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替罗非班联合丁苯酞治疗超时间窗急性脑梗死患者对血清 HO-1、NO、VEGF、Ang-1 的影响 *

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摘要 目的：探讨替罗非班联合丁苯酞治疗超时间窗急性脑梗死患者对血清血红素加氧酶 -1（HO-1）、一氧化氮（NO）、血管生成素 -1（Ang-1）、血管内皮生长因子（VEGF）的影响。**方法：**选择 2018 年 1 月到 2020 年 1 月在我院接受治疗的 141 例超时间窗急性脑梗死患者，采用随机数表法分为联合组（n=71）和单药组（n=70）。单药组给予丁苯酞治疗，联合组在单药组的基础上给予替罗非班治疗。比较两组临床疗效、HO-1、NO、VEGF、Ang-1、美国国立卫生研究院卒中量表（NIHSS）、Barthel 指数（Barthel）、凝血酶时间（TT）、凝血酶原时间（PT）、纤维蛋白原（FIB）水平变化情况及药物并发症发生情况。**结果：**治疗后，两组总有效率比较差异显著（P<0.05）；治疗前，联合组和单药组血清 HO-1、NO、VEGF、Ang-1 比较无显著差异；治疗后联合组和单药组血清 HO-1、NO、VEGF 随着时间的推移而降低，且联合组均低于单药组，Ang-1 随着时间的推移而升高，且联合组均高于单药组，差异显著（P<0.05）；治疗前，联合组和单药组 NIHSS、Barthel 比较无显著差异；治疗后联合组和单药组 NIHSS 随着时间的推移而降低，且联合组均低于单药组，Barthel 随着时间的推移而升高，且联合组均高于单药组，差异显著（P<0.05）。**结论：**在超时间窗急性脑梗死患者中应用替罗非班联合丁苯酞效果显著，可能与其可有效改善血清 HO-1、NO、VEGF、Ang-1 水平有关，且不增加不良反应。

关键词：替罗非班；丁苯酞；超时间窗；急性脑梗死；血红素加氧酶 -1；一氧化氮；血管生成素 -1；血管内皮生长因子

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Effect of Tirofiban Combined with Butylphthalide on Serum HO-1, NO, VEGF and ANG-1 in Patients with Acute Cerebral Infarction Beyond Time Window*

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ABSTRACT Objective: To study Effect of tirofiban combined with butylphthalide on serum Heme oxygenase-1 (HO-1), nitric oxide (NO), angiogenin-1 (ANG-1), vascular endothelial growth factor (VEGF) in patients with acute cerebral infarction beyond time window. **Methods:** 141 patients with acute cerebral infarction beyond the time window treated in our hospital from January 2018 to January 2020 were selected and divided into combination group (n=71) and single drug group (n=70) by random number table method. The mono-drug group was given butylphthalide treatment, and the combination group was given tirofiban treatment on the basis of mono-drug group. Clinical efficacy, HO-1, NO, VEGF, ANG-1, the National Institutes of Health Stroke Scale (NIHSS), Barthel index (Barthel), thrombin time (TT), prothrombin time (PT), fibrinogen (FIB) levels and the incidence of drug complications were compared between the two groups. **Results:** After treatment, the total effective rate of the two groups was significantly different (P<0.05); before treatment, there was no significant difference in serum HO-1, no, VEGF, Ang-1 between the combined group and the single drug group; after treatment, the serum HO-1, no, VEGF in the combined group and the single drug group decreased with time, and the combined group was lower than the single drug group, and Ang-1 increased with time, and the combined group was higher than the single drug group, the difference was significant Before treatment, there was no significant difference in NIHSS and Barthel between the combined group and the single drug group; after treatment, NIHSS in the combined group and the single drug group decreased with the passage of time, and Barthel in the combined group increased with the passage of time, and the combined group was higher than the single drug group, the difference was significant (P<0.05). **Conclusion:** The effect of tirofiban combined with butylphthalide in patients with acute cerebral infarction over time window is significant, which may be related to the effective improvement of serum HO-1, no, VEGF, Ang-1 levels, and does not increase adverse reactions.

Key words: Tirofiban; Butylphthalide; Over time window; Acute cerebral infarction; Heme oxygenase-1; Nitric oxide; Angiopoietin-1; Vascular endothelial growth factor

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前言

超时间窗急性脑梗死指发病 6-7 h 后虽及时接受治疗，但神经功能缺损症状未得到改善，属于急性脑梗死中的特殊病种，可加重病情严重程度，增加致死率[1-3]。有研究显示[4]，因血管再通治疗被 " 时间窗 " 约束，导致多数超时间窗急性脑梗死患者错过最佳治疗时间，增加不良预后的发生率，因此对超时间窗急性脑梗死患者给予有效、科学的治疗方式对改善患者预后具有重要意义。丁苯酞是治疗脑梗死的常用药物，能改善脑血流灌注，促进神经功能修复；替罗非班是一种血小板糖蛋白受体拮抗剂，能抑制血小板聚集，改善血液循环[5,6]。有研究显示，血清 HO-1、NO、VEGF、Ang-1 在急性脑梗死中表达异常，可能参与了疾病的发展[7]。HO-1 是血红素代谢过程中的重要酶，当脑组织缺血损伤时会被诱导升高，通过抑制缺血再灌注损伤中的炎症反应保护脑组织；NO 是参与动脉粥样硬化形成的重要因子，其水平变化可反映脑梗死的进展；VEGF 是研究最广泛的促血管生长因子，其水平增高有利于脑梗死患者侧支循环的形成；Ang-1 是调节脉管系统的主要因子，当脑组织缺血时可抑制炎症及微血管的退行性病变[8-10]。因此，血清 HO-1、NO、VEGF、Ang-1 水平可作为诊治急性脑梗死的重要指标。本研究分析替罗非班联合丁苯酞治疗超时间窗急性脑梗死患者对血清 HO-1、NO、VEGF、Ang-1 的影响。

1 资料与方法

1.1 一般资料

选择 2018 年 1 月到 2020 年 1 月在我院接受治疗的 141 例超时间窗急性脑梗死患者，研究已获得我院伦理委员会批准实施。采用随机数表法分为 2 组，联合组 71 例，其中男 45 例，女 26 例，年龄 52~66 岁，平均（58.56± 6.13）岁；单药组 70 例，其中男 42 例，女 28 例，年龄 51~69 岁，平均（59.62± 8.21）岁。两组基线资料无明显差异，可比较。

诊断标准：参照《中国急性缺血性脑卒中诊治指南 2018》[11]：(1)急性起病；(2)局灶神经功能缺损(一侧面部或肢体无力或麻木，语言障碍等)，少数为全面神经功能缺损；(3)影像学出现责任病灶或症状体征持续 24 h 以上；(4) 排除非血管性病因；(5) 脑 CT / MRI 排除脑出血。

纳入标准：（1） 符合上述诊断标准；（2） 未见大面积梗死；（3）入院前未进行相关治疗者；（4）首次发病。排除标准：（1）伴有严重心、肾器官疾病者；（2）伴有呼吸衰竭、脑出血者；（3）自身免疫性疾病者；（4）符合实施抗凝、溶栓或降纤治疗的患者；（5）药物、酒精滥用史；（6）依从性较差者；（7）既往脑梗死患者；（8）肝肾功能严重不全者；（9）近期半年存在输血、手术、感染以及出血等情况者；（10）病历资料缺失或随访失联者；（11）对本次研究药物过敏者。

1.2 方法

单药组给予丁苯酞治疗：丁苯酞（规格：0.1 g，生产厂家：石药集团恩必普药业有限公司，国药准字 H20050299）0.2 g，口服，1d3 次。联合组在单药组的基础上给予替罗非班治疗：替罗非班（规格：50 mL：12.5 mg，生产厂家：DSM Pharmaceuticals, Inc.，国药准字：H20150589）50 mL/ 次，1d1 次，两组均治疗 28 d。

1.3 观察指标

采集肘静脉血 4 mL，提取血清，采用双抗体夹心酶联免疫吸附法测定 HO-1、NO、VEGF、Ang-1；PT、TT、FIB 水平采用凝血仪测定。神经功能缺损评分：分值越高，神经功能缺损越严重，两组患者量表评定均有神经内科主任医师进行评定；观察不良反应情况。

疗效评定标准：NIHSS 评分减少 >89%；有效：NIHSS 评分减少 46%~88%；无效：临床症状无明显改善甚至加重。

1.4 统计学分析

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

2 结果

2.1 不同组别临床治疗效果评价

治疗后，两组总有效率比较差异显著（$P<0.05$）见表 1。

表 1 不同组别临床治疗效果评价[n(%)]

Table 1 Clinical efficacy evaluation of different groups[n(%)]

Groups	n	Excellent	valid	Invalid	Total effective rate
Joint group	71	35(49.30)	29(40.85)	7(9.86)	64(90.14)
Single drug group	70	28(40.00)	23(32.86)	19(27.14)	51(72.86)
x^2 value					7.001
P value					0.008

2.2 不同组别血清 HO-1、NO、VEGF、Ang-1 检查结果比较

治疗前，联合组和单药组血清 HO-1、NO、VEGF、Ang-1 比较无显著差异；治疗后联合组和单药组血清 HO-1、NO、VEGF 随着时间的推移而降低，且联合组均低于单药组，Ang-1 随着时间的推移而升高，且联合组均高于单药组，差异显著（$P<0.05$），见表 2。

2.3 两组神经功能评分水平比较

治疗前，联合组和单药组 NIHSS、Barthel 比较无显著差异；治疗后联合组和单药组 NIHSS 随着时间的推移而降低，且联合组均低于单药组，Barthel 随着时间的推移而升高，且联合组均高于单药组，差异显著（$P<0.05$），见表 3。

3 讨论

脑梗死发病率较高，占脑血管疾病中占比 75%以上，超时

表 2 不同组别血清 HO-1、NO、VEGF、Ang-1 检查结果比较($\bar{x}\pm s$)

Table 2 Comparison of serum HO-1, NO, VEGF and ANG-1 in different groups($\bar{x}\pm s$)

Groups	n	HO-1(ng/mL)		NO(μmol/L)		VEGF(pg/mL)		Ang-1(ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Joint group	71	5.03± 2.35	3.21± 0.74	104.21± 12.31	73.26± 10.38	174.25± 26.58	102.39± 15.54	1.02± 0.21	1.46± 0.31
Single drug group	70	5.06± 2.48	3.98± 0.87	104.05± 12.64	88.59± 11.36	176.18± 27.06	136.58± 12.59	0.97± 0.24	1.21± 0.18
t value		0.074	5.664	0.076	8.367	0.427	14.343	1.317	5.845
P value		0.941	0.000	0.939	0.000	0.669	0.000	0.189	0.000

表 3 两组神经功能评分水平比较($\bar{x}\pm s$,分)

Table 3 Comparison of neurological function scores between the two groups($\bar{x}\pm s$, points)

Groups	n	NIHSS		Barthel	
		Before treatment	After treatment	Before treatment	After treatment
Joint group	71	11.69± 5.25	3.15± 0.87	52.95± 2.37	72.35± 2.12
Single drug group	70	11.83± 5.56	5.37± 1.26	53.15± 2.12	61.34± 2.28
t value		0.154	12.189	0.528	29.700
P value		0.878	0.000	0.598	0.000

间窗急性脑梗死属于急性脑梗死中的特殊病种,早期无明显症状,发病后 48 h 易造成神经功能损伤,是超时间窗急性脑梗死患者致残的重要因素[12,13]。有研究认为[14],超时间窗急性脑梗死早期进展主要是由于血流动力学改变,导致脑部血流不畅,导致脑组织缺血缺氧坏死,缺血损伤发生进展加重神经功能恶化,晚期是由于血栓形成,扩大脑水肿,继发瀑布炎症反应,最终加重症状。发病率及病死率较高,据调查显示,我国脑梗死发病 3 月后死亡率为 9.0%~9.6%,严重威胁人们的生命[15,16]。有学者发现,超时间窗急性脑梗死患者因受溶栓治疗时间窗的限制,导致多数患者失去最佳治疗机会[17]。因此,给予患者有效治疗,是改善患者血液供应,恢复神经功能,对改善患者预后具有重要意义。

临床治疗脑梗死的方法较多,经临床证实,联合治疗的方式能提高急性脑梗死的临床疗效,改善患者预后[18,19]。丁苯酞为人工合成的消旋体,能促进微循环重构,直接通过血脑屏障,阻断脑梗死所致脑损伤的病理环节,保护脑组织,保持血管的完整结构,增加脑部缺血组织的血流[20-22]。替罗非班是血小板受体 GPII b / III a 的特异性拮抗剂,是一种新型抗血小板聚集药物,能阻断血小板凝集,抑制血栓形成,保护脑组织,减轻神经细胞损伤,改善脑组织微循环,有效恢复患者受损脑组织功能[23,24]。有研究显示,替罗非班治疗脑卒中效果良好,且对进展性脑卒中患者的刺激性较小[25]。本研究对比分析了替罗非班联合丁苯酞与单独使用丁苯酞治疗超时间窗急性脑梗死的治疗效果,结果显示,联合治疗的患者总有效率明显高于单药组,本文从安全性方面来看,治疗期间均未发生明显不良反应,证实了联合治疗的安全性。分析其原因可能是因为丁苯酞有抗血小板作用,可改善脑缺血导致的氧化应激损伤;替罗非班则能避免过度神经元细胞诱导的炎症因子聚集,从而抑制体内的炎症反应,与丁苯酞联合发挥协同作用,从而提高治疗效果。本研究进一步分析了治疗期间神经功能评分水平及凝血功能水平的变化情况,结果显示,联合组患者 NIHSS、FIB 低于对照组,Barthel、TT、PT 高于对照组,证实了替罗非班联合丁苯酞能通过改善患者神经功能水平及凝血功能水平提高治疗效果。Gao H Q[26]等研究也显示,替罗非班可短时间起抗血小板聚集的作用,避免血栓形成,抑制血小板聚集,同时还能促使脑动脉血流快速恢复,增强脑细胞再灌注。分析其原因可能是因为丁苯酞能促进微循环重构,保持血管的完整结构,增加脑部缺血组织的血流;替罗非班进入患者机体后可抑制纤维蛋白原,改善缺血程度,促进损伤脑组织细胞的修复,两者联合治疗,加强对抗血小板凝聚作用,减轻血栓后续氧化应激及对神经功能损伤,从而改善患者神经功能。

有文献报道,多种细胞因子参与了超时间窗急性脑梗死的发生与发展[27]。HO-1 是血红素加氧酶家族中的成员之一,其水平在脑组织缺血损伤时升高,通过抑制缺血再灌注损伤过程中的氧化反应保护脑组织[28]。NO 具有神经元之间的信使物质作用,可参与血管平滑肌舒张等神经和调节血压等心血管功能变化过程,当脑组织缺血缺氧时可产生大量 NO,加速脑组织坏死[29,30]。VEGF 是在垂体率泡星状细胞纯化出的一类功能性蛋白,也是血管再生的主要因子,有利于血管内皮细胞的增殖及黏附,缓解脑组织损伤,还能促进血管生长,确保血管的正常功能,当发生急性脑梗死时,患者在严重脑缺血状态下可激活 VEGF,导致其水平升高[31,32]。Ang-1 是间质血管新生的主要蛋白,属于血管保护性指标,能促进血管形成,影响组织损伤的修复,同时还能提高内皮细胞敏感性,改善神经功能受损情况[33]。有研究显示,Ang-1 可保护受损神经元,参与梗死区域血管的重建,通过多种机制参与急性脑梗死的发生[34,35]。本研究将血清

HO-1、NO、VEGF、Ang-1 作为评估超时间窗急性脑梗死治疗疗效的重要指标，结果显示，联合组患者血清 HO-1、NO、VEGF 明显低于单药组，Ang-1 高于单药组，分析其原因可能是因为丁苯酞可增加缺血区毛细血管数量，提高脑血液灌注量，促进侧支循环的形成；替罗非班可改善患者脑血管痉挛和缺血程度，促进脑组织修复，恢复了脑部血液循环，改善血管内皮损伤，从而改善患者血清 HO-1、NO、VEGF、Ang-1 水平。

综上所述，在超时间窗急性脑梗死患者中应用替罗非班联合丁苯酞效果显著，可有效改善血清 HO-1、NO、VEGF、Ang-1 水平，且不增加不良反应。

参 考 文 献(References)

[1] Zhang W, Zuo P, Wang F, et al. Clinical Study on Treatment of Patients with Acute Cerebral Infarction by Huayu Tongluo Decoction Combined with Edaravone Injection [J]. E3S Web of Conferences, 2020, 185(8): 03011

[2] Xu J, Li P, He B, et al. A NEW THREE-DIMENSIONAL Co (II) -MIXED-LIGAND MOF: A PROTECTIVE EFFECT AGAINST ACUTE CEREBRAL INFARCTION BY REDUCING THE HS-CRP CONTENT AND INFLAMMATORY RESPONSE [J]. Journal of Structural Chemistry, 2020, 61(7): 1132-1137

[3] Zeng J, Wang F, Feng H, et al. Influencing Factors of Recanalization after Intravenous Thrombolysis with Urokinase in Acute Cerebral Infarction Patients[J]. European Neurology, 2020, 83(2): 1-5

[4] Cao J X, Liu L, Sun Y T, et al. Escitalopram improves neural functional prognosis and endothelial dysfunction in patients with acute cerebral infarction[J]. Restorative Neurology and Neuroscience, 2020, 38 (5): 385-393

[5] Pan L, Jin J, Huang R, et al. Application of transcranial Doppler in prognosis assessment of nerve function in patients with acute cerebral infarction after intracranial mechanical thrombectomy [J]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue, 2020, 32(7): 835-839

[6] Zhang W, Cheng J, Zhang Y, et al. Analysis of CT and MRI Combined Examination for the Diagnosis of Acute Cerebral Infarction [J]. Journal of the College of Physicians and Surgeons Pakistan, 2019, 29(9): 898-899

[7] Toyama M, Nakayama M, Fukaya K, et al. Early cardiac surgery for infective endocarditis with acute extensive cerebral infarction[J]. Indian Journal of Thoracic and Cardiovascular Surgery, 2020, 36(4): 1-4

[8] Mallory R. A RARE CASE OF ACUTE SIMULTANEOUS CARDIO-CEREBRAL INFARCTION WITH REVIEW OF MECHANISM OF ONSET AND OPTIMAL MANAGEMENT [J]. Journal of the American College of Cardiology, 2020, 75(11): 3036

[9] Chen, Zhang, Y-Q, et al. Correlations of acute myocardial infarction complicated by cerebral infarction with insulin resistance, adiponectin and HMGB1 [J]. European review for medical and pharmacological sciences, 2019, 23(10): 4425-4431

[10] Sasaki T, Yasuda T, Abe D, et al. A Case of Multiple Cerebral Infarction Preceding Acute Exacerbation of Idiopathic Thrombocytopenic Purpura[J]. Journal of Stroke and Cerebrovascular Diseases, 2019, 28 (3): 789-791

[11] Neurology branch of Chinese Medical Association, cerebrovascular disease group of Neurology branch of Chinese Medical Association. Guidelines for diagnosis and treat ment of acute ischemic stroke in China, 2018[J]. Chinese Journal of Neurology, 2018, 51(9): 666-682

[12] Debeaumarche H, Din A A E, Thouant P, et al. Progression in cerebral microbleeds number after acute myocardial infarction: Harmful role of triple antithrombotic therapy [J]. Archives of Cardiovascular Diseases Supplements, 2020, 12(1): 5-6

[13] Li J, Cao S, Hu W, et al. Intravascular Mechanical Thrombectomy for a Patient with Systemic Lupus Erythematosus and Acute Cerebral Infarction with Antiphospholipid Syndrome[J]. International Journal of Psychological and Brain Sciences, 2020, 5(1): 21

[14] Shenghua Z, Rui-Cong D, Hua H E. Effect of Yiqi Tongnao Decoction on Acute Cerebral Infarction of Qi Deficiency and Blood Stasis [J]. E3S Web of Conferences, 2020, 185(24): 03015

[15] Lee S H, Jung J M, Kim K Y, et al. Intramural Hematoma Shape and Acute Cerebral Infarction in Intracranial Artery Dissection: A High-Resolution Magnetic Resonance Imaging Study[J]. Cerebrovascular Diseases, 2020, 49(3): 1-8

[16] Park C, Lee E K, Kim S M, et al. Acute Kidney Injury after Administering Dapagliflozin to a Diabetic Patient with Acute Cerebral Infarction[J]. Korean Journal of Medicine, 2020, 95(6): 404-408

[17] Dang Y Y, Zhang Z H, Shen C S. Carotid Artery Stenting for the Treatment of Fatal Acute Cerebral Infarction Associated with Aortic Dissection[J]. Neurology India, 2020, 68(1): 185

[18] Chieh-Ni, Kao, Yu-Wei, et al. Acute cerebral infarction caused by atrial thrombus originating from left upper pulmonary vein stump after left upper lobe trisegmentectomy[J]. General Thoracic and Cardiovascular Surgery, 2020, 68(2): 206-207

[19] Deguchi I, Osada T, Takao M. Prescription status of oral anticoagulants in patients with acute cerebral infarction with non-valvular atrial fibrillation at the time of stroke onset[J]. Journal of Cardiology, 2020, 75(5): 544-548

[20] Xin M, Hao Y, Huang G, et al. The efficacy and safety of salvianolic acids on acute cerebral infarction treatment: A protocol for systematic review and meta analysis[J]. Medicine, 2020, 99(23): e20059

[21] Shao S J, Zhang G Z, Zhao L, et al. Microcatheter infusion of bolus-dose tirofiban for acute ischemic stroke due to distal intracranial artery occlusion[J]. Medicine, 2020, 99(30): e21366

[22] Nettersheim F, Hohmann C, Pfister R, et al. Schwere Tirofiban-induzierte Thrombozytopenie und thrombotische Mikroangiopathie nach perkutaner Koronarintervention [J]. Dmw Deutsche Medizinische Wochenschrift, 2019, 144(02): 109-113

[23] Wang H, Li X, Liu C, et al. Effects of Oral Antiplatelet Agents and Tirofiban on Functional Outcomes of Patients with Non-Disabling Minor Acute Ischemic Stroke[J]. Journal of Stroke and Cerebrovascular Diseases, 2020, 29(8): 104829

[24] Huo X C, Miao Z R. Consensus interpretation on "Expert consensus on clinical application of tirofiban in atherosclerotic cerebrovascular disease" [J]. Chinese Journal of Contemporary Neurology and Neurosurgery, 2020, 20(5): 381-385

[25] Kim Y W, Sohn S I, Yoo J, et al. Local tirofiban infusion for remnant stenosis in large vessel occlusion: tirofiban ASSIST study [J]. BMC Neurology, 2020, 20(1): 284

(下转第 2887 页)

[18] Brown EN, Pavone KJ, Naranjo M. Multimodal General Anesthesia: Theory and Practice[J]. Anesth Analg, 2018, 127(5): 1246-1258

[19] Nishiyama T. Changes in heart rate variability during anaesthesia induction using sevoflurane or isoflurane with nitrous oxide [J]. Anaesthesiol Intensive Ther, 2016, 48(4): 248-251

[20] 谭卫华, 曾慧, 刘健萍, 等. FloTrac/Vigileo 监测右美托咪定滴鼻复合七氟醚吸入诱导对先天性心脏病患儿血流动力学的影响[J]. 现代中西医结合杂志, 2018, 27(31): 3426-3429

[21] Sperna Weiland NH, Hermanides J, van der Ster BJP, et al. Sevoflurane based anaesthesia does not affect already impaired cerebral autoregulation in patients with type 2 diabetes mellitus[J]. Br J Anaesth, 2018, 121(6): 1298-1307

[22] 罗亮, 刘少星, 朱波, 等. 低体质量小儿心脏手术中应用七氟醚全身麻醉诱导的效果及其对血流动力学的影响[J]. 现代生物医学进展, 2019, 19(4): 763-766

[23] Palanca BJA, Avidan MS, Mashour GA. Human neural correlates of sevoflurane-induced unconsciousness[J]. Br J Anaesth, 2017, 119(4): 573-582

[24] Høyer KF, Nielsen TS, Risis S, et al. Sevoflurane Impairs Insulin Secretion and Tissue-Specific Glucose Uptake In Vivo [J]. Basic Clin Pharmacol Toxicol, 2018, 123(6): 732-738

[25] Gao C, He XF, Xu QR, et al. Sevoflurane downregulates insulin-like growth factor-1 to inhibit cell proliferation, invasion and trigger apoptosis in glioma through the PI3K/AKT signaling pathway [J]. Anticancer Drugs, 2019, 30(7): e0744

[26] Zhou L, Wang L, Hu X. PTEN in propofol-induced insulin resistance in mouse primary hepatocytes [J]. Exp Ther Med, 2018, 16 (6): 4831-4835

[27] 贺艳兰, 彭七华, 刘海根, 等. 丙泊酚与七氟醚对腹腔镜子宫肌瘤切除术患者胰岛功能的影响 [J]. 海南医学, 2018, 29 (12): 1679-1682

[28] Kim H, Han J, Jung SM, et al. Comparison of sevoflurane and propofol anesthesia on the incidence of hyperglycemia in patients with type 2 diabetes undergoing lung surgery[J]. Yeungnam Univ J Med, 2018, 35(1): 54-62

[29] 陈甜子, 角述兰, 杨柳, 等. 瑞芬太尼在全身麻醉中应用的研究进展[J]. 医学综述, 2017, 23(7): 1393-1396, 1401

[30] 官彬, 朱帅, 严军. 七氟烷吸入麻醉对小儿腹腔镜疝修补术后呼吸功能及 CRP、补体水平的影响[J]. 河北医科大学学报, 2019, 40(9): 1086-1089

(上接第 2938 页)

[26] Gao H Q, Xu S D, Li J R, et al. Tirofiban Promotes the Proliferation of Human Umbilical Vein Endothelial Cells InVitro Via Enhanced Vascular Endothelial Growth Factor Expression [J]. Transplantation Proceedings, 2020, 52(1): 419-422

[27] Ghonim A A, Mostafa A, Emara A, et al. Clinical outcome of intracoronary versus intravenous high-dose bolus administration of tirofiban in diabetic patients undergoing primary percutaneous coronary intervention [J]. Cardiovascular journal of Africa, 2019, 30(5): 285-289

[28] Vlachou M, Didagelos M, Kouparanis A, et al. Bridging with Tirofiban During Temporary Withdrawal of Oral Antiplatelets for Two Major Surgical Procedures in High Ischaemic Risk Patients [J]. The Open Cardiovascular Medicine Journal, 2019, 13(1): 1-4

[29] Felix, Sebastian, Nettersheim, et al. Severe tirofiban-induced thrombocytopenia and thrombotic microangiopathy after percutaneous coronary intervention [J]. Deutsche medizinische Wochenschrift (1946), 2019, 144(2): 109-113

[30] Canpolat U, Yorgun H, Aytemir K. Treatment of Sinus Node Artery Occlusion During Anterior Left Atrial Tachycardia Ablation Using Intracoronary Tirofiban [J]. JACC: Clinical Electrophysiology, 2019, 5(7): 870-871

[31] Wu C, Sun C, Wang L, et al. Low-Dose Tirofiban Treatment Improves Neurological Deterioration Outcome After Intravenous Thrombolysis[J]. Stroke, 2019, 50(12): 3481-3487

[32] Ding X, Gu A, Yang Q, et al. Intra-arterial tirofiban in a male nonagenarian with acute ischemic stroke: A case report [J]. Open Life Sciences, 2019, 14(1): 515-518

[33] Fu Z, Xu C, Liu X, et al. Safety and Efficacy of Tirofiban in Acute Ischemic Stroke Patients Receiving Endovascular Treatment: A Meta-Analysis[J]. Cerebrovascular Diseases, 2020, 49(4): 1-9

[34] Wang H, Feng M. Influences of different dose of tirofiban for acute ST elevation myocardial infarction patients underwent percutaneous coronary intervention[J]. Medicine, 2020, 99(23): e20402

[35] Moukafih B, Moutaouakkil Y, Adaoui A, et al. valuation de l'utilisation d'un inhibiteur de la glycoprotéine IIb/IIIa, Agrastat dans un centre de cardiologie au Maroc [J]. Le Pharmacien Hospitalier et Clinicien, 2020, 55(1): 24-29