

血尿酸水平与缺血性卒中相关分析

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摘要 目的 研究血尿酸水平与缺血性卒中的相关性。方法 选择缺血性卒中患者(病例组)100例和健康体检者(对照组)100例,分别测定空腹血尿酸(UA)、总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白(LDL-C)、高密度脂蛋白(HDL-C),并对病例组进行颈部动脉超声检查、NIHSS评分、BI指数计算。比较两组尿酸水平及病例组不同血尿酸水平下UA、TC、TG、LDL-C、HDL-C的指标变化及NIHSS评分、BI指数、颈部血管斑块形成率的差别。结果 病例组和对对照组空腹血尿酸升高的例数,分别为46例和17例,分别占46%和17%,血尿酸平均浓度分别为 $485.96 \pm 76.03 (\mu\text{mol/L})$ 和 $343.12 \pm 61.46 (\mu\text{mol/L})$,差异有统计学意义。病例组尿酸结果明显高于对照组,两组比较有显著性差异($P < 0.01$)。病例组UA、TC、TG、LDL-C、HDL-C水平较正常对照组差异有显著意义($P < 0.05$)。对病例组血尿酸水平、颈部血管超声结果、NIHSS评分、BI指数进行分析。病例组患者血尿酸水平与病情及预后平行关系,即血尿酸水平高,颈部血管斑块形成率高,病情重,预后差。结论 高尿酸血症(HUA)是缺血性卒中重要的危险因素,是防治缺血性卒中的综合因素之一。

关键词 血尿酸 缺血性卒中 血脂测定 颈部血管斑块形成

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The Relation of Blood Uric Acid and Acute Ischemic Stroke

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ABSTRACT Objective: The relation of blood uric acid and acute ischemic stroke is researched. Methods: We have selected 100 examples of acute ischemic stroke and health people to compare. The fasting serum uric acid (UA), total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL-C) and high density lipoprotein (HDL-C) are measured. At the same time, the carotid artery ultrasound examination, the NIH Stroke Scale and Barthel index of the case group are calculated. For two groups of Uric acid level with the index changing of UA, TC, TG, LDL-C, HDL-C at the various levels are compared. The difference among the NIH Stroke Scale, Barthel index and formation rate of atheromatous plaque in carotid arteries is analyzed. Results: The quantity of the case group and Control group of fasting serum uric acid, are equal to 46 and 17, respectively. Here the percentages are 46% and 17%. The average consistency of Serum uric acid are $485.96 \pm 76.03 (\mu\text{mol/L})$ and $343.12 \pm 61.46 (\mu\text{mol/L})$. The difference has a statistics. The result of UA in case group is higher than control group. The compression of the two groups have significant difference ($P < 0.01$). The UA, TC, TG, LDL-C, HDL-C of case group is more significant than natural group ($P < 0.05$). For the level of UA in case group, the result of the carotid artery ultrasound, the NIH Stroke Scale and Barthel index are analyzed. The UA level of patients at case group has parallel relationship with patients' condition and prognosis, namely the level of UA is high, formation rate of atheromatous plaque in carotid arteries is high, patients' condition is heavy, and prognosis is bad. Conclusions: Hyperuricemia is important dangerous factor of ischemic stroke, and is one of synthesis factors preventing ischemic stroke.

Key words: Blood uric acid; Acute ischemic stroke; Lipid determination; Formation rate of atheromatous plaque in carotid arteries

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前言

近年来,由于我国生活水平的提高,饮食结构的改变,各种原因引起缺血性卒中的发病逐渐增多,预防已知的、探求未知的危险因素,成为降低发病率、死亡率关键。目前公认的缺血性卒中危险因素有年龄、血压、冠心病、心房纤颤、吸烟、糖尿病、高血脂等,颈动脉粥样硬化是全身动脉粥样硬化的一个“窗

口”,是缺血性卒中最重要的病因和危险因素^[1,2]。大量临床文献表明,高尿酸血症(high serum uric acid HUA)与上述缺血性卒中的危险因素相关联^[3,4,5],HUA有逐年增高趋势,但血尿酸是一个尚未引起人们足够重视的生化指标,血尿酸轻度升高在临床上可无任何症状,尿酸盐在血中浓度成过饱和状态即可沉积,引起脏器及血管损害。研究证实,高尿酸血症除明确与痛风的发病有关外,也是脑血管病的危险因素之一^[6],vigam等^[7]研究表明,血尿酸水平与急性缺血性卒中发病率、病死率有关。目前缺乏充足的证据证实其是缺血性卒中的重要危险因素。本研究通过观察100例缺血性卒中患者的血尿酸水平、血脂、颈部血管斑块形成率及神经功能缺损程度,探讨血尿酸水平与缺血性卒

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中相互关系,为缺血性卒中防治提供理论依据。

1 资料与方法

1.1 一般资料

选择 2011 年 2 月-2011 年 8 月哈尔滨医科大学附属第四医院收治的发病在 24 小时内缺血性卒中患者 100 例,设为病例组,男 56 例,女 44 例,年龄 40-75 岁(平均 58.28 ± 10 岁)。全部病例均符合第四届全国脑血管病学术会议修订的标准^[8],并经头 CT 或头 MRI 证实。选择健康体检者 100 例,设为对照组,男 58 例,女 42 例,年龄 40-75 岁(平均 55.76 ± 11 岁)。两组均排除高血压病、冠心病、糖尿病、自身免疫系统疾病、肾脏病、血液病等影响血尿酸水平的疾病。

1.2 方法

1.2.1 标本收集 所有试验对象均于清晨空腹抽取肘静脉血 3ml,离心后取上层血清,于 -70°C 冰箱冰冻保存。

1.2.2 U A 和血脂测定 采用罗氏 7600 全自动生化分析仪检

测,试剂盒由罗氏生物科技股份有限公司提供。

1.2.3 缺血性卒中患者评分 NIHSS 评分和 BI 指数

1.2.4 缺血性卒中患者颈部血管超声检查 患者入院后 24-72 h 采用菲力普 HDI-5000 彩色超声检查仪进行颈部动脉超声检查。颈部动脉内膜光滑、完整者为正常,颈部动脉内膜-中层厚度(IMT) $>1.2\text{ mm}$ 为动脉粥样硬化斑块形成。检查者均由同一高年资技师操作。

1.3 统计学处理

数据用均数、标准差($\bar{x} \pm s$)表示,两独立样本均数比较用 t 检验,并进行参数间的相关性分析,采用 SPSS 11.5 统计软件处理。

2 结果

病例组血清 UA 水平与病情及预后平行关系,即血尿酸水平高,颈部血管斑块形成率高、病情重、预后差。

表 1 病例组 UA 水平与 NIHSS 评分、BI 指数、颈部血管斑块形成率

Table1 The NIH Stroke Scale,Barthel index,and formation rate of atheromatous plaque in carotid arteries associated with the level of UA in case group

U A	The NIH Stroke Scale	Barthel index	Formation rate of atheromatous plaque in carotid arteries
Normal(54%)	1.8	80.62	30.04%
Increased(46%)	4.34	70.41	57.5%

病例组血清 UA、TC、LDL-C、VLDL-C 水平较正常对照组 差异有显著意义($P < 0.05$)。

表 2 病例组与对照组血尿酸、血脂含量测定结果($\bar{x} \pm s$)

Table2 The levels of UA and lipids between case group and control group ($\bar{x} \pm s$)

Group	U A($\mu\text{mol/L}$)	TC (mmol/L)	TG(mmol/L)	LDL-C (mmol/L)	VLDL-C (mmol/L)	HDL-C (mmol/L)
Case group	$485.96 \pm 76.03^*$	5.43 ± 0.87	2.53 ± 2.64	$3.01 \pm 0.72^*$	$0.57 \pm 0.56^*$	1.43 ± 0.34
Control group	343.12 ± 61.46	4.35 ± 0.46	1.46 ± 0.35	2.53 ± 0.47	0.24 ± 0.07	1.45 ± 0.27

注:与对照组比较,* $P < 0.05$

Note: * $P < 0.05$ versus the corresponding item of control group

病例组 UA 平均值、UA 异常比明显高于对照组。

表 3 病例组与对照组 UA 平均值及正常、异常比例

Table 3 The average level of UA ,the ratio of normals and the ratio of abnormals between the case group and control group

Group	Average level of UA ($\mu\text{mol/L}$)	The ratio of normals	The ratio of abnormals
Case group	443.5 ± 78.4	54%	46%
Control group	316.3 ± 76.9	83%	17%

3 讨论

本试验纳入对象时,排除高血压病、冠心病、糖尿病、自身免疫系统疾病、肾脏病、血液病影响血尿酸水平的疾病,以及服用影响尿酸水平药物的患者。试验表明,病例组合并高尿酸血症的比例高达 46%,明显高于对照组 17%。同时发现血尿酸水平与缺血性卒中患者病情及预后较好的平行关系。试验结果显示病例组血尿酸、血脂均高于对照组,差异有显著意义($P < 0.05$)。病例组血清血尿酸水平高,则颈部血管斑块形成率高、病情重、预后差,并与文献报道相一致^[9]。但是,HUA 动脉粥样硬化性心脑血管病发生发展过程中确切的病理机制尚不清楚,实验研究提示有以下可能^[18-20]:尿酸是嘌呤代谢的终产物,随血尿酸浓度升高血尿酸逐渐以尿酸盐形式析出,不溶解的尿酸盐可

形成针形结晶并大量存在于动脉粥样硬化斑块中,而且结晶被细胞摄取后会激活补体、启动炎症反应,其可溶性尿酸是前炎症因子,它能刺激单核细胞趋化因子-1 的产生,还能激活循环中的血小板,损伤血管内皮,通过阴离子交换器,可溶性尿酸能够进入血管平滑肌细胞,影响细胞内的氧化还原反应,激活丝裂原激活的蛋白激酶(Erk1/2 和 p38)、环加氧酶 2(COX-2)和核转录因子,促进了 TXA-2、PDGF、PDGF 受体和 MCP-1 的合成,刺激平滑肌细胞的增生。同时高尿酸引起血脂代谢异常,尿酸水平升高可使其在肾脏大量沉积,可通过物理作用阻塞肾小管,影响细胞正常功能,导致 HDL 大量排放,ApoA 降低,LDL 大量堆积,HUA 可促进 LDL 氧化,增加脂质过氧化、氧自由基生成,平滑肌细胞增生。以上机制促进动脉粥样硬化及血栓形

成,而动脉粥样硬化是缺血性卒中机制中最重要的环节及因素^[10-13]。随血尿酸浓度增加,尿酸以尿酸钠盐形式析出,同时使介质中离子强度增加,导致血浆蛋白与红细胞静电排斥力降低,蛋白在红细胞表面的吸附增强,红细胞膜变硬,红细胞变形性降低,导致全血粘度增加。

已有国内外大量临床资料证实,HUA可能是急性缺血性卒中危险因素之一^[14-15]。迄今,至少有20个大规模试验,进行血尿酸与心脑血管疾病关系的研究,其中多数支持HUA可以作为动脉粥样硬化、心脑血管病的重要独立预测因素^[16-17]。尿酸有抗氧化作用,但在某些情况如VitC水平低下时(常见于脑血管病),可产生促氧化作用^[21],导致预后不良,Cherubini等^[22]的研究结果支持这一解释。

综上所述,血尿酸水平升高可影响血脂代谢,对动脉粥样硬化斑块形成有协同作用,促进缺血性卒中的发生、发展。因此该研究提示早期检测、控制尿酸水平可能是控制血脂辅助手段,是防治缺血性卒中的又一积极手段,重视血尿酸水平的研究对探讨其它代谢因素在缺血性卒中的发病机制中的作用有一定的实用价值,提高对尿酸的认识,改善饮食结构,可降低缺血性卒中的发生、发展。

参考文献(References)

- [1] Handa N, Matsumoto M, Maeda H, et al. Ischemic stroke events and carotid athero-sclerosis[J]. Stroke, 1995, 26:1781-1786
- [2] 王拥军.应加强颈动脉粥样硬化的基础和临床研究[J].中华神经科杂志, 2001, 34(5):257
Wang YJ. Both of the basical and clinial researches of carotid atherosclerosis should be strengthen[J]. Chin J Neurol, 2001, 34(5):257
- [3] Brand FN, McGee DL, Kannel WB, et al. Hyperuricemia as a risk factor of coronary heart Disease: The Framingham Study[J]. Am J Epidemiol, 1985, 121:11-18
- [4] Bonora E, Targher G, Zenere MB, et al. Relation ship of uric acid con-centration to cardiovascular risk factors in Young men. Role of obesity and central fat distribution. The Verona Young Men Atherosclerosis Risk Factors Study[J]. Int J Obes Relat Metad Disord, 1996, 20: 975-980
- [5] Rathmann W, Funkhouser E, Yer R, et al. Relations of hyperuricemia with thevarious components of the Insulin resistance syndrome in young black and white adults: the CARDIA study. Coronary Artery Risk Devel-opment in Young Adults [J]. Ann Epidemiol, 1998, 8: 250-261
- [6] J Handa N, Matsumoto M, Maeda H, et al. Ischemic stroke events and carotid athemsclerosis. R∞ llts of the Osaka Follow-up Study for UI • trasonographic Assessment of Carotid Atherosclerosis (the OSACA Study)[J]. Stroke, 1995, 26(10): 1781-1786
- [7] Vigna GB, Bolzan M, Romagmoni F, et al. Lipids and other risk fac-tots selected by diseriminant analysis in symptomatic patients with supraaortie and peripheral atherosclerosis [J]. Circulation, 1992, 85 (6) 2205-2011
- [8] Handa N, Matsumoto M, Maeda H, et al. Ischemic stroke events and carotid athemsclerosis. R∞ llts of the Osaka Follow-up Study for UI. Trasonographie Assessment of Carotid Atherosclerosis (the OSACA Study)[J]. Stroke, 1995, 26(10) :1781-1786
- [9] Weir cJ, Muir SW, Walters MR, et al. Serum ufate a8 sn independent predictor of poor outcome and future vascular events after acute stroke[J]. Stroke, 2003, 34:1951-1957
- [10] Freedman DS, Williamson DF, centr EW, et al. Relation of serum acid to mortality and ischemic heart disease. The NHANEST Epidemiologic Follow-up study[J]. Am J Epidemiol, 1995, 141: 637-644
- [11] Fuster V, Badiman L, Badiomon JJ, et al. The pathogenesis of coronary artery disease and the acute coronary syndromes[J]. N Engl J Med, 1992, 326:310-318
- [12] 李秀峰.尿酸 - 冠心病的一个危险因素[J]. 美国医学会杂志(中文版), 1994, 13(4):139-140
Li Xiu-feng. Uric acid: a risk factor of Coronary heart disease [J]. Journal of the American Medical Association (Chinese Edition), 1994, 13(4):139-140
- [13] 易兴阳, 余昌明, 潘光强, 等.颈动脉粥样硬化与颈动脉粥样硬化性脑梗死关系探讨[J].中华神经科杂志, 1999, 32:210-225
Yi XY, Yu CM, Pan GQ, et al. Explore the relationship between carotid atherosclerosis and cerebral atherosclerotic infarction [J]. Chin J Neurol, 1999, 32:210-225
- [14] Weir CA, Muir SW, Walters MR, et al. Serum urae as an independent predictor of poor outcome and future vascular events after acute stroke[J]. Stroke, 2003, 34(8) :1951-1956
- [15] Wong KY, Mac Walter RS, Fraser HW, et al. Urate predicts subsequent cardiac death in stroke survivors[J]. Eur Heart J, 2002, 23(10):788-793
- [16] Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study. 1971.1992. National Health and Nutrition Examination Survey [J]. JAMA, 2000, 283(18) : 2404-2410
- [17] Niskanen LK, Laaksonen DE, Nyyssonen K, et al. Uric acid level as a risk factor for cardiovascular and all cause mortality in middle-aged men: a prospective cohort study [J]. Arch Intern Med, 2004, 164(14) : 1546-1551
- [18] Johson RJ, Kang D, Feig DI. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? [J]. Hypertension, 2003, 41: 1183
- [19] Alderman MH, Aiyer KJ. Uric acid role in cardiovascular disease and effect of losartan[J]. Curr Med Res Opin, 2004, 20(3) :369-379
- [20] 党爱民, 刘国仗.尿酸与心血管事件[J].中华心血管病杂志, 2003, 31(6) :478-480
Dang AM, liu GZ. uric acid and Cardiovascular events [J]. Chinese Journal of Cardiology, 2003, 31(6): 478-480
- [21] Abuja PM. Ascorbate prevents prooxidant effects of urate in oxidation of human low density lipoprotein[J]. Febs Lett, 1999, 446 :305-308
- [22] Cherubini A, Polidori MC, Bregnocchi M, et al. Antioxidant profile and early outcome Stroke patients[J]. Stroke, 2000, 31: Z295-2300