

doi: 10.13241/j.cnki.pmb.2017.14.031

脑蛋白水解物对缺血性脑血管病患者血流动力学及神经功能的影响*

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摘要 目的:探讨脑蛋白水解物对缺血性脑血管病患者血流动力学、血脂水平及神经功能的影响。**方法:**92例缺血性脑血管病患者依据抽签法分作对照组与观察组,各46例,对照组采用常规治疗,观察组在常规治疗基础上结合脑蛋白水解物治疗,观察并比较两组患者的全血低切黏度、全血高切黏度、血浆黏度、红细胞压积、纤维蛋白原、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)、神经功能、脑血管储备能力、屏气指数以及临床效果。**结果:**治疗后,两组血流动力学均低于治疗前,且观察组低于对照组($P<0.05$);两组TC、TG、LDL-C均低于治疗前,且观察组低于对照组($P<0.05$);两组HDL-C均高于治疗前,且观察组高于对照组($P<0.05$);两组NIHSS均低于治疗前,且观察组低于对照组($P<0.05$);两组脑血管储备能力及屏气指数均高于治疗前,且观察组高于对照组($P<0.05$)。观察组治疗有效率高于对照组,差异具有统计学意义($P<0.05$)。**结论:**脑蛋白水解物可有效调节缺血性脑血管病患者血流动力学及血脂水平,改善神经功能。

关键词:缺血性脑血管病;脑蛋白水解物;血流动力学;神经功能

中图分类号:R743 **文献标识码:**A **文章编号:**1673-6273(2017)14-2725-04

Effects of Brain Protein Hydrolysate on Hemodynamics and Neural Function of Patients with Ischemic Cerebrovascular Disease*

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ABSTRACT Objective: To study the effects of brain protein hydrolysate on hemodynamics, blood lipid levels and neural function in patients with ischemic cerebrovascular disease. **Methods:** 92 patients with ischemic cerebrovascular disease who were treated in our hospital were selected and randomly divided into the control group and the observation group, with 46 cases in each group. The patients in the control group were treated with the conventional method, while the patients in the observation group were treated with the brain protein hydrolysate on the basis of the conventional treatment. Then the levels of the whole blood low shear viscosity, whole blood high shear viscosity, plasma viscosity, erythrocyte pressure volume, fibrinogen, total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL-C) and high density lipoprotein (HDL-C) and the nerve function, cerebrovascular reserve capacity, breathless index and the clinical effect in the two groups were observed and compared before and after the treatment. **Results:** After treatment, the hemodynamics of the two groups were significantly lower than before, and the observation group was lower than that of the control group ($P<0.05$); the levels of TC, TG and LDL-C in the two groups were lower than before, and the observation group was lower than that of the control group ($P<0.05$); the levels of HDL-C in the two groups were higher than before, and the observation group was higher than that of the control group ($P<0.05$); the NIHSS in the two groups were lower than before, and the observation group was lower than that of the control group ($P<0.05$); the cerebrovascular reserve capacity and breath holding index of the two groups were higher than before, and the observation group were higher than those of the control group ($P<0.05$). The effective rate in the observation group was higher than that of the control group ($P<0.05$). **Conclusion:** Brain protein hydrolysate can effectively regulate hemodynamics and blood lipid levels in patients with ischemic cerebrovascular disease and improve the neurological function.

Key words: Ischemic cerebrovascular disease; Brain protein hydrolysate; Blood flow dynamics; Nerve function

Chinese Library Classification (CLC): R743 **Document code:** A

Article ID:1673-6273(2017)14-2725-04

前言

缺血性脑血管病是因各种诱因造成脑组织部分血流减少或者中断,进而导致失语、感觉障碍、瘫痪等临床症状,致残率

及病死率均较高,预后不良^[1]。血流动力学异常、脂代谢紊乱是缺血性脑血管病的常见危险因素^[2,3]。缺血性脑血管病能够诱导脑组织缺血坏死,并形成缺血暗带,造成不同程度的神经功能损伤。近年来,脑蛋白水解物已广泛运用于脑血管疾病的治疗,

* 基金项目:陕西省自然科学基金研究计划项目(2012JM4004)

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(收稿日期:2016-11-12 接受日期:2016-11-30)

但关于其治疗效果报道不一^[4]。本研究就探讨脑蛋白水解物对缺血性脑血管病患者血流动力学、血脂水平及神经功能的影响。

1 资料与方法

1.1 一般资料

选择我院 2014 年 2~2015 年 2 月收治的缺血性脑血管病患者 92 例,均符合《各类脑血管疾病诊断要点》中的相关诊断标准^[5],同时经脑部影像学等检查确诊。纳入无明确手术指征,发病至入院时间在 12 h 内,伴意识不清、失语、偏瘫等症状,近 7 天无抗血小板药物使用史。将合并肿瘤、自身免疫系统障碍、肝肾功能不全、过敏体质者予以排除。本研究已签署家属知情同意书,且通过我院伦理委员会批准,依据抽签法分作对照组与观察组,各 46 例。对照组有 28 例男性,18 例女性;年龄 45~70 岁,平均(62.37±1.49)岁;发病至入院时间 1~12 h,平均(3.48±0.27)h;疾病类型:有 23 例缺血性脑卒中,14 例脑梗塞,9 例脑梗死。观察组有 26 例男性,20 例女性;年龄 43~72 岁,平均(62.21±1.43)岁;发病至入院时间 1~12h,平均(3.45±0.24)h;疾病类型:有 22 例缺血性脑卒中,16 例脑梗塞,8 例脑梗死。比较两组基础资料无差异($P>0.05$),有比较性。

1.2 方法

对照组采用常规治疗,即予以饮食控制、抗凝、调节血脂、脱水、保持水电解质平衡等常规治疗,必要时予以吸氧。观察组在常规治疗基础上结合脑蛋白水解物治疗,15~25 mL 脑蛋白水解物+250 mL 0.9%生理盐水稀释,予以患者静脉滴注,每天 1 次,1 个疗程为 14 天,两组均连续治疗 4 个疗程。

1.3 观察指标

于治疗前及治疗结束时抽签患者空腹外周静脉血 2 mL,

常规处理后于特定环境中保存待检。^①采用全自动血液分析仪测定患者血流动力学:全血低切黏度(low blood viscosity)、全血高切黏度(high blood viscosity)、血浆黏度(Plasma viscosity, SV)、红细胞压积(hematokrit, HCT)、纤维蛋白原(fibrinogen, FIB)。^②采用全自动生化分析仪测定血脂水平: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)。^③采用神经功能缺损程度评分(NIHSS)评估患者治疗前及治疗结束时神经功能,参照上肢运动、下肢运动、感觉、面瘫、视野、凝视、意识水平等方面评估,神经功能损伤程度与分数呈正相关。^④于治疗前及治疗结束时采用多普勒超声检测仪测定屏气前后患者两侧大脑中动脉平均流速,后计算脑血管储备能力及屏气指数值。^⑤于治疗结束时进行临床效果评估^[6]:NIHSS 减少在 91%以上,且未见病损即基本痊愈;NIHSS 间质在 46%~90%之间,中度残疾即显著进步;NIHSS 减少在 18%~45%之间即进步;NIHSS 波动在 17%以下即稳定;NIHSS 增加超过 18%即恶化。基本痊愈、显著进步、进步均判定为有效。

1.4 统计学分析

选择 SPSS18.0 行数据统计,用均数±标准差($\bar{x} \pm s$)表示计量资料,用 t 检验比较,用[n(%)]表示计数资料,用 χ^2 检验比较,等级资料用秩和检验, $P<0.05$ 有统计学意义。

2 结果

2.1 治疗前后两组患者血液动力学比较

治疗前,比较两组血液动力学无差异($P>0.05$);治疗后,两组全血低切黏度、全血高切黏度、血浆黏度、红细胞压积、纤维蛋白原均有降低,观察组低于对照组,比较差异显著($P<0.05$),见表 1。

表 1 治疗前后两组患者血液动力学比较($\bar{x} \pm s$)

Table 1 Comparison of hemodynamics between the two groups before and after treatment

Groups	N	Low blood viscosity		High blood viscosity		SV (m Pa·s)		HCT (%)		Fibrinogen (g/L)	
		(mPa·s)		(mPa·s)							
		Before	After	Before	After	Before	After	Before	After	Before	After
		treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment
Control group	46	12.58±	7.52±	5.76±	4.79±	1.83±	1.41±	48.23±	41.20±	4.07±	3.28±
		2.37	1.53	0.58	0.28	0.32	0.26	6.80	5.73	0.36	0.27
Observation group	46	12.49±	5.19±	5.74±	4.05±	1.82±	1.30±	48.14±	36.50±	4.08±	3.09±
		2.34	1.20	0.57	0.14	0.30	0.18	6.72	5.41	0.34	0.20
t		0.183	8.127	0.166	16.032	0.154	2.359	0.063	4.045	0.137	3.835
P		0.855	0.000	0.897	0.000	0.877	0.020	0.949	0.000	0.891	0.000

2.2 治疗前后两组患者血脂水平比较

治疗前,比较两组血脂水平无差异($P>0.05$);治疗后,两组 TC、TG、LDL-C 均有降低,观察组低于对照组,两组 HDL-C 均有上升,观察组更明显,比较差异显著($P<0.05$),见表 2。

2.3 治疗前后两组患者神经功能比较

治疗前,比较两组神经功能无差异($P>0.05$);治疗后,两组 NIHSS 均有降低,观察组低于对照组,比较差异明显($P<0.05$),见表 3。

2.4 治疗前后两组患者脑血管储备能力及屏气指数比较

治疗前,比较两组脑血管储备能力及屏气指数无差异($P>0.05$);治疗后,两组脑血管储备能力及屏气指数均有升高,观察组高于对照组,差异明显($P<0.05$),见表 4。

2.5 两组临床效果比较

观察组有效率高于对照组,差异具有统计学意义($P<0.05$);两组患者治疗期间均无明显不良反应($P>0.05$)。见表 5。

3 讨论

缺血性脑血管病是临床常见的脑血管疾病,血流动力学异

表 2 治疗前后两组患者血脂水平比较($\bar{x} \pm s$)

Table 2 Comparison of blood lipid levels between the two groups before and after treatment

Groups	n	TC(mmol/L)		TG(mmol/L)		LDL-C(mmol/L)		HDL-C(mmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	46	5.35± 0.23	4.39± 0.18	2.18± 0.30	1.53± 0.25	3.82± 0.27	3.17± 0.23	1.15± 0.19	1.39± 0.23
Observation group	46	5.31± 0.20	3.86± 0.12	2.17± 0.25	1.43± 0.19	3.80± 0.25	2.76± 0.21	1.16± 0.21	1.58± 0.26
t		0.890	16.616	0.173	2.159	0.368	8.928	0.239	3.712
P		0.375	0.000	0.862	0.033	0.713	0.000	0.811	0.000

表 3 治疗前后两组患者神经功能比较($\bar{x} \pm s$)

Table 3 Comparison of neural function between the two groups before and after treatment

Groups	n	NIHSS(points)	
		Before treatment	After treatment
Control group	46	23.26± 5.17	13.79± 2.64
Observation group	46	23.32± 5.25	9.40± 1.81
t		0.054	9.301
P		0.956	0.000

表 4 治疗前后两组患者脑血管储备能力及屏气指数比较($\bar{x} \pm s$)

Table 4 Comparison of cerebrovascular reserve capacity and breathless index between the two groups before and after treatment

Groups	n	Cerebrovascular reserve capacity(%)		Breathless index	
		Before treatment	After treatment	Before treatment	After treatment
Control group	46	18.32± 2.67	26.74± 3.11	0.73± 0.12	1.06± 0.21
Observation group	46	18.26± 2.63	34.18± 3.57	0.74± 0.15	1.29± 0.28
t		0.108	10.657	0.353	4.457
P		0.913	0.000	0.724	0.000

表 5 两组患者临床效果比较[(n)%]

Table 5 Comparison the clinical effect between the two groups

Groups	n	Recovery	Effective	Progress	Stable	Deterioration	Efficient rate
Control group	46	11(23.91)	13(28.26)	9(19.56)	8(17.39)	5(10.86)	33(71.73)
Observation group	46	15(32.60)	19(41.30)	7(15.21)	4(8.69)	1(2.17)	41(89.13)
z/χ^2		2.043					4.420
P		0.041					0.035

常在其发生、发展中起着关键作用^[7]。全血黏度低切升高能够提示红细胞的聚集能力增强,红细胞变形能力减弱时则可使全血黏度高切升高^[8]。血浆黏度升高时可造成血浆中的大分子物质在红细胞周围聚集,诱导网络结构的形成,造成红细胞压积增加,进而引起脑血流灌注形成阻滞,使脑血供不足,导致脑组织及营养物质出现不同程度的缺氧^[9]。血浆纤维蛋白原的浓度高,可起聚合作用,能够加速动脉粥样斑块的发展,致使官腔出现狭窄,引起脑血流下降^[10]。本研究显示,治疗前患者血流动力学指标均明显升高,提示缺血性脑血管病患者多伴不同程度的血

流动力学异常。有研究指出,血脂代谢紊乱是导致缺血性脑血管病的另一重要因素,TC 作为机体重要物质,能够介导细胞膜形成;TG 能够为机体提供能量,还可促进肝脏、脂肪等组织合成^[11]。LDL-C 的浓度过高,能够促进动脉粥样硬化斑块的形成,阻滞血管;HDL-C 作为机体重要的脂蛋白,对血管内的血垢、多余血脂具有清除作用,进而清洁血管^[12]。本研究发现,治疗前患者 TC、TG、LDL-C 显著升高,HDL-C 降低,进一步证实此类患者存在血脂代谢紊乱。提示尽早治疗能够使缺血性脑血管病患者的预后得到一定改善^[13]。

脑蛋白水解物是一种活性肽,其分子量小,存在良好的脂溶性,能够直接透过血脑屏障,起到治疗作用^[14]。本研究表示,脑蛋白水解物治疗后血流动力学指标低于常规治疗者,提示脑蛋白水解物能够缓解脑部的血液循环,使脑组织缺血、缺氧得到有效改善^[15]。同时本研究显示,脑蛋白水解物治疗后血脂水平改善更明显,提示脑蛋白水解物能够利于血脂代谢的调节,进而改善动脉粥样硬化的形成。有关研究表明,脑血供不足能够促进乳酸过度产生,导致酸性中毒;同时导致神经末梢对于兴奋性氨基酸的调节出现异常,降低神经细胞灭活兴奋氨基酸的能力,引起神经元损伤,导致神经功能受损^[16]。有学者指出,早期若能确保可逆性损伤神经元的充分血流灌注,可有效改善神经功能^[17]。本研究显示,脑蛋白水解物治疗后NIHSS低于常规治疗者,提示脑蛋白水解物对神经功能有保护作用,考虑与其可有效改善脑部血流灌注,同时可使神经元蛋白的合成加快,利于轴突的生长发育,造成脑组织抗氧化能力增加,避免不良因素对中枢神经系统的刺激^[18,19]。相关研究报道,缺血性脑血管疾病发生时可导致侧支循环代偿出现不足,诱导脑动脉扩张,继而启动脑血管储备能力的代偿反应,屏气指数能够客观提示脑血管储备及扩张状态^[20]。本研究显示,脑蛋白水解物治疗后脑血管储备能力及屏气指数更高,提示其可增加脑血流灌注的代偿能力,提高脑血管功能。且经脑蛋白水解物治疗后有效率明显高于常规治疗者,提示其可有效改善患者神经功能,减轻残疾程度,改善预后。

综上,脑蛋白水解物可有效调节缺血性脑血管病患者血流动力学及血脂水平,改善神经功能。

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