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尤瑞克林联合血管内介入对急性脑梗死患者神经功能、炎症因子和血液流变学的影响 *

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摘要 目的:探讨血管内介入联合尤瑞克林对急性脑梗死(ACI)患者炎症因子、血液流变学以及神经功能的影响。**方法:**选取我院于2017年4月~2019年12月间收治的80例ACI患者,采用随机数字表法分为对照组($n=40$)和研究组($n=40$),对照组给予血管内介入溶栓治疗,研究组在对照组基础上联合尤瑞克林治疗,比较两组患者疗效、神经功能、炎症因子、血液流变学和不良反应。**结果:**研究组治疗14 d后的临床总有效率为90.00%(36/40),高于对照组的72.50%(29/40)($P<0.05$)。两组治疗14 d后血清白介素-6(IL-6)、白介素-1 β (IL-1 β)、单核细胞趋化蛋白-1(MCP-1)水平、美国国立卫生研究院卒中量表(NIHSS)评分以及血浆黏度、全血黏度高切、全血黏度低切、红细胞聚集指数均较治疗前下降,且研究组低于对照组($P<0.05$)。两组不良反应发生率比较差异无统计学意义($P>0.05$)。**结论:**尤瑞克林联合血管内介入治疗ACI患者,疗效显著,可有效改善机体神经功能、炎症因子和血液流变学,且安全性较好。

关键词:尤瑞克林;血管内介入;急性脑梗死;神经功能;炎症因子;血液流变学

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Effects of Urinary Kallidinogenase Combined with Intravascular Intervention on Neurological Function, Inflammatory Factors and Hemorheology in Patients with Acute Cerebral Infarction*

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ABSTRACT Objective: To investigate the effect of urinary kallidinogenase combined with intravascular intervention on neurologic function, inflammatory factors and hemorheology in patients with acute cerebral infarction (ACI). **Methods:** 80 patients with ACI who were admitted to our hospital from April 2017 to December 2019 were selected, they were randomly divided into control group ($n=40$) and study group ($n=40$). The control group was given intravascular thrombolytic therapy, and the study group was treated with urinary kallidinogenase on the basis of the control group. The efficacy, neurological function, inflammatory factors, hemorheology and adverse reactions of the two groups were compared. **Results:** The total clinical effective rate of the study group at 14d after treatment was 90.00% (36/40), which was higher than 72.50% (29/40) of the control group ($P<0.05$). The levels of serum interleukin-6 (IL-6), interleukin-1 β (IL-1 β), monocyte chemotactic protein 1 (MCP-1), National institutes of health stroke scale (NIHSS) score, plasma viscosity, high whole blood viscosity, low whole blood viscosity and red blood cell aggregation index of the two groups at 14 d after treatment decreased than those before treatment, and the study group was lower than the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Urinary kallidinogenase combined with intravascular intervention in the treatment of ACI is effective, which can effectively improve the nervous function, inflammatory factors and hemorheology, and which has a good safety.

Key words: Urinary kallidinogenase; Intravascular intervention; Acute cerebral infarction; Neurological function; Inflammatory factors; Hemorheology

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前言

急性脑梗死(ACI)是因为局部脑组织出现供血障碍,导致脑组织缺血、缺氧性坏死,引发机体神经功能障碍的一类疾病^[1]。随着人们饮食结构的改变,以及我国人口老龄化进程的加快,ACI的发病率呈逐渐升高趋势,若未能予以治疗,将增加致残、致死风险^[2]。现临床有关ACI的治疗尚无特效方案,其主要治疗原则为有效恢复脑组织的血液灌注量,保护脑缺血半暗带^[3]。血管内介入溶栓治疗是治疗ACI的主要方法,可有效控制患者病情,改善梗死区域的缺血、缺氧症状^[4]。但由于ACI患者一旦发病,即可引发内皮细胞损伤、白细胞激活等身体内部的反应,进一步产生局部炎症反应,而局部炎症反应又可促使梗死面积扩大而导致严重的神经功能缺损^[5]。单纯的血管内介入溶栓治疗并不能彻底的逆转神经功能损伤。尤瑞克林具有良好的改善脑侧支重建循环的作用,既往常用于治疗轻-中度急性血栓性脑梗死患者^[6]。本院通过对我院收治的部分ACI患者予以尤瑞克林联合血管内介入治疗,疗效显著,报道如下。

1 资料与方法

1.1 一般资料

选取我院于2017年4月~2019年12月间收治的80例ACI患者,纳入标准:(1)诊断标准参考全国第五届脑血管病学术会议制定的相关标准^[7];(2)均为首次发病,且经头颅CT或磁共振成像检查确诊;(3)发病至入院时间<72h;(4)对本次研究用药无禁忌者;(5)签署知情同意书。排除标准:(1)合并精神障碍无法沟通交流者;(2)合并有出血者或凝血功能障碍者;(3)合并严重心、肝、肾功能不全者;(4)伴有颅内动脉瘤或静脉畸形者;(5)合并感染、免疫缺陷类疾病者。采用随机数字表法分为对照组(n=40)和研究组(n=40),其中研究组男24例,女16例,年龄47~76岁,平均(60.51±6.97)岁;发病时间:9~70h,平均(35.47±4.87)h;梗死部位:大脑皮质12例,小脑15例,皮质下13例;梗死基本类型:大动脉粥样硬化型7例,小动脉闭塞型13例,心源性梗死型12例,不明原因型8例。对照组男25例,女15例,年龄49~76岁,平均(61.09±7.24)岁;发病时间:6~71h,平均(35.82±5.91)h;梗死部位:小脑10例,皮质下14例,大脑皮质16例;梗死基本类型:心源性梗死型10例,大动脉粥样硬化型9例,不明原因型8例,小动脉闭塞型13例。两组一般资料比较无差异($P>0.05$),均衡可比。本研究获得我院医学伦理委员会批准。

1.2 方法

两组均给予血管内介入溶栓治疗,具体操作如下:采用

Seldinger穿刺法,行脑血管造影,采用微导管尖端尽量接近闭塞病变血管区域,随后选用阿替普酶(Boehringer Ingelheim Pharma GmbH & Co.KG,注册证号:S20160054,规格:50 mg/支)进行溶栓治疗,治疗期间严密监测患者心率、平均动脉压等。介入治疗后给予常规基础对症治疗,包括丹参川芎嗪(吉林四长制药有限公司,国药准字H22026448,规格:5 mL),将10 mL丹参川芎嗪溶入250 mL 0.9%氯化钠注射液,静脉滴注,1次/d,连续应用14 d。阿司匹林(拜耳医药保健有限公司,国药准字J20171021,规格:阿司匹林100 mg),100 mg/次,1次/d,连续应用14 d。同时两组患者均给予降糖、降压与调脂药物。在以上基础上,研究组给予尤瑞克林(广东天普生化医药股份有限公司,国药准字H20052065,规格:0.15PNA单位)治疗,将0.15PNA单位的尤瑞克林溶入100 mL 0.9%氯化钠注射液,静脉滴注,1次/d,连续应用14 d。

1.3 观察指标

(1)记录两组治疗14 d后的临床疗效。总有效率=(治愈例数+显效例数+有效例数)/总例数×100%。治愈:临床症状消失,病残程度0级,美国国立卫生研究院卒中量表(NIHSS)评分减少90%-100%;显效:临床症状基本消失,病残程度1~3级,NIHSS评分降低46%-89%;有效:临床症状有所好转,NIHSS评分降低18%-45%;无效:临床症状无变化,NIHSS评分降低18%或增加^[8]。(2)于治疗前、治疗14 d后采用NIHSS评价患者神经功能,NIHSS含15项内容,每项0~2分,总分30分,分数越高,神经功能缺损越严重。(3)记录两组治疗期间不良反应发生情况。(4)于治疗前、治疗14 d后抽取患者清晨空腹肘静脉血3 mL,经常规离心处理(3800 r/min离心12 min,离心半径8 cm)分离上清液置于-30℃冰箱中待测。选用上海吉泰远成生物科技有限公司试剂盒,采用酶联免疫吸附法检测血清白介素-6(IL-6)、白介素-1β(IL-1β)、单核细胞趋化蛋白-1(MCP-1)水平。采用EB-5000型自动血液流变检测仪(上海欧加华医疗仪器有限公司)检测血液流变学指标:全血黏度低切、全血黏度高切、血浆黏度、红细胞聚集指数。

1.4 统计学方法

采用SPSS22.0进行统计分析。计量资料用均值±标准差($\bar{x} \pm s$)的形式表示,采用t检验,计数资料以率(%)的形式表示,采用 χ^2 检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组总有效率比较

研究组治疗14 d后的临床总有效率为90.00%(36/40),高于对照组的72.50%(29/40)($P<0.05$);详见表1。

表1 两组总有效率比较 例(%)

Table 1 Comparison of total effective rate between two groups [n(%)]

Groups	Cure	Markedly effective	Effective	Invalid	Total effective rate
Control group(n=40)	8(20.00)	12(30.00)	9(22.50)	11(27.50)	29(72.50)
Study group(n=40)	12(30.00)	16(40.00)	8(20.00)	4(10.00)	36(90.00)
χ^2					4.021
P					0.045

2.2 两组神经功能状况比较

对照组治疗前 NIHSS 评分为(14.18± 2.95)分,治疗 14 d 后 NIHSS 评分为(10.26± 2.17)分,低于治疗前($t=6.770, P=0.000$);研究组治疗前 NIHSS 评分为(14.25± 2.74)分,治疗 14d 后 NIHSS 评分为(6.41± 0.97)分,低于治疗前($t=17.059, P=0.000$);研究组治疗 14 d 后 NIHSS 评分低于对照组($t=13.591,$

$P=0.000$)。

2.3 两组炎症因子水平比较

两组治疗前 IL-6、IL-1 β 、MCP-1 比较无差异 ($P>0.05$);两组治疗 14 d 后 IL-6、IL-1 β 、MCP-1 均较治疗前下降,且研究组低于对照组 ($P<0.05$);详见表 2。

表 2 两组炎症因子水平比较($\bar{x} \pm s$)

Table 2 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	IL-6(pg/mL)		IL-1 β (pg/mL)		MCP-1(pg/mL)	
	Before treatment	14 d after treatment	Before treatment	14 d after treatment	Before treatment	14 d after treatment
Control group(n=40)	6.94± 1.03	5.31± 0.89*	12.63± 2.05	8.21± 1.34*	6.88± 1.19	4.72± 0.91*
Study group(n=40)	6.98± 1.02	4.67± 0.71*	12.58± 2.36	4.85± 1.25*	6.81± 1.07	2.15± 0.78*
t	0.175	3.555	0.101	11.596	0.277	13.562
P	0.862	0.001	0.920	0.000	0.783	0.000

Note: compared with before treatment, * $P<0.05$.

2.4 两组血液流变学指标比较

两组治疗前血浆黏度、全血黏度低切、红细胞聚集指数、全血黏度高切比较无差异 ($P>0.05$),两组治疗 14 d 后血浆黏度、

全血黏度低切、红细胞聚集指数、全血黏度高切均较治疗前降低,且研究组低于对照组 ($P<0.05$),详见表 3。

表 3 两组血液流变学指标比较($\bar{x} \pm s$)

Table 3 Comparison of hemorheology indexes between the two groups($\bar{x} \pm s$)

Groups	Low whole blood viscosity (mPa·s)		High whole blood viscosity (mPa·s)		Plasma viscosity(mPa·s)		Red blood cell aggregation index	
	Before	14 d after	Before	14 d after	Before	14 d after	Before	14 d after
	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment
Control group (n=40)	21.89± 3.45	15.91± 2.27*	6.72± 0.31	5.51± 0.38*	2.03± 0.24	1.61± 0.25*	24.18± 4.67	18.86± 3.79*
Study group (n=40)	21.96± 3.18	10.73± 2.05*	6.76± 0.35	4.24± 0.29*	1.98± 0.28	1.12± 0.24*	23.96± 4.63	13.12± 2.65*
t	0.094	10.711	0.541	14.751	0.857	8.942	0.212	7.850
P	0.925	0.000	0.590	0.000	0.394	0.000	0.833	0.000

Note: compared with before treatment, * $P<0.05$.

2.5 两组不良反应发生情况比较

对照组出现腹泻、恶心各 1 例、2 例呕吐,不良反应发生率为 10.00%(4/40);研究组出现 1 例恶心、3 例腹泻、2 例呕吐,不良反应发生率为 15.00%(6/40)。两组不良反应发生率比较无差异($\chi^2=0.457, P=0.499$)。

3 讨论

ACI 是临床常见的脑血管疾病,多发于中老年群体,该病的临床表现主要为眩晕、耳鸣、头痛、半身不遂等。该病的主要病理基础为颅内动脉血栓栓塞或血栓形成,导致脑组织血流中断,若闭塞血管内血流灌注未及时恢复则可引发一系列组织损伤^[9-11]。ACI 的发病机制复杂,目前,已知的 ACI 发生、发展进程及状态均与血管内皮功能失调关系密切^[12]。随着研究的深入,人们发现炎症反应、血液流变学异常均参与了动脉粥样硬化的

发生、发展全过程。当机体出现内皮细胞损伤时,血管壁可继发炎症细胞的黏附并释放炎症因子,进而激活凝血机制,引起血液流变学异常从而再次形成血栓,加重机体病情程度^[13-15]。现临床针对 ACI 的治疗重点主要在于开通堵塞脑血管,恢复脑组织供血。血管内介入治疗是急诊治疗 ACI 的首要方法,可促进梗死血管再通,恢复组织灌注血流^[16,17]。然而,有学者指出血管内介入治疗易发生缺血再灌注损伤,且局部注射阿替普酶将增加脑出血风险^[18]。因此,如何进一步优化治疗方法已成为目前临床研究的焦点。尤瑞克林是尿液蛋白水解酶提取物之一,既往研究认为尤瑞克林可以在 ACI 后迅速开启二级侧支循环,继而增加脑血流,改善神经功能缺失^[19,20]。

本次研究结果显示,与单纯的血管内介入治疗相比,尤瑞克林联合血管内介入治疗 ACI 患者,可有效改善机体神经功能,进一步提高治疗效果。究其原因,患者通过血管内介入治

疗,对患者注入阿替普酶,阿替普酶是一种纤溶酶原激活剂,可通过将纤溶酶原转化为纤溶酶而溶解血栓,进而阻止脑组织供血动脉进一步狭窄或闭塞^[21,22]。而尤瑞克林可通过激活自身激肽原酶-激肽系统,促使激肽原向血管舒张素与激肽转化,起到扩张缺血区血管的作用,改善缺血脑组织的血氧供应,从而保护缺血区半暗带,促进神经元修复与新生血管形成,有效保护患者神经功能^[23,24]。本次研究结果还显示,两组患者治疗后炎症因子和血液流变学指标均有所改善,且研究组的改善效果更佳,表明尤瑞克林联合血管内介入治疗 ACI 患者可有效阻止疾病进展,降低机体损伤程度。这可能是因为尤瑞克林进入人体后,可活化激肽原,进而产生赖氨酰缓激肽、缓激肽、胰激肽等多种激肽类活性物质,而这些激肽类物质与相应的受体结合后可影响多种信号传导途径,进而发挥促进血管舒张、抑制炎症反应等生物学效应^[25,26]。此外,尤瑞克林可促进脑损伤新生血管形成,并解除微血管痉挛,抑制血小板聚集,从而改善机体血液流变学状态^[27,28]。另两组不良反应发生率比较无差异,可见尤瑞克林联合血管内介入治疗安全可靠。这可能与尤瑞克林可选择性的作用于脑缺血区的血管,而对正常区域的脑血管几乎无负面影响有关^[29,30]。本次研究尚存在样本量偏小、未能观察不同剂量用药疗效的不足,后续研究中将扩大样本量、设置不同剂量用药的分组以获取更为准确的数据。

综上所述,尤瑞克林联合血管内介入治疗 ACI 患者,疗效显著,可有效改善机体神经功能、炎症因子和血液流变学,且安全性较好。

参考文献(References)

- [1] Sun Z, Xu Q, Gao G, et al. Clinical observation in edaravone treatment for acute cerebral infarction [J]. Niger J Clin Pract, 2019, 22(10): 1324-1327
- [2] 蔡珍飞, 吴肖萍, 曹丹. 2017 年台州地区急性脑梗死发生的流行特征[J]. 实用预防医学, 2019, 26(10): 1247-1250
- [3] Liu X, Rao S, Wang J. Intravenous thrombolysis in combination with mild hypothermia therapy in the treatment of acute cerebral infarction [J]. Pak J Med Sci, 2019, 35(4): 1161-1166
- [4] 宋贺, 张金峰, 唐蕊, 等. 急性脑梗死患者经导管选择性脑动脉内介入溶栓治疗的回顾性研究[J]. 河北医药, 2019, 41(13): 2022-2025
- [5] Teng L, Meng R. Long Non-Coding RNA MALAT1 Promotes Acute Cerebral Infarction Through miRNAs-Mediated hs-CRP Regulation [J]. J Mol Neurosci, 2019, 69(3): 494-504
- [6] 陆伟恒, 罗成宏, 廖成钜, 等. 尤瑞克林联合阿司匹林对急性脑梗死患者血清学指标及临床疗效的影响 [J]. 实用医学杂志, 2017, 33(21): 3615-3618
- [7] 陈伟群, 王新德. 全国第五届脑血管病学学术会议纪要 [J]. 中华神经科杂志, 2000, 33(4): 252
- [8] 雷俊杰, 冯可, 莫志怀, 等. 急性脑梗死 CISS 分型与同型半胱氨酸及 NIHSS 评分的关系[J]. 广东医学, 2018, 39(z1): 114-116
- [9] Wang N, Liu L, Jiang X, et al. Acute multiple cerebral infarction combined with cerebral microhemorrhage in Polycythemia vera: A case report[J]. Exp Ther Med, 2019, 18(4): 2949-2955
- [10] Zeng X, Hu J, Liang X, et al. Acute cerebral infarction following a Trimeresurus stejnegeri snakebite: A case report [J]. Medicine (Baltimore), 2019, 98(23): e15684
- [11] 樊文萍, 黄学莲, 马凤英, 等. 丹红注射液治疗急性脑梗死的临床疗效分析[J]. 现代生物医学进展, 2018, 18(9): 1772-1775
- [12] Hidaka M, Yamaguchi S, Koyanagi Y, et al. Reocclusion of the treated vessel due to endothelial injury after mechanical thrombectomy in a patient with acute ischaemic stroke[J]. BMJ Case Rep, 2019, 12(8): e228937
- [13] Liu YX, Cao QM, Ma BC. Pathogens distribution and drug resistance in patients with acute cerebral infarction complicated with diabetes and nosocomial pulmonary infection[J]. BMC Infect Dis, 2019, 19(1): 603
- [14] QiaoZhen X, AiGuo M, Tong W, et al. Correlation between of small dense low-density lipoprotein cholesterol with acute cerebral infarction and carotid atherosclerotic plaque stability [J]. J Clin Lab Anal, 2019, 33(6): e22891
- [15] Zhang W, Cheng J, Zhang Y, et al. Analysis of CT and MRI Combined Examination for the Diagnosis of Acute Cerebral Infarction[J]. J Coll Physicians Surg Pak, 2019, 29(9): 898-899
- [16] 汪宁, 张保朝, 温昌明, 等. 血管内介入治疗急性脑梗死的临床疗效及对患者血清神经元特异性烯醇化酶、脑钠肽及神经生长因子的影响[J]. 中国临床医生杂志, 2018, 46(7): 798-800
- [17] Zheng M, Wang X, Yang J, et al. Changes of complement and oxidative stress parameters in patients with acute cerebral infarction or cerebral hemorrhage and the clinical significance [J]. Exp Ther Med, 2020, 19(1): 703-709
- [18] 史哲, 卫景沛, 张茗, 等. 尤瑞克林联合阿替普酶治疗超早期脑梗死的近期疗效观察[J]. 北京医学, 2015, 37(5): 498-499
- [19] Dong Y, Qu J, Zhang Z, et al. Human urinary kallidinogenase in treating acute ischemic stroke patients: analyses of pooled data from a randomized double-blind placebo-controlled phase IIb and phase III clinical trial[J]. Neurol Res, 2020, 42(4): 286-290
- [20] Qian Y, Lyu Y, Jiang M, et al. Human urinary kallidinogenase or edaravone combined with butylphthalide in the treatment of acute ischemic stroke[J]. Brain Behav, 2019, 9(12): e01438
- [21] Lee C, Na JU, Lee JH, et al. Characteristics of blood tests in patients with acute cerebral infarction who developed symptomatic intracranial hemorrhage after intravenous administration of recombinant tissue plasminogen activator [J]. Clin Exp Emerg Med, 2019, 6(2): 160-168
- [22] Xu H. Efficacy of different doses of alteplase thrombolysis on acute ischemic stroke in patients[J]. Pak J Pharm Sci, 2019, 32(5(Special)): 2465-2469
- [23] Chen L, Geng L, Chen J, et al. Effects of Urinary Kallidinogenase on NIHSS score, mRS score, and fasting glucose levels in acute ischemic stroke patients with abnormal glucose metabolism: A prospective cohort study[J]. Medicine (Baltimore), 2019, 98(35): e17008
- [24] 黄成兰. 尤瑞克林联合舒血宁治疗对脑梗死患者 NIHSS 评分、疗效及预后的影响[J]. 中国急救医学, 2018, 38(z2): 127
- [25] 李丹, 韩冰. 醒脑静注射液、尤瑞克林联合治疗对脑梗死病人神经功能缺损及脑血流动力学的影响[J]. 中西医结合心脑血管病杂志, 2018, 16(7): 846-848

- Breast Cancer by the Long Non-Coding RNA H19 [J]. *Int J Mol Sci*, 2017, 18(11): 2319
- [15] Zong W, Ju S, Jing R, et al. Long non-coding RNA-mediated regulation of signaling pathways in gastric cancer [J]. *Clin Chem Lab Med*, 2018, 56(11): 1828-1837
- [16] Scholz CJ, Weber H, Jungwirth S, et al. Explorative results from multistep screening for potential genetic risk loci of Alzheimer's disease in the longitudinal VITA study cohort [J]. *J Neural Transm (Vienna)*, 2018, 125(1): 77-87
- [17] Fox AH, Nakagawa S, Hirose T, et al. Paraspeckles: Where Long Noncoding RNA Meets Phase Separation [J]. *Trends Biochem Sci*, 2018, 43(2): 124-135
- [18] Li C, Liu T, Zhang Y, et al. LncRNA-ZDHHC8P1 promotes the progression and metastasis of colorectal cancer by targeting miR-34a[J]. *Eur Rev Med Pharmacol Sci*, 2019, 23(4): 1476-1486
- [19] Cui X, Yi Q, Jing X, et al. Mining Prognostic Significance of MEG3 in Human Breast Cancer Using Bioinformatics Analysis[J]. *Cell Physiol Biochem*, 2018, 50(1): 41-51
- [20] Jin L, Cai Q, Wang S, et al. Long noncoding RNA MEG3 regulates LATS2 by promoting the ubiquitination of EZH2 and inhibits proliferation and invasion in gallbladder cancer[J]. *Cell Death Dis*, 2018, 9(10): 1017
- [21] Yang Z, Li H, Li J, et al. Association Between Long Noncoding RNA MEG3 Polymorphisms and Lung Cancer Susceptibility in Chinese Northeast Population[J]. *DNA Cell Biol*, 2018, 37(10): 812-820
- [22] Xu J, Su C, Zhao F, et al. Paclitaxel promotes lung cancer cell apoptosis via MEG3-P53 pathway activation [J]. *Biochem Biophys Res Commun*, 2018, 504(1): 123-128
- [23] 孟菲菲, 司君利, 刘璐, 等. 长链非编码 RNA MEG3 在胃癌中的表达及其与预后的关系[J]. *中国肿瘤临床*, 2016, 43(15): 659-662
- [24] Cui X, Jing X, Long C, et al. Long noncoding RNA MEG3, a potential novel biomarker to predict the clinical outcome of cancer patients: a meta-analysis[J]. *Oncotarget*, 2017, 8(12): 19049-19056
- [25] Baratieh Z, Khalaj Z, Honardoost MA, et al. Aberrant expression of PlncRNA-1 and TUG1: potential biomarkers for gastric cancer diagnosis and clinically monitoring cancer progression [J]. *Biomark Med*, 2017, 11(12): 1077-1090
- [26] Esfandi F, Taheri M, Kholghi Oskooei V, et al. Long noncoding RNAs expression in gastric cancer [J]. *J Cell Biochem*, 2019, 120(8): 13802-13809
- [27] 熊乐, 卢婧, 刘安文. 长链非编码 RNA TUG1 在恶性肿瘤中的研究进展[J]. *临床与实验病理学杂志*, 2017, 33(4): 425-428
- [28] Ji TT, Huang X, Jin J, et al. Inhibition of long non-coding RNA TUG1 on gastric cancer cell transference and invasion through regulating and controlling the expression of miR-144/c-Met axis[J]. *Asian Pac J Trop Med*, 2016, 9(5): 508-512
- [29] 曹丽华, 殷丹丹, 夏成才, 等. lncRNA TUG1 在胰岛 β 细胞分泌胰岛素中的功能研究[J]. *现代生物医学进展*, 2017, 17(25): 4847-4851
- [30] Ren K, Li Z, Li Y, et al. Long Noncoding RNA Taurine-Upregulated Gene 1 Promotes Cell Proliferation and Invasion in Gastric Cancer via Negatively Modulating miRNA-145-5p [J]. *Oncol Res*, 2017, 25(5): 789-798

(上接第 2559 页)

- [26] Deguchi I, Osada T, Kimura H, et al. A case of acute cerebral infarction associated with an accessory middle cerebral artery in a patient who underwent thrombectomy[J]. *Acute Med Surg*, 2019, 7(1): e459
- [27] Novotny V, Khanevski AN, Bjerkreim AT, et al. Short-Term Outcome and In-Hospital Complications After Acute Cerebral Infarcts in Multiple Arterial Territories[J]. *Stroke*, 2019, 50(12): 3625-3627
- [28] Wang R, Zeng J, Wang F, et al. Risk factors of hemorrhagic transformation after intravenous thrombolysis with rt-PA in acute cerebral infarction[J]. *QJM*, 2019, 112(5): 323-326
- [29] Duan X, Zhang D, Wang K, et al. Comparative study of xuesaitong injection and compound salvia miltiorrhizae injection in the treatment of acute cerebral infarction: a meta-analysis [J]. *J Int Med Res*, 2019, 47(11): 5375-5388
- [30] Ni T, Fu Y, Zhou W, et al. Carotid plaques and neurological impairment in patients with acute cerebral infarction[J]. *PLoS One*, 2020, 15(1): e0226961