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奥扎格雷与银杏达莫对老年急性脑梗塞患者血清 Cys-C 和 IL-6 的影响 *

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摘要 目的:探讨奥扎格雷联合银杏达莫对老年急性脑梗塞患者血清胱抑素 C(Cys-C), 白介素 -6(IL-6)及临床疗效的影响。**方法:**收集我院收治的 150 例急性脑梗塞患者,随机分为实验组和对照组,每组 75 例。两组患者入院后均给予抗血小板聚集,保护脑细胞等治疗措施,对照组患者给予银杏达莫注射液治疗;实验组患者在对照组的基础上给予奥扎格雷注射液治疗,治疗连续 4 周。观察并比较两组患血清 Cys-C、IL-6、患者神经功能缺损评分(NIHSS)以及治疗的总有效率。**结果:**与治疗前相比,治疗后两组患者的血清 Cys-C、IL-6 以及 NIHSS 水平均下降,差异具有统计学意义($P<0.05$);与对照组相比,实验组患者的 Cys-C、IL-6 以及 NIHSS 水平较低,差异具有统计学意义($P<0.05$);与对照组相比,实验组患者的治疗总有效率较高,差异具有统计学意义($P<0.05$)。**结论:**奥扎格雷联合银杏达莫能够降低老年急性脑梗塞患者血清 Cys-C、IL-6 水平,临床疗效较好,提高了治疗效果。

关键词:奥扎格雷;银杏达莫;急性脑梗塞;血清胱抑素 C;IL-6

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Effect of Ozagrel Combined with Ginkgo Leaf Extract and Dipyridamole Injection on Serum Cystatin C and IL-6 Level and in Elderly Patients with Acute Cerebral Infarction*

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ABSTRACT Objective: To investigate the effect of ozagrel combined with ginkgo leaf extract and dipyridamole on serum cystatin C (Cys-C) and interleukin 6 (IL-6) level and the clinical efficacy in senile patients with acute cerebral infarction. **Methods:** 150 cases of elderly patients with acute cerebral infarction were randomly divided into experimental group and control group, 75 cases in each group. After admission, the patients in the two groups were given anti platelet aggregation, brain cells protection drugs, etc., and the control group were treated with ginkgo leaf extract and dipyridamole injection; and the patients in the experimental group were given ozagrel sodium injection on the basis of the control group, once a day, continuously treated for 4 weeks. The serum Cys-C and IL-6 level, neurological function deficit score (NIHSS) and the treatment of total efficiency was observed and compared between two groups. **Results:** compared with before treatment, the serum Cys-C, IL-6 and NIHSS levels were decreased after treatment in the two groups of patients, and the difference was statistically significant ($P<0.05$); compared with the control group, Cys-C, IL-6 and NIHSS level was lower in the experimental group, and the difference was statistically significant ($P<0.05$); compared with the control group, the total effective rate was higher in the experimental group with statistical significance ($P<0.05$). **Conclusions:** Ozagrel sodium combined with ginkgo leaf extract and dipyridamole can reduce serum cystatin C and IL-6 levels in the treatment of senile acute cerebral infarction, and can obtain good clinical curative effect.

Key words: Ozagrel; Ginkgo Dipyridamole; Acute cerebral infarction; Cystatin C; IL-6

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前言

脑梗塞是由于各种原因引起的脑血管闭塞而产生的脑功能以及神经的损害而发生的临床综合征^[1]。急性脑梗塞(Acute

cerebral infarction, ACI)的发病率占全部脑血管病变类型的 75%,我国的急性脑梗塞发病率高于世界平均水平^[2]。有研究证实,高龄是急性脑梗死的重要危险因素,目前临床对于老年的急性脑梗死的治疗方法较多,但疗效并不理想^[3]。奥扎格雷为血

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栓素 A2(TXA2)合成酶的抑制剂,能阻碍前列腺素 H2(PGH2)生成 TXA2,能抑制血小板聚集,降低血黏度,同时具有解除血管痉挛的功效,可扩张脑血管,改善微循环,增加脑部的血液供应,减轻神经功能的损害程度^[4,5]。银杏达莫具有抗血小板活化因子(PAF)的功效,被认为是天然 PAF 受体的拮抗剂。有动物实验已经证实^[6],银杏内酯对大脑具有保护作用,其成分银杏黄酮苷能够清除氧自由基,抑制脂质的过氧化,保护脑细胞。本实验通过观察老年急性脑梗塞患者血清胱抑素 C(Cys-C),血清白介素-6(IL-6)水平的变化,探讨奥扎格雷联合银杏达莫对老年急性脑梗塞的治疗作用,现将结果报道如下。

1 资料与方法

1.1 临床资料

收集 2014 年 1 月~2016 年 1 月于我院就诊或住院治疗的 150 例急性脑梗塞患者,随机分为实验组和对照组,每组 75 例。实验组组内男性 43 例,女性 32 例,患者平均年龄(66.65±0.87)岁;对照组内男性 41 例,女性 34 例,患者平均年龄(67.23±0.94)岁。所有患者均符合中华医学会神经病学分会制定的《中国急性缺血性脑卒中诊治指南 2010》中关于急性脑梗死的诊断标准,并经 CT、MRI 等影像学检查确诊。所有患者均无心血管、胃肠道疾病以及肾功能不全;无恶性肿瘤;无意识障碍;无脑出血;无过敏反应;所有患者均签署知情同意书进行实验措施。两组患者一般资料相比具有可比性(P>0.05)。

1.2 方法

两组患者入院后均给予相应的治疗措施,包括抗血小板聚集,保护脑细胞等,对照组患者给予银杏达莫注射液(国药准字 H14023515 山西普德药业股份有限公司)10 mL+0.9 %氯化钠注射液 500 mL,静脉滴注,1 次/d;实验组患者在对照组的基础上给予奥扎格雷钠注射液(H20000216 海南碧凯药业有限公司)80 mg+0.9 %氯化钠注射液 250 mL,静脉滴注,1 次/d;治疗连续 4 周,治疗期间根据患者情况及时调整药量。

1.3 检测指标及评价方法

1.3.1 血清胱抑素-C(Cys-C)水平检测 患者于治疗前后取外周静脉血 3 mL,离心取上清,采用免疫透射比浊法,检测患者血清胱抑素 C(Cys-C)水平。

1.3.2 血清白介素-6(IL-6)水平检测 取所有患者治疗前后外周静脉血 2 mL,离心取上清,于-80℃条件下保存待检,采用 ELISA 法,检测患者血清白介素-6(IL-6)水平。

1.3.3 神经功能缺损评分(NIHSS) 患者于治疗前后参照美国卫生研究院卒中量表对患者的神经功能缺损评分(National Institutes of Health Stroke Scale,NIHSS)进行检测,其评分水平越高,患者的神经功能缺损程度越严重。

1.3.4 疗效评价 治疗后对患者的治疗效果进行判定:患者功能缺损的评分(NIHSS)减少在 75 %以上为痊愈;患者 NIHSS 减少在 50 %~75 %之间为显效;患者 NIHSS 减少在 25 %~50 %之间为好转;患者 NIHSS 减少量低于 25 %为无效。

1.3.5 患者不良反应情况检测 治疗期间对患者恶心、呕吐、腹泻、头晕、发热、心律失常等不良反应的发情况进行统计。

1.4 统计学分析

采用 SPSS 19.0 统计软件进行分析。计量数据采用 t 检验,以均数±标准差($\bar{x} \pm s$)表示;计数资料采用卡方检验,%表示。

所有数据比较,以 P<0.05 认为差异有统计学意义。

2 结果

2.1 患者治疗前后血清胱抑素 C(Cys-C)水平比较

治疗后,两组患者的 Cys-C 水平与治疗前相比均下降(P<0.05),与对照组相比,实验组患者 Cys-C 水平较低(P<0.05),具体见表 1。

表 1 患者治疗前后 Cys-C 水平比较(mg/L, $\bar{x} \pm s$)

Table 1 Comparison of the serum Cys-C level between two groups before and after treatment(mg/L, $\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	1.28± 0.24	0.72± 0.16* [#]
Control group	1.25± 0.21	1.01± 0.19*

Note: Compared with before treatment, *P<0.05; Compared with the control group, [#]P<0.05.

2.2 两组患者治疗前后 IL-6 水平比较

与治疗前相比,治疗后两组患者的血清 IL-6 水平均下降(P<0.05),与对照组相比,实验组患者的血清 IL-6 水平较低(P<0.05),具体见表 2。

表 2 患者治疗前后 IL-6 水平比较(pg/mL, $\bar{x} \pm s$)

Table 2 Comparison of the serum IL-6 level between two groups before and after treatment (pg/mL, $\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	15.38± 1.14	8.86± 1.35* [#]
Control group	14.95± 0.98	11.33± 1.04*

Note: Compared with before treatment, *P<0.05; Compared with the control group, [#]P<0.05.

2.3 患者神经功能缺损评分(NIHSS)比较

治疗后,两组患者 NIHSS 水平与治疗前相比均下降(P<0.05),与对照组相比,实验组患者的 NIHSS 水平较低(P<0.05),具体见表 3。

表3 患者治疗前后 NIHSS 水平比较($\bar{x} \pm s$)

Table 3 Comparison of the NIHSS level between two groups before and after treatment($\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	23.47± 1.26	11.53± 1.17* [#]
Control group	23.81± 1.13	15.41± 1.61*

Note: Compared with before treatment, *P<0.05; Compared with the control group, [#]P<0.05.

2.4 患者临床疗效比较

治疗后,实验组的治疗总有效率为 97.33 %,对照组为 81.33 %,实验组与对照组相比治疗总有效率较高,差异有统计学意义(P<0.05),具体见表 4。

2.5 患者不良反应发生情况比较

对照组患者中恶心 2 例,头晕 2 例,发热 1 例,心律失常 1

例,不良反应发生率为8%;实验组患者中恶心1例,头晕1例,不良反应发生率为2.67%,症状均较轻,经对症治疗后均好

转,对实验未产生影响。两组患者不良反应发生率无明显差异($P>0.05$)。

表4 患者临床疗效比较(%)

Table 4 Comparison of the clinical curative effect in two groups(% , $\bar{x} \pm s$)

	Cured	Excellent	Effective	Invalid	Total effective rate
Experimental group	45(60.0)	19(25.33)	9(12.0)	2(2.67)	73(97.33)*
Control group	33(44.0)	20(26.67)	8(10.67)	14(18.67)	61(81.33)

Note: Compared with the control group, * $P<0.05$.

3 讨论

急性脑梗塞由于脑组织缺血缺氧,因此临床出现一系列的神经功能缺损症状^[7]。已有研究证实,导致脑血管闭塞的原因包括:动脉粥样硬化斑块破裂,脂核内物质释放,血小板发生聚集,形成血栓,或其他部位形成的血栓随血流进入大脑,血栓逐渐增大,闭塞动脉或者堵塞分支血管;低血压造成的毛细血管缺血、缺氧,使供血区的脑组织出现坏死或凋亡等均可以导致急性脑梗塞的发生^[8]。研究表明^[9],血管的损伤引起的炎症反应,进而导致的血管内皮损伤是脑梗塞发病的重要因素。因此改善梗死区的血液循环,防止脑梗塞进一步加重是治疗的重点^[11]。

白细胞介素-6(IL-6)主要由巨噬细胞以及T淋巴细胞分泌,具有多种免疫调节功能以及生物学活性^[12]。IL-6能够刺激内皮细胞释放趋化因子,增加细胞的粘附性,对于炎症反应具有促进作用,同时可引起内皮细胞的损伤,产生氧自由基,引起病灶局部神经细胞死亡^[13]。有研究表明,在急性脑梗塞发病的过程中,血清IL-6水平会发生异常升高,至恢复期水平下降,其原因可能是脑组织缺血坏死后,炎细胞大量浸润,产生免疫应答反应,导致IL-6水平升高^[14]。在脑梗塞局部脑组织发生缺血时,IL-6可以作为重要的促炎因子,引起局部的炎症过度反应,破坏血脑屏障,同时还具有促凝血作用,诱导患者血栓形成,进一步加重病情^[15]。我们的实验结果表明,两组患者治疗前血清IL-6水平均升高,治疗后,两组患者的血清IL-6水平均下降,其中实验组患者的IL-6水平较低,这与之前的研究结果一致,提示我们的治疗措施能够降低患者血清IL-6水平,改善患者病情。

有研究证实^[16],脑梗塞患者的血清Cys-C水平呈异常升高。Cys-C是人体内的蛋白酶抑制剂,参与蛋白水解的调控^[17],Cys-C与蛋白酶相互作用,参与了多种心脑血管疾病过程,与动脉粥样斑块的稳定性关系密切,且能够调节炎症反应过程。近年来的研究表明^[18-20],Cys-C是脑血管疾病的危险因素,能够调节细胞外基质的水平以及半胱氨酸蛋白酶的活性。我们的实验结果表明,治疗后,两组患者的血清Cys-C水平均下降,实验组患者的血清Cys-C水平与对照组相比较低,提示奥扎格雷联合银杏达莫对急性脑梗塞具有较好的治疗效果。

综上所述,奥扎格雷联合银杏达莫能够降低老年急性脑梗塞患者血清胱抑素C、IL-6水平,临床疗效较好。

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