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阿司匹林联合神经节苷脂治疗脑梗塞的临床疗效观察*

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摘要 目的:探讨阿司匹林联合神经节苷脂治疗脑梗塞的临床疗效及可能机制。**方法:**选择我院 2015 年 5 月到 2018 年 3 月接诊的 90 例脑梗塞患者,依照抽签法将其分为实验组和对照组,每组 45 例。两组患者均给予常规支持治疗,对照组在此基础上给予阿司匹林治疗,实验组在对照组的基础上给予单唾液酸四己糖神经节苷脂(Monosialyl tetrahexose ganglioside, GM1)治疗。据患者美国国立卫生研究院卒中量表(National Institutes of Health Stroke Scale, NIHSS)和 Barthel 指数评分的改善情况,比较两组的疗效,以及治疗前后血清过氧化脂质(lipid peroxide, LPO)、超氧化物歧化酶(superoxide dismutase, SOD)、丙二醛(malondialdehyde, MDA)、一氧化氮(nitric oxide, NO)水平的变化。**结果:**治疗后,实验组有效率为 96.86%,显著高于对照组(78.13%, $P<0.05$)。两组治疗后血清 SOD 水平及 Barthel 指数均较治疗前显著上升,而血清 LPO、MDA、NO 水平及 NIHSS 评分均较治疗前显著下降,实验组血清 SOD 水平及 Barthel 指数显著高于对照组,血清 LPO、MDA、NO 水平及 NIHSS 评分均明显低于对照组($P<0.05$)。**结论:**阿司匹林联合 GM1 能提高脑梗塞的疗效,可能与有效提高血清 SOD 水平及降低 LPO、MDA、NO 水平有关。

关键词:阿司匹林;单唾液酸四己糖神经节苷脂;脑梗塞;过氧化脂质(LPO);超氧化物歧化酶(SOD)

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Curative Efficacy of Aspirin Combined with Ganglioside in the Treatment of Cerebral Infarction*

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ABSTRACT Objective: To investigate the curative efficacy and possible mechanisms of aspirin combined with ganglioside in the treatment of cerebral infarction. **Methods:** 90 cases of cerebral infarction patients received in our hospital from May 2015 to March 2018 were selected, they were divided into the experimental group and the control group according to the lottery method, with 45 cases in each group. They were given routine supportive treatment, the control group was given aspirin treatment, and the experimental group was given monosialyl tetrahexose ganglioside (GM1) sodium injection based on the basis of control group. According to the improvement of National Institutes of Health Stroke Scale (NIHSS) and Barthel index scores, the efficacy and changes of serum lipid peroxide (LPO), superoxide dismutase (SOD), malondialdehyde (MDA) and nitric oxide (NO) levels before and after treatment were compared two groups. **Results:** After treatment, the effective rate of experimental group was 96.86%, which was significantly higher than that of the control group (78.13%, $P<0.05$). After treatment, the serum SOD level and Barthel index were significantly increased than those before treatment, while the serum LPO, MDA, NO levels and NIHSS score in both groups were significantly decreased than those before treatment, and the serum SOD level and Barthel index in the experimental group were significantly higher than that of the control group, the serum LPO, MDA, NO levels and NIHSS scores in the experimental group were significantly lower than that of the control group ($P<0.05$). **Conclusion:** Aspirin combined with GM1 can improve the curative effect of cerebral infarction, which may be related to the effective increase of serum SOD level and the decrease of LPO, MDA and NO levels.

Key words: Aspirin; Monosialyl tetrahexose ganglioside; Cerebral infarction; Lipid peroxidation(LPO); Superoxide dismutase(SOD)

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前言

脑梗塞又称缺血性脑卒中,是临床上脑卒中患者最常见的类型,多发于中老年,约占总数的 80%^[1],死亡率高,患者预后不

佳,可致残。颈动脉系统和椎-基底动脉系统栓塞为脑梗塞的主要病因,少有先前症状,发病急促,患者多因突发脑水肿、眩晕和昏迷入院,日后主要有偏瘫、失语、偏侧感觉障碍等神经损伤样症状和脑出血、脑疝等并发症^[2]。能否及时有效治疗脑梗

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塞,减少神经损伤程度,提高预后患者生活水平在临床上广受关注。

单唾液酸四己糖神经节苷脂 (Monosialyl tetrahexose ganglioside, GM1)是临床上应用较多的一种中枢神经修复药物^[3],而阿司匹林对血小板凝集有抑制作用,常用于缺血性心脏病和血栓治疗^[4]。血清血清过氧化脂质(lipid peroxide, LPO)、超氧化物歧化酶 (superoxide dismutase, SOD)、丙二醛(malondialdehyde, MDA)、一氧化氮(nitric oxide, NO)水平提示神经细胞因缺血,受氧自由基损伤的程度^[5]。本研究选择了 68 例脑梗塞患者,分别给予单纯阿司匹林治疗和联合 GM1 治疗,通过对患者治疗前后的美国国立卫生研究院卒中量表 (National Institutes of Health Stroke Scale, NIHSS)和 Barthel 评分变化的比较,探讨了阿司匹林联合神经节苷脂治疗脑梗塞的疗效及对患者血清 LPO、SOD、MDA、NO 水平的影响,以期为临床实践提供理论支持。

1 资料与方法

1.1 一般资料

选择我院 2015 年 5 月到 2018 年 3 月接诊的 90 例脑梗塞患者,依照抽签法分为实验组和对照组,所有患者及其家属均被告知并同意参与该研究,并经得我院伦理委员会批准实施。入选标准:患者均进行过影像学检查和实验室检查 (CT 及 MRI),结果符合《临床 CT 诊断急性脑梗塞》中的标准^[6],NIHSS 评分在 6 分以上。排除标准:对本研究相关药物过敏,脑部肿瘤及感染,心肝肾功能障碍等合并其他脏器疾病。实验组 45 例,年龄(55.3± 8.5)岁,男性 28 例,女性 17 例,发病时间(12.3± 3.8)h;对照组 45 例,年龄(58.0± 6.5)岁,男性 27 例,女性 18 例,发病时间(11.5± 4.0)h。所有患者均为颈内动脉脑梗塞。患者多出现偏瘫,失语和偏侧感觉障碍。两组患者年龄、性别、症状、合并症、发病时间、NIHSS 评分差异无明显统计学意义($P>0.05$),见表 1。

表 1 两组患者基本资料比较

Table 1 Comparison of the basic data between the two groups

	Control group(45 case)	Experimental group(45 case)	t/χ^2 value	P value
Age	58.0± 6.5	55.3± 8.5	1.6927	0.0941
Male/female	27/18	28/17	0.047	0.829
Come on time	11.5± 4.0	12.3± 3.8	0.9727	0.3334
NIHSSscore	9± 3.0	9± 3.0	0.0000	1.0000
Clinical symptoms			0.0388	0.9808
Hemiplegia	45(100.00)	45(100.00)		
Aphasia	19(42.22)	18(40.00)		
Lateral sensory disturbance	42(93.33)	43(95.56)		
Complications			0.3274	0.8489
High blood pressure	21(46.67)	22(48.89)		
Diabetes	17(37.78)	14(31.11)		
Hyperlipidemia	22(48.89)	23(51.11)		

1.2 方法

两组患者均给予常规支持治疗,如控制血压血糖、抗感染、保持电解质平衡、链激酶溶血栓等,期间进行实时临床记录和护理,对照组在此基础上给予口服阿司匹林(Bayer Health Care Manufacturing S.R.L, 100 mg/片, 国药准字 J20130078)100 mg 治疗,每日一次,实验组基于对照组加以 100 mg 单唾液酸四己糖神经节苷脂钠(齐鲁制药有限公司,20 mg/支, 国药准字 H20046213)和 250 mL 生理盐水配制的注射液,进行滴注,每日一次,治疗疗程两周。

1.3 观察指标

1.3.1 疗效观察 两组患者治疗前和治疗后分别进行 NIHSS 和 Barthel 指数评分,比较治疗后两组患者的两项评分,根据 NIHSS 的改善程度对治疗效果进行划分。检测两组患者治疗前后血清 LPO、SOD、MDA、NO 水平的变化。

1.3.2 观察指标评价 按照《日常生活能力评定 Barthel 指标

量表》^[7],61-99 分为轻度功能障碍或具备自理能力;41-60 分为中度功能障碍;40 分以下为重度功能障碍。按照 NIHSS 的改善程度对疗效的划分^[8]:基本痊愈、显著有效、一般有效、基本无效。基本痊愈:患者治疗后 NIHSS 评分降低 90%;显著有效:患者治疗后 NIHSS 评分降低 45%以上;一般有效:患者治疗后 NIHSS 评分降低 18%以上;无效:患者治疗后 NIHSS 评分降低 18%以下,至无改观。

1.3.3 指标测定 分别取两组患者入院时和治疗两周后的清晨空腹外周静脉血 5 mL,3000 r/min 离心 15 min 取得血清,氮蓝四唑光化还原法测定 SOD,硫代巴比妥酸反应物法测定 LPO,丙二醛测试盒测定 MDA,微盘法测定 NO。

1.4 统计学分析

采用 SPSS18.0 处理本研究数据,计量资料以均数± 标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验,计数资料以[例(%)]表示,组间比较采用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

治疗后, 实验组有效率为 97.78%, 显著高于对照组 (77.78%, $P < 0.05$), 具体数据见表 2。

2.1 两组疗效的对比

表 2 两组临床疗效的比较[例(%)]

Table 2 Comparison of the clinical efficacy between the two groups[n(%)]

Groups	Basic recovery	Significantly effective	Generally valid	Invalid	Effective rate
Control group(n=45)	11(24.44)	19(42.22)	5(11.11)	10(22.22)	35(77.78)
Experimental group (n=45)	19(42.22)	14(31.11)	11(24.44)	1(2.22)	44(97.78)
χ^2					8.389
P					0.004

2.2 两组治疗前后 NIHSS 和 Barthel 评分变化的比较

治疗前, 两组 NIHSS 和 Barthel 指数评分比较差异无统计学意义 ($P > 0.05$); 治疗后, 两组患者 NIHSS 和 Barthel 指数评分

均较治疗前明显改善 ($P < 0.05$), 且实验组 Barthel 指数显著高于对照组 ($P < 0.05$), NIHSS 明显低于对照组 ($P < 0.05$), 具体数据见表 3。

表 3 两组治疗前后 NIHSS 和 Barthel 指标评分的变化比较

Table 3 Comparison of the NIHSS and Barthel index before and after treatment between two groups

Item	Groups	Barthel	NIHSS
Control group(n=45)	Before treatment	47± 9.7	9.0± 3.0
	After treatment	65± 11.4	4.0± 3.5
Experimental group(n=45)	Before treatment	46± 9.4	9.0± 3.0
	After treatment	74± 12.8	2.5± 2.1
t/pControl inner value		8.0669, 0.0000	7.2761, 0.0000
t/pIn-group value		11.8275, 0.0000	11.9071, 0.0000
t/pIntra - group value before treatment		0.4966, 0.6207	0.0000, 1.0000
t/pAfter treatment, the value in the group		3.5222, 0.0007	2.4652, 0.0156

2.3 两组治疗前后血清 LPO、SOD、MDA、NO 水平的比较

治疗前, 两组血清 LPO、SOD、MDA、NO 水平比较差异无统计学意义 ($P > 0.05$); 治疗后, 两组血清 SOD 水平均较治疗前

显著上升, 而血清 LPO、MDA、NO 水平均较治疗前显著下降, 实验组血清 SOD 水平较对照组明显升高, 血清 LPO、MDA、NO 水平显著低于对照组 ($P < 0.05$), 具体数据见表 4。

表 4 两组治疗前后血清 LPO、SOD、MDA、NO 水平的比较($\bar{x} \pm s$)

Table 4 Comparison of the serum LPO, SOD, MDA and NO levels before and after treatment between the two groups($\bar{x} \pm s$)

Item	Groups	LPO (nmol/mL)	SOD (nU/mL)	MDA (mmol/L)	NO (μ mol/mL)
Control group(n=45)	Before treatment	7.50± 0.86	75.60± 19.47	7.63± 2.13	45.15± 3.78
	After treatment	5.76± 0.69	79.13± 16.58	6.72± 0.91	38.53± 4.17
Experimental group (n=45)	Before treatment	7.51± 0.15	76.12± 16.40	7.59± 2.20	44.19± 3.56
	After treatment	4.58± 0.92	90.36± 14.11	5.05± 1.21	31.88± 5.51
t/pControl inner value		10.5862, 0.0000	0.9259, 0.3569	2.6354, 0.0099	7.8902, 0.0000
t/pIn-group value		21.0857, 0.0000	4.4154, 0.0000	6.7862, 0.0000	12.5881, 0.0000
t/pIntra - group value before treatment		0.0768, 0.9389	0.1370, 0.8913	0.0876, 0.9304	1.2402, 0.2181
t/pAfter treatment, the value in the group		6.8832, 0.0000	3.4602, 0.0008	7.3994, 0.0000	6.4557, 0.0000

3 讨论

脑梗塞患者多合并高血压、高血脂症、糖尿病和心脏类疾病^[9,10],其症状复杂,严重程度随脑损伤部位及面积、栓塞动脉大小、缺血程度和合并症类型而不同,轻度患者可无临床症状或出现短暂性发作(眩晕,反复性肢体瘫痪等),严重者伴有肢体瘫痪、昏迷、失语、急性癫痫等症状,以基底核区、双侧额叶、颞叶区发病多见。脑梗塞的病理改变主要是脑梗塞病灶内的组织血液循环障碍,神经细胞缺血缺氧坏死,并出现缺血出血带环绕以及周围组织炎症反应^[11,12]。颈动脉系统和椎-基底动脉系统的动脉粥样硬化是最常见的病因,动脉壁的增厚,血管腔的狭窄以及脱落的小栓子随血流栓塞下级动脉,导致相应供血脑组织缺血缺氧损伤,供血动脉内血流迟缓甚至停滞。由于内源性凝血启动,血小板凝聚,导致血液凝固,又加重了脑组织的缺血缺氧损伤,最终引起坏死^[12]。

临床研究表明^[13,14]在治疗脑梗塞过程中,及时疏通栓塞动脉,恢复缺血出血带供血和保护已受损神经细胞是关键。阿司匹林和单唾液酸四己糖神经节苷脂(GM1)均为临床常用药物,但鲜有联合治疗脑梗塞的案例。阿司匹林为抑制血小板凝聚、抗血栓药物,多为预防性治疗心肌梗塞和脑缺血,对疏通栓塞动脉,恢复缺血出血带供血具有重要意义,可显著降低脑梗塞患者的死亡率。国外研究证实^[15]单独阿司匹林治疗急性脑梗塞的有效率均在75%上下,但有5%病例出现肠道出血,30-40%病例出现阿司匹林抵抗。本研究结果显示78%患者经阿司匹林治疗有效,未见肠道出血和阿司匹林无效病例。单唾液酸四己糖神经节苷脂可促进神经重构(Neuroplasticity),加速神经修复,改善脑部血流动力学特征,保护营养受损的神经细胞等。Prasad M等^[16]通过对新生儿缺血缺氧性脑病的治疗前后各项病状体征的研究发现GM1对神经组织有亲和性,能通过血脑屏障,嵌入神经细胞,起到保护和营养作用,经GM1治疗的患儿病状体征改善较明显,有效率约92%。Takizawa S^[17]通过NIHSS和Barthel评分对比二磷酸胞嘧啶胆碱和GM1对治疗脑梗塞的效果,发现其较GM1更优,有效率达94%,并发现其具有减轻脑部水肿、增强钠泵活性的功效。本研究结果表明单唾液酸四己糖神经节苷脂能够促进神经修复,对患者恢复神经功能和自理能力具有重要作用,联合治疗的有效率更高。

脑细胞缺血缺氧损伤的机制尚不明确,现认为是多种因素共同参与的结果^[18,19],如自由基、炎症介质、蛋白酶等,其中自由基的损伤机制经广泛研究,是目前应用于临床治疗脑梗塞以及其他神经细胞损伤衰老疾病较成熟的病理基础^[20,21]。自由基是一种具有高活性,含有多个不成对电子的原子或基团,又称"游离基",包括氧自由基和氮自由基^[22,23]。本研究的血清观测指标中,过氧化脂质(LPO)即属于氧自由基,一氧化氮(NO)为氮自由基。脑细胞损伤时可生成并释放大量的自由基,在体内堆积,并与生物膜上的不饱和脂肪酸发生过氧化物反应,引发脑细胞本身及其他细胞生物膜破坏和功能障碍。丙二醛(MDA)为氧自由基和不饱和脂肪酸的稳定产物,具有断裂和失活DNA、RNA的作用^[24]。Aizawa Y等的研究表明^[25]MDA可用来间接测量血清氧自由基水平。NO是自由基产物最初的形式,是体内重要的信使分子,可舒张血管,减活血小板,防血栓、动脉粥样硬

化,具有脑血管调节作用^[26,27]。当发生脑缺血时,自由基和相关代谢产物能够激活一氧化物合成酶(NOS),致血清NO水平升高。超氧化物歧化酶(SOD)可有效清除体内氧自由基,保护生物膜,其活性的高低对神经功能进行性衰退和衰老具有重要意义^[28,29]。Wang Y等的研究^[30]表明大量氧自由基能够消耗SOD,所以血清SOD水平的显著下降提示脑细胞缺血缺氧损伤的发生。本研究结果显示所有脑梗塞患者血清SOD水平均显著低于健康水平,联合治疗的患者血清SOD水平上升幅度以及LPO、MDA、NO水平下降幅度大于单纯治疗,提示联合治疗使脑梗塞患者体内自由基生成量下降,降解上升,脑细胞缺血缺氧损伤被阻滞。

综上所述,阿司匹林联合单唾液酸四己糖神经节苷脂能在抗血栓血小板的同时阻滞脑细胞损伤和促进神经修复,提高脑梗塞的疗效,这可能与有效提高血清SOD水平及降低LPO、MDA、NO水平有关。

参考文献(References)

- [1] Bong J B, Kang H G, Choo I S. Acute cerebral infarction after pyrethroid ingestion[J]. *Geriatrics & Gerontology International*, 2017, 17(3): 510-511
- [2] Jia W, Xie Y, Zhao S, et al. Dengzhanxin injection for cerebral infarction[J]. *Medicine*, 2017, 96(32): e7674
- [3] Tang S C, Luo C J, Zhang K H, et al. Effects of dl-3-n-butylphthalide on serum VEGF and bFGF levels in acute cerebral infarction [J]. *Eur Rev Med Pharmacol Sci*, 2017, 21(19): 4431-4436
- [4] Zhang C, Zhao S, Zang Y, et al. The efficacy and safety of Dl-3n-butylphthalide on progressive cerebral infarction: A randomized controlled STROBE study[J]. *Medicine*, 2017, 96(30): e7257
- [5] Long Y, Zhan Q, Yuan M, et al. The Expression of microRNA-223 and FAM5C in Cerebral Infarction Patients with Diabetes Mellitus[J]. *Cardiovascular Toxicology*, 2017, 17(1): 42
- [6] Nan W G. Clinical analysis of CT diagnosis of acute cerebrovascular disease[J]. *World Latest Medicine Information*, 2016, 16(60): 132-136
- [7] Liu W, Unick J, Galik E, et al. Barthel Index of activities of daily living: item response theory analysis of ratings for long-term care residents[J]. *Nursing research*, 2015, 64(2): 88-99
- [8] Kwah L K, Diong J. National Institutes of Health Stroke Scale (NIHSS) [J]. *Journal of physiotherapy*, 2014, 60(1): 61
- [9] Galea J, Brough D. The role of inflammation and interleukin-1 in acute cerebrovascular disease [J]. *Journal of inflammation research*, 2013: 6121-6128
- [10] Wan J L, Ma Z W. The Value of Mean Platelet Volume for Prognosis of Patients with Acute Cerebral Infarction [J]. *Clinical Laboratory*, 2017, 63(11): 1801
- [11] Arboix A. Intrahospital stroke: hidden side of acute cerebrovascular disease[J]. *Medicine clínica*, 2011, 137(11): 495-496
- [12] He X, Li D R, Cui C, et al. Clinical significance of serum MCP-1 and VE-cadherin levels in patients with acute cerebral infarction [J]. *European Review for Medical & Pharmacological Sciences*, 2017, 21(4): 804
- [13] Schmidt M, Lamberts M, Olsen A S, et al. Cardiovascular safety of non-aspirin non-steroidal anti-inflammatory drugs: review and position paper by the working group for Cardiovascular

- Pharmacotherapy of the European Society of Cardiology[J]. European Heart Journal, 2016, 37(13): 1015
- [14] Zhang Y, Qiu B, Wang J, et al. Effects of BDNF-Transfected BMSCs on Neural Functional Recovery and Synaptophysin Expression in Rats with Cerebral Infarction [J]. Molecular Neurobiology, 2017, 54(5): 1-12
- [15] Kardel Amatty. Clinical evaluation of monosialonic acid four gangue ganglioside sodium injection in the treatment of acute cerebral infarction[J]. World Latest Medicine Information, 2015, 15(12): 4-9
- [16] Prasad M, Lerman LO, Lerman A. Carotid Stiffness and Cerebrovascular Disease: The Physiology Beyond the Anatomy[J]. Journal of the American College of Cardiology, 2015, 66 (19): 2126-2128
- [17] Takizawa S. Free radical production in ischemic cerebrovascular disease[J]. Nihon Ronen Igakkai Zasshi, 2003, 40(4): 319-321
- [18] Chang CC, Lee CT, Lan TH, et al. Effects of antidepressant treatment on total antioxidant capacity and free radical levels in patients with major depressive disorder[J]. Psychiatry research 2015, 230(2): 575-580
- [19] Wang T, Gong Y, Shi Y, et al. Feasibility of dual-low scheme combined with iterative reconstruction technique in acute cerebral infarction volume CT whole brain perfusion imaging [J]. Experimental & Therapeutic Medicine, 2017, 14(1): 163-168
- [20] Kobayashi A, Tamura A, Ichihara T, et al. Factors associated with changes over time in medication-taking behavior up to 12 months after initial mild cerebral infarction onset [J]. J Med Invest, 2017, 64 (1): 85-95
- [21] Çay S, Köse M, Tümer F, et al. SOD activity and DNA binding properties of a new symmetric porphyrin Schiff base ligand and its metal complexes [J]. Spectrochimica acta. Part A, Molecular and biomolecular spectroscopy, 2015, 151821-151838
- [22] Liu S, Wu J R, Zhang D, et al. Comparative efficacy of Chinese herbal injections for treating acute cerebral infarction: a network meta-analysis of randomized controlled trials [J]. BMC Complementary & Alternative Medicine, 2018, 18(1): 120
- [23] Shen J, Zhao Z, Shang W, et al. Fabrication and evaluation a transferrin receptor targeting nano-drug carrier for cerebral infarction treatment [J]. Artificial Cells, Nanomedicine, and Biotechnology, 2019, 47(1): 192-200
- [24] Li M J, Xiao H, Qiu Y X, et al. Identification of potential diagnostic biomarkers of cerebral infarction using gas chromatography-mass spectrometry and chemometrics[J]. RSC Advances, 2018, 8(41): 22866-22875
- [25] Aizawa Y, Nakai T, Saito Y, et al. Calcified Amorphous Tumor-Induced Acute Cerebral Infarction. [J]. International Heart Journal, 2018, 59(1): 240-242
- [26] Hwang JH, Kumar VR, Kang SY, et al. Effects of Flower Buds Extract of Tussilago farfara on Focal Cerebral Ischemia in Rats and Inflammatory Response in BV2 Microglia [J]. Chinese journal of integrative medicine, 2018, 24(11): 844-852
- [27] Cheng X, Svensson M, Yang Y, et al. Focal, but not global, cerebral ischaemia causes loss of myenteric neurons and upregulation of vasoactive intestinal peptide in mouse ileum[J]. International journal of experimental pathology, 2018, 99(1): 38-45
- [28] Fan C, Zhang L, He Z, et al. Reduced Severity of Outcome of Recurrent Ipsilateral Transient Cerebral Ischemia Compared with Contralateral Transient Cerebral Ischemia in Rats[J]. Journal of stroke and cerebrovascular diseases: the official journal of National Stroke Association, 2017, 26(12): 2915-2925
- [29] Chen YF, Wang YW, Huang WS, et al. Trans-Cinnamaldehyde, An Essential Oil in Cinnamon Powder, Ameliorates Cerebral Ischemia-Induced Brain Injury via Inhibition of Neuroinflammation Through Attenuation of iNOS, COX-2 Expression and NF κ -B Signaling Pathway[J]. Neuromolecular medicine, 2016, 18(3): 322-333
- [30] Wang Y, Zhang H, Wang Z, et al. Therapeutic effect of nerve growth factor on canine cerebral infarction evaluated by MRI[J]. Oncotarget, 2018, 9(3): 3741-3751

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- [24] 李杰, 王琦, 冯萍灵, 等. 清热化痰法对 AECOPD 大鼠血清中性粒细胞弹性蛋白酶水平的影响研究 [J]. 中国药师, 2014, 17(5): 722-724
- [25] Liu H, Archer NK, Dillen CA, et al. Staphylococcus aureus Epicutaneous Exposure Drives Skin Inflammation via IL-36- Mediated T Cell Responses[J]. Cell Host Microbe, 2017, 22(5): 653- 666. e5
- [26] Honda K, Wada H, Nakamura M, et al. IL-17A synergistically stimulates TNF- α -induced IL-8 production in human airway epithelial cells: A potential role in amplifying airway inflammation [J]. Exp Lung Res, 2016, 42(4): 205-216
- [27] Ehrhardt H, Pritze T, Oak P, et al. Absence of TNF- α enhances inflammatory response in the newborn lung undergoing mechanical ventilation [J]. Am J Physiol Lung Cell Mol Physiol, 2016, 310(10): L909-L918
- [28] Zhuan B, Yu Y, Yang Z, et al. Mechanisms of oxidative stress effects of the NADPH oxidase-ROS-NF- κ B transduction pathway and VPO1 on patients with chronic obstructive pulmonary disease combined with pulmonaryhypertension [J]. Eur Rev Med Pharmacol Sci, 2017, 21(15): 3459-3464
- [29] Al-Azzawi MA, Ghoneim AH, Elmadbouh I. Evaluation of Vitamin D, Vitamin D Binding Protein Gene Polymorphism with Oxidant - Antioxidant Profiles in Chronic Obstructive Pulmonary Disease [J]. J Med Biochem, 2017, 36(4): 331-340
- [30] 李杰, 王林洋, 程涓, 等. 清热化痰法对 AECOPD 痰热证大鼠模型病理肺组织的影响[J]. 天津中医药大学学报, 2016, 35(1): 31-35