效控制H型高血压——预防脑卒中的新思路[J]. 中华内科杂志, 2008, 47(12): 976–977.]
- [6] Genoud V, Lauricella AM, Kordich LC, *et al.* Impact of homocysteine-thiolactone on plasma fibrin networks[J]. J Thromb Thrombolysis, 2014, Mar 23. [Epub ahead of print]
- [7] Huo Y. Practice of translational medicine in H-type hypertension[J]. China Med Tribune, 2012-09-20(P.C12). [霍勇. H型高血压转化医学实践[N]. 中国医学论坛报, 2012-09-20 (C12版).]
- [8] Wang G. Characteristics and treatment of hypertension in the elderly[J]. Chin Foreign Med Res, 2011, 9(33): 136–137. [王光. 老年人高血压的特点及治疗[J]. 中外医学研究, 2011, 9(33): 136–137.]

- [9] Baszczuk A, Kopczyński Z, Thielemann A. Endothelial dysfunction in patients with primary hypertension and hyperhomocysteinemia[J]. *Postepy Hig Med Dosw* (Online), 2014, 68: 91–100.
- [10] Zhang T, Lyu CF, Liu K, *et al.* Analysis of the correlations of age, gender, blood uric acid and lipids with plasma homocysteine in hypertensive patients[J]. *Pract Prev Med*, 2013, 20(7): 786–788. [张涛, 吕纯芳, 刘琨, 等. 高血压患者血浆同型半胱氨酸与年龄、性别、尿酸及血脂的相关性分析[J]. *实用预防医学*, 2013, 20(7): 786–788.]
- [11] Feng SQ, Ye P, Luo LM, *et al.* Relationship between serum homocysteine and metabolic syndrome: a cross-sectional study of 1680 community-dwelled citizens of Beijing City[J]. *Chin J Epidemiol*, 2012, 33(3): 256–259. [冯胜强, 叶平, 骆雷鸣, 等. 北京市1680名社区居民血清同型半胱氨酸与代谢综合征关系的横断面研究[J]. *中华流行病学杂志*, 2012, 33(3): 256–259.]
- [12] Monfared A, Azimi SZ, Kazemnezhad E, *et al.* Hyperhomocysteinemia and assessment of its associated factors in renal transplant recipients: a single-center study in northern Iran[J]. *Transplantation*, 2014, 98(1): 66–71.
- [13] Ozkan Y, Yardim-Akaydin S, Imren E, *et al.* Increased plasma homocysteine and allantoin levels in coronary artery disease: possible link between homocysteine and uric acid oxidation[J]. *Acta Cardiol*, 2006, 61(4): 432–439.
- [14] Hoffman M. Alterations of fibrinogen structure in human disease[J]. *Cardiovasc Hematol Agents Med Chem*, 2008, 6(3): 206–211.
- [15] Yu LY, Wang HT, Song H, *et al.* Association between carotid atherosclerosis degree and thrombelastograph and risk factors in the patients with H-type hypertension[J]. *Chin J Hypertens*, 2011, 19(12): 1163–1168. [于立妍, 王华亭, 宋辉, 等. H型高血压患者颈动脉粥样硬化程度与血栓弹力图及危险因素的相关性[J]. *中华高血压杂志*, 2011, 19(12): 1163–1168.]
- [16] Li FR, Xie CP. Comparative study on the effect of enalapril maleate and folic acid tablets and enalapril tablets in H-type hypertension[J]. *Pract J Card Cereb Pneurol Vasc Dis*, 2013; 21(9): 26–28. [李芙蓉, 谢春苹. 马来酸依那普利叶酸片与依那普利片治疗H型高血压的疗效对比研究[J]. *实用心脑血管病杂志*, 2013, 21(9): 26–28.]

(编辑: 周宇红)