doi: 10.13241/j.cnki.pmb.2019.06.034

尤瑞克林联合静脉溶栓治疗急性脑梗塞的临床疗效及对血浆血小板、D-D、Fg 水平的影响 *

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摘要 目的:探讨尤瑞克林联合静脉溶栓治疗急性脑梗塞的临床疗效及对血浆血小板、D- 二聚体(D-D)、纤维蛋白原(Fg)水平的影响。**方法:**选择 2015 年 5 月至 2018 年 5 月我院接诊的急性脑梗塞患者 65 例作为研究对象,根据随机数表法分为观察组(n=35)和对照组(n=30)。对照组采用静脉溶栓治疗,观察组采用尤瑞克林联合静脉溶栓治疗。比较两组治疗后的临床疗效,治疗前后血浆血小板、D-D、Fg、美国国立卫生研究院卒中量表(NIHSS)评分、改良 Barthel 指数评定量表(MBI)水平的变化及不良反应的发生情况。**结果:**治疗后,观察组临床疗效总有效率为 94.29%,显著高于对照组(73.33%,*P<0.05*)。两组患者治疗前血浆血小板、D-D、Fg 水平、NIHSS、MBI 评分比较差异均无统计学意义(*P>0.05*);治疗后,两组患者血浆血小板、D-D、Fg 水平及 NIHSS 评分均较治疗前明显降低,且观察组患者以上指标均显著低于对照组(*P<0.05*);两组患者治疗治疗后 MBI 评分均较治疗前显著升高,且观察组 MBI 评分显著高于对照组(*P<0.05*)。两组患者不良反应总发生率分别为 2.86%、13.33%,组间比较差异无统计学意义(*P>0.05*)。**结论:**尤瑞克林联合静脉溶栓治疗急性脑梗塞患者的临床效果显著优于单用静脉溶栓治疗,这可能与其更有效改善改善患者血浆血小板、D-D、Fg 水平有关。

关键词:尤瑞克林;静脉溶栓;急性脑梗塞;血小板;D- 二聚体;纤维蛋白原

中图分类号:R743 **文献标识码:**A **文章编号:**1673-6273(2019)06-1156-04

Curative Efficacy of Eureklin Combined with Intravenous Thrombolysis in the Treatment of Acute Cerebral Infarction and Its Effects on the Plasma Platelet, D-D, Fg Levels*

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ABSTRACT Objective: To study the curative efficacy of Eureklin combined with intravenous thrombolysis in the treatment of acute cerebral infarction and its effects on the plasma platelet, D- dimer (D-D), fibrinogen (Fg) levels. **Methods:** 65 cases of patients with acute cerebral infarction treated in our hospital from May 2015 to May 2018 were selected as the subjects, The patients were divided into the observation group (n=35) and the control group (n=30) according to the random number table method. The control group was given intravenous thrombolysis, and the observation group was treated by intravenous thrombolysis on the basis of control group. The clinical efficacy after treatment, the changes of plasma platelet, D-D, Fg, NIHSS score, modified barbi index rating scale (MBI) before and after treatment and the occurrence of adverse reactions were compared between two groups. **Results:** After treatment, the total effective rate of observation group was 94.29%, which was significantly higher than that of the control group (73.33%, *P<0.05*). There was no significant difference in the plasma platelet, D-D, Fg level, NIHSS, MBI scores between the two groups before treatment (*P>0.05*). After treatment, the plasma platelets, D-D, Fg levels and NIHSS scores in both groups were significantly lower than before treatment, and the above indicators in the observation group were significantly lower than those in the control group (*P < 0.05*). MBI scores of patients in both groups were significantly higher after treatment than before treatment, and the MBI scores in the observation group were significantly higher than those in the control group (*P<0.05*). The total incidence of adverse reactions in the two groups was 2.86% and 13.33%, respectively, with no statistically significant difference between the two groups (*P>0.05*). **Conclusion:** The clinical effect of intravenous thrombolysis combined with eureklin is significantly better than that of intravenous thrombolysis alone in the treatment of acute cerebral infarction patients, which may be related to the more effective improvement of plasma platelet, D-D and Fg levels of patients.

Key words: Eureklin; Intravenous thrombolysis; Acute cerebral infarction; Platelets; D-dimer; Fibrinogen

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

Article ID: 1673-6273(2019)06-1156-04

* 基金项目:江苏省自然科学基金项目(2010229)

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(收稿日期:2018-11-08 接受日期:2018-11-30)

前言

急性脑梗塞是神经内科的常见疾病,通常是因局部脑组织区域血液供应障碍导致脑组织缺血缺氧性病变坏死,多发生于中老年人,具有发病急、病程进展快、病死率高等特点[1,2],现已成为我国三大病死原因之一,严重威胁患者的生命安全[3,4]。因此,急性脑梗塞治疗应以尽快恢复血液供应,挽救缺血半暗带细胞活性为主。

临床上通常采用早期溶栓治疗急性脑梗塞。阿替普酶是由氨基酸组成的溶栓药物,能通过氨基酸与纤维蛋白结合激活纤溶酶原转变为纤溶酶,从而起到溶解血栓、疏通血管的作用[5,6]。尤瑞克林是治疗急性脑梗塞的最新药物,可有选择性的扩张缺血脑组织血管,达到减少梗死面积、改善血液循环的目的[7,8]。本研究主要探讨了尤瑞克林联合静脉溶栓治疗急性脑梗塞的临床疗效及对血浆血小板、D-D、Fg 水平的影响,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 5 月至 2018 年 5 月我院收治的急性脑梗塞患者 65 例进行研究,我院伦理委员已批准此次研究。将所有患者随机分为两组,观察组男 19 例,女 16 例;年龄 54~83 岁,平均(69.85± 8.57)岁;对照组男 16 例,女 14 例;年龄 52~81 岁,平均(68.46± 8.13)岁;两组一般资料比较差异无统计学意义($P>0.05$),具有可比性。

纳入标准[9]:(1)符合《急性脑梗塞》的诊断标准,并通过头部 CT、MRI 等检查得以确诊;(2)无早期大面积梗死;(3)未出现脑出血。排除标准:(1)合并严重脑外伤者;(2)认知障碍者;(3)妊娠期及哺乳期妇女;(4)有颅内出血倾向者。

1.2 治疗方法

两组患者入院后均采用调脂、抗血小板、活血化瘀、改善脑循环、营养神经等药物,按中国急性缺血性脑卒中诊治指南[10]进行治疗。对照组给予阿替普酶(规格:20 mg/ 支,生产厂家:Boehringer Ingelheim Pharma GmbH&Co, KG, 国药准字 S20120035) 0.9 mg/Kg (最大剂量为 90 毫克),其中在 1min 内静脉注射 10%的剂量,剩下的 90%剂量在 1h 内静脉滴注。观察组在对照组的基础上加用尤瑞克林 (规格:0.15PNA 单位 / 瓶,生产厂家:广东天普生化医药股份有限公司,国药准字 H20052065)0.15PNAU 加入 0.9%氯化钠注射液 100 mL 静脉滴注,1 天 1 次。

1.3 观察指标

收集患者静脉血 3 mL,用 3000 r/min 转速离心 20 min 后将血清分离,放在 -80℃ 冰箱以备检测。血小板使用全自动血小板聚集仪光电比浊法检测,血清 D-D 使用酶联免疫吸附测定,Fg 水平采用双缩脲法检测。所有操作均严格按照说明书进行操作;日常生活活动能力评定采用改良 Barthel 指数量表:总分 100 分,分值越高,自理能力越强;NIHSS 评分量表:正常或近乎正常:0~1 分;轻度卒中:1~4;中度卒中:5~15 分;中 ~ 重度卒中:15~20 分;重度卒中:21~42 分;记录不良反应发生情况。

疗效评定标准[11]:显效:可自理生活,NIHSS 减少 > 90%;有效:自觉症状明显改善,NIHSS 减少 > 46%;无效:NIHSS 减少 < 17%。显效 + 有效 = 总有效率。

1.4 统计学分析

以 spss18.0 软件包处理数据,计量资料用均数± 标准差($\bar{x}\pm s$)表示,均为正态分布,组间比较使用独立样本 t 检验,计数资料以率表示,组间比较采用 x^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组患者疗效比较

治疗后,两组患者总有效率分别为 94.29%、73.33%,观察组总有效率显著高于对照组($P<0.05$),见表 1。

表 1 两组患者临床疗效的比较[例(%)]

Table 1 Comparison of the clinical efficacy between the two groups[n(%)]

Groups	n	Effective	Valid	Invalid	Total effective rate
Observation group	35	19(54.29)	14(40.00)	2(5.71)	33(94.29)
Control group	30	13(43.33)	9(30.00)	8(26.67)	22(73.33)
x^2 value					5.448
P value					0.020

2.2 两组患者治疗前后血浆血小板、D-D、Fg 水平的比较

两组患者经治疗后血浆血小板聚集率、D-D、Fg 水平均较治疗前明显降低,且观察组患者血浆血小板聚集率、D-D、Fg 水平均显著低于对照组($P<0.05$),见表 2。

2.3 两组患者治疗前后 NIHSS、MBI 评分比较

治疗后,两组 NIHSS 评分较治疗前明显下降,MBI 评分较治疗前显著升高,且观察组 MBI 评分显著高于对照组,NIHSS 评分显著低于对照组($P<0.05$),见表 3。

2.4 两组患者不良反应发生情况的比较

两组患者不良反应总发生率分别为 2.86%、13.33%,组间比较差异无统计学意义($P>0.05$),见表 4。

3 讨论

脑梗塞的发生主要是因脑组织局部血流灌注减少或中断,导致脑组织的缺氧或缺血,最终出现生理功能丧失[12,13]。脑梗塞前期无明显症状,局灶性神经体征在数分钟至数小时达到高峰,是一个复杂的、有多个病理生理环节参与的过程[14,15]。有研究显示脑缺血损伤主要包括炎症反应损伤、细胞因子释放及氧

表 2 两组患者治疗前后血浆血小板、D-D、Fg 水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the plasma platelet, D-D and Fg levels between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Platelet aggregation (%)		D-D(mg/L)		Fg(mg/L)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	35	71.89± 20.14	37.13± 22.31	0.86± 0.27	0.30± 0.12	5.24± 1.28	3.29± 1.54
Control group	30	70.97± 19.28	51.89± 20.07	0.87± 0.29	0.46± 0.14	5.13± 1.63	4.23± 1.58
t value		0.187	2.784	0.144	4.962	0.305	2.424
P value		0.852	0.007	0.886	0.000	0.762	0.018

表 3 两组患者治疗前后 NIHSS、MBI 评分比较($\bar{x}\pm s$)

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

Groups	n	NIHSS		MBI	
		Before the treatment	After treatment	Before the treatment	After treatment
Observation group	35	15.75± 6.42	5.02± 3.01	25.38± 4.23	69.35± 7.07
Control group	30	15.85± 7.62	8.17± 5.23	26.02± 4.18	51.32± 8.63
t value		0.057	3.028	0.611	9.259
P value		0.954	0.004	0.543	0.000

表 4 两组患者不良反应发生情况比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between the two groups [n(%)]

Groups	n	Blood in the urine	Subcutaneous ecchymosis	Alimentary tract hemorrhage	The total incidence of
Observation group	35	1	0	0	1(2.86)
Control group	30	1	2	1	4(13.33)
x^2 value					2.497
P value					0.114

自由基毒性损伤等[16,17]。既往通常使用溶栓治疗该病，能使血管再通，恢复其局部脑组织供血。

阿替普酶，是一种新型溶栓药物，是由 526 个氨基酸组成的糖蛋白，能减轻神经功能损伤，使血栓内的纤溶酶原转变成纤溶酶，从而发挥溶解血栓的作用。但是血栓溶解后会形成新的栓子，激活血小板再次形成血栓，因而需要与其他药物联合用药以控制急性脑梗塞的发展[18,19]。尤瑞克林是国家一类新药，主要成分及化学名称为人尿激肽原酶，可选择性扩张缺血脑组织微血管，改善局部脑血流，且具有一定的神经保护作用，能够抑制神经细胞的凋亡，促进脑缺血后神经干细胞增殖和迁移，最终起到神经修复作用[20,21]。也有研究显示尤瑞克林可有效改善急性脑梗塞患者的炎症反应[22]。本研究结果显示联合尤瑞克林治疗的患者的临床总有效率高达 94.29%，明显高于单独使用静脉溶栓治疗的患者，且患者 NIHSS 评分显著低于单药治疗者，MBI 评分明显高于单药治疗者，提示联合用药能提高患者的临床疗效，改善患者日常生活活动能力和病情严重程度。此外，两组患者不良反应总发生率比较差异无统计学意义，提示联合用药是安全的。Muramatsu K[23]等研究显示尤瑞克林能明显改善急性脑梗塞患者的神经损伤，分析是因为尤瑞克林具有较强抗脂质过氧化作用，能有效清除机体的有效自由基，减轻神经损伤，保护脑组织。

血浆血小板是从骨髓成熟的巨核细胞胞浆解脱落下来的小块胞质，能够迅速黏附于创伤处，并聚集成团，形成较松软的止血栓子[24,25]。D-D 是一种由纤维蛋白溶解酶产生的交联纤维蛋白溶解凝块，可以维持机体内血液的流动和修复组织，对血管的通透性有至关重要的作用[26,27]。Fg 是由肝脏合成的促进血小板聚集的凝血蛋白，促进平滑肌和内皮细胞的生长，增加血液粘滞性，引起内皮细胞损伤[28,29]。本研究结果显示联合用药患者的血浆血小板聚集率、D-D、Fg 水平显著低于单药治疗的患者，提示联合尤瑞克林能有效改善患者的血液高凝聚状态，这与 Ke X J[30]等研究结果相似。分析是因为尤瑞克林作用于内皮细胞释放大量纤溶酶原激活剂，可提高其活性，促进血栓快速溶解，同时阻断血小板聚集，降低外周血管阻力，降低血液粘度，改善血管微循环。

综上所述，尤瑞克林联合静脉溶栓治疗急性脑梗塞患者的临床效果显著优于单用静脉溶栓治疗，这可能与其更有效改善改善患者血浆血小板、D-D、Fg 水平有关。

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