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早期颈内动脉支架置入对动脉粥样硬化脑梗患者 血清 Lp-PLA2 和 Hcy 水平的影响 *

刘福德¹ 王建懿^{1Δ} 陈 晨¹ 于 嘉² 商苏杭¹

(1 西安交通大学第一附属医院神经内科 陕西 西安 710000; 2 空军军医大学第二附属医院神经外科 陕西 西安 710038)

摘要 目的: 探讨早期颈内动脉支架置入(carotid artery stenting, CAS)对动脉粥样硬化脑梗死患者血清脂蛋白相关磷脂酶 2(lipoprotein-associated phospholipase 2, LP-PLA2)和同型半胱氨酸(Homocysteine, Hcy)水平的影响。**方法:** 选择 2018 年 8 月到 2021 年 4 月在西安交通大学第一附属医院诊治的颈动脉重度狭窄性脑梗死患者 86 例作为研究对象,根据治疗方法将患者分为早期 CAS 组与对照组各 43 例,对照组给予药物保守治疗,2 周后脑梗死稳定后再给予手术,CAS 组在对照组基础上治疗 3~5 d 后给予颈内动脉支架置入治疗,检测两组患者血清 Lp-PLA2 和 Hcy 水平变化情况。**结果:** CAS 组治疗后 7 d 的总有效率为 97.7%,高于对照组的 86.0%($P<0.05$)。CAS 组治疗后 7 d 的高灌注综合征、脑出血、低血压、心动过缓等并发症发生率为 4.7%,对照组无出现高灌注综合征、脑出血、低血压、心动过缓等并发症,对比差异无统计学意义($P>0.05$)。两组治疗后 7 d 的颈内动脉相对脑血流量与脑血容量高于治疗前($P<0.05$),CAS 组高于对照组($P<0.05$)。两组治疗后 7 d 的血清 Lp-PLA2、Hcy 含量低于治疗前($P<0.05$),CAS 组低于对照组($P<0.05$)。**结论:** 早期颈内动脉支架置入在动脉粥样硬化脑梗死患者的应用能抑制 Lp-PLA2、Hcy 的表达,改善患者的血流动力学变化,从而促进提高治疗效果,在临床上的应用具有很好的安全性。

关键词: 颈内动脉支架置入;动脉粥样硬化;脑梗;脂蛋白相关磷脂酶 2;同型半胱氨酸;血流动力学

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Effects of Early Internal Carotid Artery Stent Placement on Serum Lp-PLA2 and Hcy Levels in Patients with Atherosclerotic Cerebral Infarction*

LIU Fu-de¹, WANG Jian-yi^{1Δ}, CHEN Chen¹, YU Jia², SHANG Su-hang¹

(1 Department of Neurology, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710000, China;

2 Department of Neurosurgery, Second Affiliated Hospital of Air Force Military Medical University, Xi'an, Shaanxi, 710038, China)

ABSTRACT Objective: To investigate the effect of early internal carotid artery stenting (CAS) on serum lipoprotein-associated phospholipase 2 (LP-PLA2) and homocysteine (Hcy) levels in patients with atherosclerotic cerebral infarction. **Methods:** A total of 86 patients with severe carotid artery stenotic cerebral infarction who were diagnosed and treated in the First Affiliated Hospital of Xi'an Jiaotong University from August 2018 to April 2021 were selected as the research subjects. According to the treatment method, the patients were divided into the early CAS group and the control group, 43 cases in each group. The control group were given conservative drug treatment, and after 2 weeks the cerebral infarction was stabilized before surgery. The CAS group was given internal carotid artery stenting after 3-5 days of treatment on the basis of the control group, and the changes of serum Lp-PLA2 and Hcy levels in the two groups were detected. **Results:** After 7 days of treatment, the total effective rate at 7 days were 97.7% in the CAS group, which were higher than 86.0% in the control group ($P<0.05$). The incidence rates of complications such as hyperperfusion syndrome, cerebral hemorrhage, hypotension, bradycardia in the CAS group were 4.7% after 7 days of treatment, and there were no cases of hyperperfusion syndrome, cerebral hemorrhage, hypotension, bradycardia occurred in the control groups that compared were not difference ($P<0.05$). The internal carotid artery relative cerebral blood flow and cerebral blood volume in the two groups were higher than those before treatment ($P<0.05$), and the CAS group was higher than the control group ($P<0.05$). There were no significant difference in the control group before and after treatment ($P>0.05$). The levels of Lp-PLA2 and Hcy in serum 7 days after treatment in the two groups were lower than those before treatment ($P<0.05$), and those in the CAS group were lower than those in the control group ($P<0.05$). **Conclusion:** The application of early internal carotid artery stenting in patients with atherosclerotic cerebral infarction can inhibit the expression of Lp-PLA2 and Hcy, and improve the hemodynamic changes of patients, thereby promoting the improvement of the therapeutic effect, and having good safety in clinical application.

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作者简介:刘福德(1986-),男,硕士,主治医师,研究方向:脑血管病的介入诊断和治疗,电话:18161823657, E-mail:doctor860814@163.com

Δ 通讯作者:王建懿(1992-),女,博士,助理研究员,研究方向:脑血管病的病因及损伤机制,

电话:18700995296, E-mail:doctor860814@163.com

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前言

脑梗死是大脑细胞和组织缺血坏死的一种疾病,以急性发病多见,具有致残率高、死亡率高等特征^[1,2]。动脉粥样硬化是脑梗死的重要原因之一,颈内动脉狭窄程度为 70-79% 的患者卒中风险高达 19%^[3,4]。随着人们生活习惯的改变、生活水平的不断提高与饮食结构的变化,脑梗的发病人数逐渐上升^[5]。目前脑梗的治疗方法较多,颈内动脉支架置入(carotid artery stenting, CAS)是治疗颈内动脉重度狭窄的主要治疗方法,具有微创、无颈部手术切口、术后恢复快等优点,还可提高普通药物治疗的有效性^[6,7]。同时随着检验技术的高速发展,越来越多的检验项目应用到脑梗的诊治中^[8,9]。LP-PLA2 是磷脂酶家族中重要成员之一,其高表达增加脑血管疾病的风险,还可以预测血管炎症、促进动脉粥样硬化形成^[10,11]。同型半胱氨酸(Homocysteine, Hcy)是诱发脑梗的独立危险因素之一,其表达水平与颈动脉斑块稳定性之间有着一定的关系^[12,13]。本文具体探讨了早期 CAS 对动脉粥样硬化脑梗患者血清 Lp-PLA2 和 Hcy 水平的影响,以探

讨颈内动脉支架置入的应用效果与机制。

1 资料与方法

1.1 研究对象

选择 2018 年 8 月到 2021 年 4 月在西安交通大学第一附属医院诊治的动脉粥样硬化脑梗患者 86 例作为研究对象,纳入标准:符合脑梗的诊断标准;多普勒超声、CT 血管成像检查明确颈内动脉粥样硬化性重度狭窄为责任病变;年龄 20-80 岁,具有支架置入指征;临床资料、影像学资料完整者;排除标准:合并传染性疾病者;合并自身免疫系统障碍者;心肝肾功能不全者;妊娠与哺乳期妇女;精神疾病患者;体弱难以耐受手术者;颈动脉高度迂曲者;颈动脉完全闭塞者。

根据治疗方法将患者分为早期 CAS 组与对照组各 43 例,两组患者的一般临床资料对比差异无统计学意义($P>0.05$)。见表 1。本医院伦理委员会批准了此次研究,患者及家属均对研究知情同意。

表 1 一般临床资料
Table 1 General clinical data

Groups	n	BMI(kg/m ²)	Gender (male / female)	Age (years)	Blood sugar (mmol/L)	Disease time(h)
CAS group	43	22.87±6.63	23/20	56.92±6.19	5.42±1.16	26.13±6.18
Control group	43	23.48±5.87	22/21	56.19±4.88	5.84±1.47	27.06±7.74
t/ χ^2		0.452	0.047	0.607	1.471	0.616
P		0.652	0.828	0.545	0.145	0.540

1.2 治疗方法

对照组:给予充分抗血小板聚集药物治疗,口服每日口服波立维(国药准字 J20040006,杭州赛诺菲圣德拉堡民生制药有限公司)75 mg 与阿司匹林(国药准字 J20130078,拜耳公司)100 mg,2 周后脑梗死稳定后再给予手术。

早期 CAS 组:在对照组基础上治疗 3~5 d 后给予颈内动脉支架置入治疗。全身肝素化,局部麻醉下行右侧股动脉穿刺,采用微导丝通过狭窄处,根据狭窄动脉的直径和长度选择合适的自膨式支架,释放保护伞,球囊扩张,放置到正确位置后释放支架,逐步撤出扩张球囊和颈内动脉保护装置。

1.3 观察指标

(1) 所有患者都在治疗前与治疗 7d 进行(National Institute of Health stroke scale, NIHSS)评分,(显效+有效)/组内例数×100.0%=总有效率。显效:治疗前与治疗 7d NIHSS 评分减少率≥80.0%;有效:治疗前与治疗 7d NIHSS 评分减少率≥40.0%~80.0%;无效:无达到上述标准甚或恶化。(2)记录与观察两组患者治疗后 7 d 出现的并发症情况,包括高灌注综合征、脑出血、低血压、心动过缓等。(3)所有患者在治疗前与治疗

后 7 d 进行 CT 灌注成像,测定与记录患者的脑血流量、脑血容量变化情况。(4)所有患者在治疗前与治疗 7 d 抽取患者的静脉血 2-3 mL,低温离心后分离上层血清,采用酶联免疫法试剂盒(购自上海碧云天生物科技有限公司)检测血清 Lp-PLA2、Hcy 含量。

1.4 统计方法

选择 SPSS20.00 进行数据分析,计量资料用($\bar{x} \pm s$)表示,计数数据采用(%)表示,对比方法为 t 检验或卡方 χ^2 分析。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 总有效率对比

早期 CAS 组治疗后 7 d 的总有效率显著高于对照组($P<0.05$)。见表 2。

2.2 并发症发生情况对比

早期 CAS 组治疗后 7 d 的高灌注综合征、脑出血、低血压、心动过缓等并发症发生率为 4.7%,对照组无出现高灌注综合征、脑出血、低血压、心动过缓等并发症,对比差异无统计学意义。

义($P>0.05$)。见表 3。

表 2 两组治疗后 7 d 的总有效率对比(n)

Table 2 Comparison of total efficiency at 7d after treatment between the two groups (n)

Groups	n	Excellence	Valid	Invalid	Total effective rate
CAS group	43	38	4	1	43(100.00%)
Control group	43	23	14	6	37(86.05%)
t/χ^2					6.450
P					0.026

表 3 两组治疗后 7d 的并发症发生情况对比(n)

Table 3 Comparison of complications occurring at 7d after treatment between the two groups (n)

Groups	n	Hyperperfusion syndrome	Hyperperfusion syndrome	Hypopiesia	Bradycardia	Total
CAS group	43	0	0	1	1	2(4.7%)
Control group	43	0	0	0	0	0(0.0%)
t/χ^2						2.048
P						0.152

2.3 脑血流量与脑血容量变化对比

治疗前($P<0.05$),早期 CAS 组高于对照组($P<0.05$)。见表 4。

两组治疗后 7d 的颈内动脉相对脑血流量与脑血容量高于

表 4 颈内动脉相对脑血流量与脑血容量变化对比

Table 4 Comparison of relative internal carotid cerebral blood flow and cerebral blood volume

Groups	n	Relative brain blood flow		t	P	Relative cerebral blood volume		t	P
		Before treatment	7 d after treatment			Before treatment	7 d after treatment		
CAS group	43	0.78±0.13	1.10±0.04	24.672	0.000	0.84±0.08	1.08±0.15	18.036	0.000
Control group	43	0.79±0.09	0.92±0.03	15.699	0.000	0.85±0.05	0.92±0.09	9.177	0.002
t/χ^2		0.034	23.182			0.056	18.888		
P		0.988	0.000				0.000		

2.4 血清 Lp-PLA2、Hcy 含量变化对比

($P<0.05$),早期 CAS 组低于对照组($P<0.05$)。见表 5。

两组治疗后 7 d 的血清 Lp-PLA2、Hcy 含量低于治疗前

表 5 血清 Lp-PLA2、Hcy 含量变化对比

Table 5 Comparison of serum changes in Lp-PLA2 and Hcy

Groups	n	Lp-PLA2(μg/L)		t	P	Hcy(μmol/L)		t	P
		Before treatment	7 d after treatment			Before treatment	7 d after treatment		
CAS group	43	313.26±27.68	165.20±18.48	33.848	0.000	18.37±3.11	7.19±1.13	26.742	0.000
Control group	43	306.09±25.09	223.09±20.17	24.673	0.000	18.07±2.82	13.20±1.74	11.883	0.000
t/χ^2		0.187	19.013			0.124	15.003		
P		0.823	0.000			0.881	0.000		

3 讨论

脑血管病是由于各种原因引起的脑部血管疾病的总称,也是神经系统的多发病与常见病,其中脑梗是最为常见的一种,该病常因颈动脉粥样硬化性狭窄所致^[15]。研究显示如果动脉粥样硬化患者的脑血管储备能力受损,可导致脑梗的发生率显著

增加。颈动脉粥样硬化脑梗患者多发生于中老年,随着人口老龄化进程的加快,其发病率逐年上升^[16,17]。

早期进行颈动脉支架血运重建可减少梗死灶体积,能挽救可逆的缺血组织,增加半暗带神经细胞的存活,还可避免由于不可逆损伤或坏死组织再灌注引起的并发症^[18]。颈内动脉支架置入能降低脑梗的发生率及致残率,在临床上的应用具有很好

的效果^[19,20]。本研究显示早期 CAS 组治疗后 7 d 的高灌注综合征、脑出血、低血压、心动过缓等并发症发生率为 4.7%，对照组无出现高灌注综合征、脑出血、低血压、心动过缓等并发症，对比差异无统计学意义($P>0.05$)，表明早期颈内动脉支架置入在动脉粥样硬化脑梗患者的应用能提高治疗效果，且不会明显增加不良反应的发生，但是也有研究^[21,22]表明不同狭窄患者对 CAS 手术的反应也不相同，重度狭窄患者 CAS 术后改善效果更佳显著。

颈动脉粥样硬化性狭窄的主要原因是血液流变学和动力学的改变，导致脑组织缺血甚至坏死，造成供血区域血容量减少，使得患者出现神经功能障碍^[23,24]。并且颈动脉内侧壁的血流保持层流，有着很高的流速和很强的剪切力，剪切力异常时可引起动脉粥样硬化性斑块破裂脱落，从而诱发脑梗^[25,26]。本研究显示两组治疗后 7 d 的颈内动脉相对脑血流量与脑血容量高于治疗前($P<0.05$)，CAS 组高于对照组($P<0.05$)，表明颈内动脉支架置入在动脉粥样硬化脑梗患者的应用能改善患者的血流动力学状况，当前也研究表明^[27]颈内动脉支架置入的目的不仅仅是解决动脉粥样硬化的问题，还需要积极预防与改善缺血脑组织区域脑血流的低灌注状况，可预防缺血性脑血管事件的再次发生，本研究与其结论一致。

脑梗死是一个受多因素影响的复杂疾病，动脉粥样硬化在脑梗的发病中起着主导作用，因此采取及时有效的诊断及治疗对脑梗显得尤为重要^[28]。LP-PLA2 是脑梗的诊断和预测指标，具有较高的灵敏度和特异度^[29]。其属于磷脂家族亚型，相对分子质量约为 4.54×10^4 ，含有 441 个氨基酸，由巨噬细胞和淋巴细胞分泌合成，能水解低密度脂蛋白上的氧化卵磷脂，还可与低密度脂蛋白结合，从而动态反映血管内炎症的程度^[30]。Hcy 是蛋氨酸代谢过程中的重要中间产物，也是一种具有细胞毒性的含硫氨基酸。当 Hcy 在体内代谢途径受阻时，可使得血清 Hcy 含量升高，引起慢性病理损害，诱发各种心脑血管疾病的发生^[31,32]。本研究显示两组治疗后 7 d 的血清 Lp-PLA2、Hcy 含量低于治疗前($P<0.05$)，CAS 组低于对照组($P<0.05$)，表明颈内动脉支架置入在动脉粥样硬化脑梗患者的应用能抑制 Lp-PLA2、Hcy 的表达，与上述研究结果一致。同时在颈内动脉支架置入中，术中要求全身肝素化；当患者心率下降到 50 次/min 时，应给予阿托品、多巴胺维持血压，围手术期和术后要严格的抗血小板治疗；积极把患者的血糖与血压控制在正常范围内，术后要改变不良的生活习惯^[33,34]。由于经费限制，本次研究的病例数相对较少，尚缺乏远期疗效资料，将在后续研究中探讨分析。

总之，早期颈内动脉支架置入在动脉粥样硬化脑梗患者的应用能抑制 Lp-PLA2、Hcy 的表达，改善患者的血流动力学变化，从而促进提高治疗效果，在临床上的应用具有很好的安全性。

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