

卡马西平对癫痫患者颈总动脉内中膜厚度的影响及相关危险因素研究

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摘要 目的:观察卡马西平(CBZ)对癫痫患者颈总动脉内中膜厚度的影响,并探讨其相关危险因素。方法:选取我院就诊的40例单一服用CBZ治疗时间大于1年的癫痫患者作为试验组,另选取40名健康志愿者作为对照组。分别测量受试者左、右两侧颈总动脉内中膜厚度(CA-IMT),计算平均CA-IMT(左、右两侧CA-IMT平均值),并检测血清总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)及同型半胱氨酸(Hcy)等。对影响CA-IMT的相关危险因素(年龄、性别、体质指数、病程、服药时间等)进行多元回归分析。结果:试验组双侧CA-IMT及平均CA-IMT均较对照组显著增加($P<0.001$);试验组TC、TG、LDL-C、Hcy水平均较对照组显著升高($P<0.05$)。多元回归分析结果显示,平均CA-IMT与服药时间呈正相关($P<0.05$),即服药时间越长,患者平均CA-IMT越高。结论:服用CBZ的癫痫患者CA-IMT增加与服药时间有关,故长期服用CBZ的患者有必要定期检测血脂及Hcy。

关键词 卡马西平;癫痫;颈总动脉内中膜厚度;血脂;同型半胱氨酸

Effects of Carbamazepine on Carotid Artery Intima Media Thickness in Epileptic Patients and Relative Risk Factors

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ABSTRACT OBJECTIVE: To observe the effects of carbamazepine (CBZ) on carotid artery intima media thickness (CA-IMT) in epileptic patients and its relative risk factors. METHODS: 40 epileptic patients receiving CBZ alone more than 1 year were collected from our hospital as trial group, and other 40 healthy volunteers as control group. CA-IMT at both sides of common carotid artery were measured, and average CA-IMT (average value of CA-IMT at both sides of common carotid artery) was calculated. Blood lipid (TC, TG, LDL-C and HDL-C) and Hcy level were detected. Multivariable regression analysis were adopted to select the relative risk factors (age, gender, BMI, course of disease, duration of therapy, etc.) of CA-IMT. RESULTS: The CA-IMT of both sides and average CA-IMT were significantly increased in trial group, compared with control group ($P<0.001$). TC, TG, LDL-C and Hcy level of trial group were increased significantly, compared with control group ($P<0.05$). Multiple regression analysis revealed that the average CA-IMT was positively related to duration of therapy ($P<0.05$), i.e. the longer duration of therapy was, the higher average CA-IMT was. CONCLUSIONS: The increase of CA-IMT is associated with epileptic patients receiving CBZ. It is necessary to determine regularly blood lipid and Hcy level of patients receiving CBZ therapy for a long time.

KEY WORDS Carbamazepine; Epilepsy; Carotid artery intima-media thickness; Blood lipids; Hcy

卡马西平(CBZ)是临床常用的抗癫痫药物。据报道^[1], CBZ能导致癫痫患者总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、C反应蛋白(CRP)增高,而这些是动脉粥样硬化的危险因素。临床上常用超声检测颈总动脉内中膜厚度(CA-IMT),预测患者可能出现动脉粥样硬化的风险。因此,笔者运用超声和实验室检查方法,观察了长期服用卡马西平对癫痫患者CA-IMT的影响及相关危险因素。

1 资料与方法

1.1 一般资料

①试验组:选择40例2009年9月—2010年12月在我院神经内科门诊就诊的癫痫患者,单一服用CBZ治疗时间均大于1

年。其中,男性18例,女性22例;年龄18~40岁,平均25.8岁。所有患者均经脑电图、影像学等检查并结合临床诊断确诊。②对照组:选择40名同期健康志愿者,男、女性各20名;年龄18~40岁,平均24.5岁。排除标准:有吸烟、饮酒、感染、高血压、慢性肝炎及其他慢性疾病病史者,原先服用过其他抗癫痫药物者。本试验经医院伦理委员会批准,且受试者均签署知情同意书。两组受试者性别、年龄等比较差异无统计学意义($P>0.05$),具有可比性。

1.2 方法

1.2.1 颈动脉超声检查 采用PHILIPS HDI SonoCT 5000型彩色多普勒超声诊断仪,使用线阵探头,频率为5~12 MHz。受检者取仰卧位,头略向后仰,充分暴露颈部。检查顺序先从锁骨内侧端横向扫查颈总动脉,然后将探头沿其行走方向向头侧移位,跨过分叉部,分别检测患者双侧颈总动脉、颈内动脉和颈外动脉。于颈总动脉分叉近心端1 cm后壁处,测量

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CA-IMT,左、右两侧各测量3次,取平均值,分别测得左、右两侧平均CA-IMT。

1.2.2 实验室检查:检测血清总胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)、同型半胱氨酸(Hcy)等指标。空腹采血2~3 ml,送我院实验室完成检测。

1.2.3 身高、体质量测量 对两组受试者进行身高、体质量测量,体质量指数(BMI)=体质量/身高²。

1.2.4 统计学方法 采用SPSS 17.0软件进行统计学处理。计数资料以 $\bar{x} \pm s$ 表示,单因素采用独立样本 t 检验进行分析;多因素采用多元逐步回归分析法。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组受试者体质量、身高、BMI比较

两组受试者体质量、身高、BMI比较差异无统计学意义($P > 0.05$),详见表1。

表1 两组受试者体质量、身高、BMI比较($\bar{x} \pm s$)

Tab 1 Comparison of body weight, height and BMI between 2 groups($\bar{x} \pm s$)

组别	<i>n</i>	体质量,kg	身高,m	BMI,kg/m ²
对照组	40	52.2±1.67	1.60±0.47	20.777 5±1.486 78
试验组	40	51.6±2.73	1.58±0.56	21.157 5±1.804 54

2.2 两组受试者CA-IMT比较

与对照组比较,试验组双侧CA-IMT及平均CA-IMT均显著增高,两组受试者比较差异有统计学意义($P < 0.001$),详见表2。

表2 两组受试者CA-IMT比较(mm, $\bar{x} \pm s$)

Tab 2 Comparison of CA-IMT between 2 groups (mm, $\bar{x} \pm s$)

组别	<i>n</i>	右侧CA-IMT	左侧CA-IMT	平均CA-IMT
对照组	40	0.552 0±0.055 41	0.552 5±0.050 57	0.552 5±0.042 29
试验组	40	0.652 5±0.098 68*	0.653 3±0.095 74*	0.652 9±0.094 52*

与对照组比较: * $P < 0.001$

vs. control group: * $P < 0.001$

2.3 两组受试者血脂及Hcy水平比较

与对照组比较,试验组TC、TG、LDL-C、Hcy水平显著增高,两组比较差异有统计学意义($P < 0.05$);两组受试者HDL-C水平比较差异无统计学意义($P > 0.05$),详见表3。

表3 两组受试者血脂及Hcy水平比较(mmol/L, $\bar{x} \pm s$)

Tab 3 Comparison of blood lipid and Hcy between 2 groups(mmol/L, $\bar{x} \pm s$)

组别	<i>n</i>	TC	TG	LDL-C	HDL-C	Hcy, μ mol/L
对照组	40	3.447±0.926 62	1.010±0.311 98	1.850±0.658 54	1.235±0.154 16	6.755±1.572 6
试验组	40	4.071±0.907 10*	1.381±0.490 05*	2.198±0.880 49*	1.292±0.191 28	10.005±1.949 4*

与对照组比较: * $P < 0.05$

vs. control group: * $P < 0.05$

2.4 对影响CA-IMT的相关危险因素的回归分析

对影响CA-IMT的相关危险因素(年龄、性别、BMI、病程、服药时间等)进行多元回归分析,结果患者平均CA-IMT与服药时间呈正相关($P < 0.05$),回归方程 $y = 0.026x + 0.552$,即服药时间越长,患者平均CA-IMT越高。对影响CA-IMT的相关危险因素的回归分析结果见表4(表中病程、年龄、性别、BMI、用药总量等无显著相关性的因素数据未列出)。

3 讨论

研究^[2]表明,癫痫和/或抗癫痫药物会导致血管危险因素增

表4 平均CA-IMT作为因变量的多元回归分析结果

Tab 4 Results of multiple regression analysis using average CA-IMT as dependent variable

因素	非标准回归系数B	标准误	标准回归系数Beta	<i>t</i>	<i>P</i>
常数项	0.552	0.046		12.028	0
服药时间	0.026	0.011	0.355	2.344	0.024
病程					
年龄					
性别					
BMI					
用药总量					
<i>F</i> 修正值			0.126		
因变量预测值的标准误差			0.089 09		
模型显著水平(<i>P</i>)			0.033		
例数			40		

加和CA-IMT增高,具有发展为亚临床型动脉粥样硬化的风险。

本研究表明,服用CBZ的癫痫患者CA-IMT较正常对照组增高,与相关研究^[3]结论相同。癫痫发作导致脂质过氧化、线粒体过氧化氢及O²⁻的产生增加^[4],过氧化物的增高可直接损伤血管内皮,导致CA-IMT增加,说明癫痫本身可以导致CA-IMT增加,加快动脉粥样硬化形成。但多元回归分析表明,患者病程与CA-IMT无线性相关,这可能与试验组癫痫病程过短有关。

同时,本研究结果表明,服用CBZ的试验组患者血清TC、TG、LDL-C、Hcy水平较对照组显著增高,与相关研究^[5]结果一致。并且多元回归分析发现,CA-IMT与服药时间呈正相关,说明癫痫患者CBZ治疗时间越长,CA-IMT越高。长期服用CBZ的患者可能通过增加TC、TG、LDL-C、Hcy水平等导致CA-IMT增高。而TC、TG、LDL-C、Hcy水平增高是动脉粥样硬化的危险因素,故患者服药时间越长,患动脉粥样硬化的风险越高。CBZ导致TC、TG、LDL-C、Hcy水平改变,其可能机制为:(1)细胞色素P₄₅₀是抗癫痫药物代谢最重要的系统,同时对胆固醇代谢有重要的作用^[6]。CBZ能与胆固醇竞争性利用该种酶,使胆固醇转化减少,而使胆固醇水平增高^[7],从而导致脂质代谢紊乱。(2)CBZ能干扰叶酸代谢,导致叶酸和维生素B₁₂水平下降,Hcy水平增加^[8]。有研究^[1,9]发现,CBZ增加患者CRP水平,而CRP浓度增加与动脉粥样硬化斑块炎症反应程度相关,是动脉粥样硬化的危险因素。同时有研究^[10]指出,CBZ可导致癫痫患者亚临床型甲状腺功能低下或甲状腺功能减退,以上危险因素的改变直接诱导血管内皮细胞凋亡和功能异常,导致动脉粥样硬化形成。

综上所述,本研究发现服用CBZ的癫痫患者的CA-IMT增加,可能与癫痫和/或CBZ治疗有关,但需要进一步的前瞻性试验研究证实。因此,对长期服用CBZ的癫痫患者定期检测血脂、Hcy及进行颈动脉超声检查是必要的,对癫痫患者减少颈动脉粥样硬化及相关疾病的发生有重要的临床意义。

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尿毒清颗粒辅助治疗早期糖尿病肾病的临床观察

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摘要 目的:观察尿毒清颗粒辅助治疗早期糖尿病肾病(DN)的临床疗效。方法:选取我院133例早期DN患者,随机分成两组,对照组(65例)给予常规西药方案治疗(采用血管紧张素Ⅱ受体拮抗药类或血管紧张素转换酶抑制剂类降压药物控制尿蛋白),治疗组(68例)在对照组治疗基础上加用尿毒清颗粒每次5.0g,每日4次。两组患者均治疗24周。比较治疗前后两组患者的肾功能指标[内生肌酐清除率(Ccr)、尿微量白蛋白(MA)、糖化血红蛋白(HbA_{1c})、空腹血糖(FPG)、血清胱抑素C(Cys C)、肝功能指标[血清白蛋白(ALB)、丙氨酸氨基转移酶(ALT)、天冬氨酸氨基转移酶(AST)、血红蛋白(Hb)]、血脂指标[总胆固醇(TC)、甘油三酯(TG)]等的变化,并记录不良反应。结果:治疗组患者总有效率为83.8%,对照组患者总有效率为60.0%,两组比较差异有统计学意义($P<0.05$);治疗组治疗后Cys C、MA均较治疗前显著下降,Ccr较治疗前显著上升($P<0.05$ 或 $P<0.01$),而对照组治疗后仅Ccr较治疗前显著上升($P<0.05$);两组患者其他指标治疗前、后比较差异均无统计学意义($P>0.05$)。两组患者均未见严重不良反应发生。结论:早期DN患者在常规西药治疗基础上加用尿毒清颗粒治疗效果明显,可显著降低患者的Cys C和MA水平,改善肾小球滤过功能,且安全性较好。

关键词 尿毒清颗粒;糖尿病肾病;血清胱抑素C;尿微量白蛋白;疗效;安全性

Clinical Observation of Niaodqing Granules in the Treatment of Early Diabetic Nephropathy

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ABSTRACT OBJECTIVE: To observe the clinical efficacy of Niaodqing granules in the treatment of early diabetic nephropathy (DN). METHODS: 133 patients with early DN of our hospital were randomized into 2 groups. 65 cases of control group were given conventional therapy of western medicine (controlling urine protein by angiotensin II receptor antagonists or angiotensin converting enzyme inhibitor). 68 cases of treatment group were additionally given Niaodqing granules 5.0 g 4 times a day on the basis of control group for 24 weeks. The changes of hepatic function index (Ccr, MA, HbA_{1c}, FPG, Cys C), hepatic function index (ALB, ALT, AST, Hb) and blood lipid index (TC, TG) were compared between 2 groups before and after treatment; ADR were also recorded. RESULTS: Total effective rate of treatment group was 83.8%, and that of control group was 60.0%, there was statistical significance between 2 groups ($P<0.05$); Cys C and MA of treatment group decreased significantly after treatment, while Ccr level increased significantly ($P<0.05$ or $P<0.01$); there was no statistical significance in other index between 2 groups before and after treatment ($P>0.05$). No severe ADR was found in 2 groups. CONCLUSIONS: Niaodqing granules are effective in the treatment of early DN, can significantly reduce Cys C and MA and improve glomerular filtration function with sound safety.

KEY WORDS Niaodqing granule; Diabetic nephropathy; Cysteine C; MA; Therapeutic efficacy; Safety

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