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荷丹片联合依达拉奉治疗急性脑梗死的临床效果及对血清 IFN- γ , Ang-2, Hcy 水平的影响 *

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摘要 目的:探讨荷丹片联合依达拉奉治疗急性脑梗死的临床效果及其对血清干扰素- γ (IFN- γ)、促血管生成素 II(Ang-2)、同型半胱氨酸(Hcy)水平的影响。方法:将 102 例急性脑梗死患者按抽签法分作对照组与实验组,每组各 51 例。对照组采用依达拉奉治疗,静脉滴注 30mg 依达拉奉,早晚各 1 次;实验组基于对照组加用荷丹片治疗,口服 14.6 g 荷丹片,早中晚各 1 次。比较两组疗效、治疗前后神经功能缺损评分(NIHSS)、血清 IFN- γ 、Ang-2、Hcy、丙二醇(MDA)、超氧化物歧化酶(SOD)、白细胞介素-6、10(IL-6、IL-10)、肿瘤坏死因子- α (TNF- α)水平及不良反应的发生情况。结果:实验组总有效率、血清 Ang-2、SOD、IL-10 水平均显著高于对照组,NIHSS、血清 IFN- γ 、Hcy、MDA、IL-6、TNF- α 水平均明显低于对照组,差异均有统计学意义($P<0.05$)。两组不良反应的发生率比较差异无统计学意义($P>0.05$)。结论:荷丹片联合依达拉奉用于急性脑梗死的疗效肯定,可调节血清 IFN- γ 、Ang-2、Hcy 的表达,对氧化应激及炎症反应均有改善作用。

关键词:急性脑梗死;荷丹片;依达拉奉;临床效果;干扰素- γ ;促血管生成素 II;同型半胱氨酸

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Clinical Effect of Hedanpian Combined with Edaravone in Treatment of Acute Cerebral Infarction and Influence on Serum Levels of IFN- γ , Ang-2 and Hcy*

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ABSTRACT Objective: To research the clinical effect of HeDanPian combined with edaravone in the treatment of acute cerebral infarction and the influence on serum levels of interferon- γ (IFN- γ), promote angiogenin II (Ang-2), homocysteine (Hcy). **Methods:** 102 cases of patients with acute cerebral infarction were selected and randomly divided into the control group and the experimental group, with 51 cases in each group. The control group was treated with edaravone, intravenous infusion of 30mg edaravone, 1 time in the morning and night; The experimental group was treated based on the control group treated with HeDanPian, oral HeDanPian 14.6 g, 1 time in the early to middle. The curative effect, nerve function defect score (NIHSS), serum IFN- γ , Ang-2, Hcy, propylene glycol (MDA), superoxide disproportionation alcohol (SOD), interleukin 6, 10 (IL-6, IL-10), tumor necrosis factor- α (TNF- α) levels, incidence of adverse reactions were compared between two groups. **Results:** After treatment, the total effective rate, serum Ang-2, SOD, IL-10 levels of experimental group were higher than those of the control group ($P<0.05$), the NIHSS, serum IFN- γ , Hcy, MDA, IL-6, TNF- α levels of experimental group were lower than those of the control group ($P<0.05$). No significant difference was found in the incidence of adverse reactions was found between the two groups ($P>0.05$). **Conclusion:** HeDanPian combined with edaravone was effective in the treatment of acute cerebral infarction, which could regulate the expression of serum IFN- γ , Ang-2 and Hcy, improve the oxidative stress and inflammation.

Key words: Acute cerebral infarction; HeDanPian; Edaravone; Clinical effect; Interferon- γ ; Angiogenin II; Homocysteine

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前言

急性脑梗死是老年群体的常见疾病,主要是因脑组织局部

血液循环骤然出现障碍,产生缺血、缺氧的软化性坏死,从而出现程度不一的头晕、头痛、恶心呕吐、失语、吞咽困难、偏瘫等症^[1]。研究表明急性脑梗死是一种多机制、多因素的恶性级联反

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应,炎症、血管、自由基等反应是其中心环节,可有多种细胞因子参与^[2]。尽快恢复缺血性脑组织血供是其治疗的关键,静脉溶栓治疗虽可利于脑组织血流灌注的恢复,但可引起血管再闭塞及脑缺血再灌注损伤,且需于发病 6 h 内进行,存在一定的局限性^[3]。依达拉奉作为一种脑保护剂,具有脂溶性与水溶性,可透过血脑屏障,清除脑部组织的氧自由基^[4]。研究表明动脉粥样硬化与血脂紊乱之间有着密切联系,是急性脑梗死的独立危险因素。荷丹片是复方调脂中药,可发挥良好的降脂作用^[5]。因此,本研究主要探讨了荷丹片联合依达拉奉治疗急性脑梗死的临床效果及其可能机制。

1 资料与方法

1.1 一般资料

收集 2014 年 5 月~2016 年 5 月于我院就诊的急性脑梗死患者 102 例,均符合急性脑梗死的相关诊断标准^[6]:发病突然、于发病数小时或者 1、2 内病情达到高峰;可见耳鸣、半身不遂、口齿不清等症状;并经头颅 CT、MRI 等检查确诊。纳入首次发病;发病至入院时间在 6~12 h;生命体征基本稳定;无意识障碍。排除近期伴溶栓、抗凝治疗或者重大手术史;恶性肿瘤、严重血液或者免疫系统障碍;可见脑出血征象;过敏体质。本研究家属及患者均签署知情同意书,且经医院伦理委员会许可,按抽签法分组。对照组 29 例男,22 例女;年龄 47~73 岁,平均(62.11±2.89)岁;梗死部位:有 17 例基底节区,有 15 例脑桥,有 11 例颞叶,有 8 例小脑。实验组 32 例男,19 例女;年龄 45~75 岁,平均(61.87±2.96)岁;梗死部位:有 19 例基底节区,有 13 例脑桥,有 10 例颞叶,有 9 例小脑。两组年龄、性别分布等一般临床特征比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组均配合调脂、抗血小板、活血化痰、维持电解质平衡、神经保护、降颅内压等常规治疗,必要时进行氧疗。对照组采用依达拉奉治疗,将 30 mg 依达拉奉(江西国药有限责任公司,20 mL:30 mg,140420)溶于 100 mL 0.9%氯化钠中,予以患者于 30 min 内静脉滴注,早晚各行 1 次,连续治疗 14 d。实验组基于对照组加用荷丹片治疗,口服 1.46 g 荷丹片(石家庄康力药业有

限公司,7.3 g/片,140423),早中晚各行 1 次,连续治疗 6 个月。

1.3 观察指标

1.3.1 神经功能缺损评分(NIHSS) 评估患者入院时及治疗 14 d 时的手肌力、上肢肌力、下肢肌力、步行能力、面肌、水平凝视功能、意识、言语 8 个方面,分值为 0 至 45 分,分数越高表示神经功能缺损程度越重^[7]。

1.3.2 临床疗效观察 于治疗第 14 d 时参照 NIHSS 进行,基本痊愈:NIHSS 降低超过 91%;显著进步:NIHSS 降低在 46%至 90%;进步:NIHSS 降低在 18%至 45%;无效:降低在 17%以下,基本治愈+显著进步+进步视为总有效^[8]。

1.3.3 指标检测 于入院及治疗第 14 d 时抽取患者空腹静脉血 4 mL,以 3000 r/min 分离 10 min,于 -80 °C 环境中放置待检。按酶联免疫吸附法检测干扰素- γ (IFN- γ)、试剂盒:江苏济川医药集团;按酶联免疫双抗体夹心法检测促血管生成素 II (Ang-2)、试剂盒:济南金达药化有限公司;按放射免疫法检测同型半胱氨酸(Hcy)、试剂盒:黑龙江康麦斯药业有限公司。按硫代巴比妥酸比色法检测丙二醇(MDA)、试剂盒:重庆市顺正医药科技发展有限公司;按黄嘌呤氧化酶法检测超氧化物歧化酶(SOD)、试剂盒:贵州信邦远东药业有限公司。按电化学发光法测定白细胞介素-6、10(IL-6、IL-10),试剂盒:均为海南利能康泰制药有限公司;按免疫比浊法检测肿瘤坏死因子- α (TNF- α)、试剂盒:广东联康药业有限公司。

1.3.4 不良反应观察 对患者心电图、肝肾功能、血常规等进行定期检测,并对不良反应进行记录。

1.4 统计学分析

选择 SPSS18.0 行数据统计,计量资料用($\bar{x}\pm s$)表示,组间比较用 t 检验,计数资料用 [(例)%] 表示,用 χ^2 检验比较,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组治疗前后 NIHSS 的比较

治疗前,两组 NIHSS 比较差异无统计学意义($P>0.05$);治疗后,两组 NIHSS 均较治疗前显著降低,且实验组下降更明显,差异具有统计学意义($P<0.05$),见表 1。

表 1 比较两组治疗前后 NIHSS 的比较($\bar{x}\pm s$)

Table 1 Comparison of the NIHSS between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	Time	NIHSS(s)
Control group(n=51)	Before treatment	21.60±2.70
	After treatment	12.14±1.51 ^b
Experimental group(n=51)	Before treatment	21.07±2.62
	After treatment	9.23±1.15 ^{ab}

2.2 两组临床疗效的比较

实验组总有效率显著高于对照组,差异有统计学意义($P<0.05$),见表 2。

2.3 两组治疗前后血清 IFN- γ 、Ang-2、Hcy 水平的比较

治疗前,两组血清 IFN- γ 、Ang-2、Hcy 水平比较差异无统计学意义($P>0.05$);治疗后,两组血清 IFN- γ 、Hcy 水平均较治疗前降低,且实验组下降更明显,两组血清 Ang-2 水平均较治疗前

上升,且实验组高于对照组,差异有统计学意义($P<0.05$),见表 3。

2.4 两组治疗前后血清 SOD、MDA 水平的比较

治疗前,两组血清 SOD、MDA 水平比较差异无统计学意义($P>0.05$);治疗后,两组血清 SOD 水平均较治疗前上升,且实验组高于对照组,两组血清 MDA 水平较治疗前降低,且实验组低于对照组,差异有统计学意义($P<0.05$),见表 4。

表2 两组临床疗效的比较[(例)%]

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

Groups	Basic recovery	Significant progress	Progress	Invalid	Total effective rate
Control group(n=51)	12(23.53)	11(21.57)	15(29.41)	13(25.49)	38(74.51)
Experimental group(n=51)	19(37.25)	23(45.10)	5(9.81)	4(7.84)	47(92.15) ^a

Note: Compared with control group ^aP<0.05.

表 3 两组治疗前后血清 IFN-γ、Ang-2、Hcy 水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum IFN-γ, Ang-2 and Hcy levels between two groups before and after the treatment ($\bar{x} \pm s$)

Groups	Time	IFN-γ(ng/L)	Ang-2(ng/L)	Hcy(mmol/L)
Control group(n=51)	Before treatment	45.26± 5.65	23.28± 2.90	22.71± 2.84
	After treatment	31.85± 3.98 ^b	32.53± 4.06 ^b	16.83± 2.10 ^b
Experimental group(n=51)	Before treatment	44.79± 5.59	22.76± 2.83	23.21± 2.91
	After treatment	20.53± 2.56 ^{ab}	49.20± 6.15 ^{ab}	12.05± 1.50 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

表 4 两组治疗前后血清 SOD、MDA 水平的比较($\bar{x} \pm s$)

Table 4 Comparison of the serum SOD and MDA levels between two groups before and after the treatment ($\bar{x} \pm s$)

Groups	Time	SOD(kU/L)	MDA(μmol/L)
Control group(n=51)	Before treatment	71.60± 8.95	8.57± 1.07
	After treatment	103.75± 12.96 ^b	6.43± 0.80 ^b
Experimental group(n=51)	Before treatment	72.31± 9.06	8.43± 1.06
	After treatment	127.96± 15.98 ^{ab}	5.11± 0.64 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

2.5 两组治疗前后血清 IL-6、IL-10、TNF-α 水平的比较

均较治疗前显著下降,且实验组低于对照组,差异有统计学意义(P<0.05),见表 5。

治疗前,两组血清 IL-6、IL-10、TNF-α 水平比较差异无统

计学意义(P>0.05);治疗后,两组血清 IL-6、IL-10、TNF-α 水平

表 5 两组治疗前后血清 IL-6、IL-10、TNF-α 水平的比较($\bar{x} \pm s$)

Table 5 Comparison of the serum IL-6,IL-10 and TNF-α levels between two groups before and after the treatment ($\bar{x} \pm s$)

Groups	Time	IL-6(ng/L)	IL-10(ng/L)	TNF-α(ng/L)
Control group(n=51)	Before treatment	16.85± 2.11	12.73± 1.57	52.69± 6.56
	After treatment	11.20± 1.42 ^b	14.11± 1.76 ^b	31.57± 3.94 ^b
Experimental group(n=51)	Before treatment	16.23± 2.02	12.25± 1.54	53.20± 6.65
	After treatment	9.76± 1.23 ^{ab}	16.53± 2.06 ^{ab}	21.44± 2.68 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

2.6 两组不良反应发生情况的比较

较差异无统计学意义(P>0.05),见表 6。

两组均有皮疹、胃肠道反应、肝功能异常出现,但发生率比

表 6 两组不良反应发生情况的比较[(例)%]

Table 6 Comparison of the incidence of adverse reactions between two groups [(n)%]

Groups	Rash	Gastrointestinal reaction	Liver dysfunction	Adverse reaction rate
Control group(n=51)	2(3.92)	5(9.80)	4(7.84)	11(21.57)
Experimental group(n=51)	1(1.96)	4(7.84)	2(3.92)	7(13.72)

3 讨论

急性脑梗死是临床常见的脑血管疾病,可因脑部供应血流的动脉产生动脉粥样硬化、血栓形成,或者气体、液体等造成脑部相关动脉血流骤减、阻断所致^[9]。依达拉奉是临床治疗急性脑梗死的常用药物,可有效清除氧自由基,抗氧化损伤,且可作用

于血脑屏障,抑制脑组织的炎性及过氧化反应,减轻继发性的脑组织损伤,缓解血管内皮细胞受损,避免神经元凋亡,利于神经功能的恢复^[10]。本结果进行显示急性脑梗死患者经依达拉奉治疗后 NIHSS 有所下降,证实依达拉奉可减轻神经功能损伤,缓解神经后遗症,改善预后。

中医学认为急性脑梗死属 " 中风 " 范畴,肝肾内虚是其病

变基础,可引水湿不化,聚而生痰并阻络脉,致脏腑阴阳所失,气血不调,冲犯脑部,致脑脉痹阻,引半身不遂、言语不利、偏瘫等,临床以降浊化痰、活络通脉为治疗之契机^[12]。荷丹片中荷叶入心、肺、肝脾经,性味苦涩,可补脾健胃、止血化瘀;丹参入肝、心经,性味苦,可疏通脉络,活血化瘀;补骨脂入脾、胃经,性温,味苦,可温阳补肾;山楂可健胃化食,活血祛瘀^[13]。研究表明荷丹片具有抑制动脉粥样硬化、调节血脂、缓解微循环、清除氧自由基等功效^[14]。本研究结果显示急性脑梗死患者经依达拉奉联合荷丹片治疗后,NIHSS 显著低于单用依达拉奉者,且总有效率更高,说明二者联合治疗可缓解神经功能的损伤,促进患者恢复。

急性脑梗死者血清 IFN- γ 浓度显著高于正常者,IFN- γ 作为一种小分子多肽,主要来自于 T 辅助淋巴细胞、自然杀伤细胞等,可诱导单核巨噬细胞的激活,利于毒性因子的释放,加剧病情^[15]。Ang-2 是血管生成的主要因子,可对 Ang-1 起到竞争性抑制作用,促进血管组织的松解,提高内皮细胞敏感性,利于毛细血管的新生,缓解神经功能受损^[16]。Hcy 过高可诱导脑血管病变,引起血管内皮细胞的功能出现紊乱,诱导胆固醇及脂蛋白于血管壁内集聚,且可使一氧化氮受损,引起动脉粥样硬化^[17]。本研究结果显示:急性脑梗死患者经依达拉奉联合荷丹片治疗后血清 IFN- γ 、Hcy 水平显著降低,血清 Ang-2 水平明显上升,说明二者联合治疗可促进疾病的控制,抑制有害物质的合成及释放,减轻机体损伤。

急性脑梗死患者的缺血性神经细胞损伤、变性与凋亡反应是氧化应激和炎症反应的共同所致^[18]。机体发病时可促进氧自由基的大量生成,从而诱导其产生氧自由基的连锁反应,导致氧化损伤^[19]。SOD 能够减少氧自由基对细胞产生的损伤,并可使受损细胞得到及时修复。MDA 浓度可客观反映机体过氧化程度,及其对于组织造成的损伤状态^[20]。同时,氧自由基可诱导核酸、蛋白质、脂质等破坏,引起炎症因子的合成及释放,IL-6 作为一种前炎性介质,可刺激炎症因子的聚集、黏附,且可诱导血管内膜的新生^[21]。IL-10 为机体代表性抗炎因子,可抑制淋巴细胞、单核细胞等浸润,且可使其他前炎性因子的合成及释放受到抑制,起到抗炎作用,其水平过低可促进动脉粥样硬化的进展,增加低密度脂蛋白的表达,使斑块稳定性降低^[22]。TNF- α 可促进其他炎症因子的释放,加剧内皮细胞的损伤,增强白细胞的黏附性,使血管收缩性增加,促进斑块破裂,引起脑出血^[23]。本研究结果显示:依达拉奉联合荷丹片治疗后氧化应激及炎症反应均得到明显改善,说明二者联合治疗可利于自由基的清除,减轻氧化应激损伤,缓解患者的炎症反应程度,使脑组织损伤减轻。同时,本研究显示两组均有少数不良反应出现,但症状均相对轻微,经对症处理后均明显缓解,表明其安全性相当。综上所述,荷丹片联合依达拉奉用于急性脑梗死的疗效肯定,可调节血清 IFN- γ 、Ang-2、Hcy 的表达,且对氧化应激及炎症反应均有改善作用。

参考文献(References)

- [1] Lee MH, Kim SU, Lee DH, et al. Evaluation and Treatment of the Acute Cerebral Infarction with Convexal Subarachnoid Hemorrhage [J]. J Cerebrovasc Endovasc Neurosurg, 2016, 18(3): 271-275
- [2] Yao Y, Chen L, Xiao J, et al. Chrysin protects against focal cerebral ischemia/reperfusion injury in mice through attenuation of oxidative stress and inflammation[J]. Int J Mol Sci, 2014, 15(11): 20913-20926
- [3] Peng X, Wan Y, Liu W, et al. Protective roles of intra-arterial mild hypothermia and arterial thrombolysis in acute cerebral infarction [J]. Springerplus, 2016, 5(1): 1988
- [4] Wu S, Sena E, Egan K, et al. Edaravone improves functional and structural outcomes in animal models of focal cerebral ischemia: a systematic review[J]. Int J Stroke, 2014, 9(1): 101-106
- [5] Zhou L, Guo SN, Gao Y. Effects and Perspectives of Chinese Patent Medicines for Tonifying Qi and Promoting Blood Circulation on Patients with Cerebral Infarction [J]. Curr Vasc Pharmacol, 2015, 13(4): 475-491
- [6] Sahara N, Kuwashiro T, Okada Y. Cerebral infarction and transient ischemic attack[J]. Nihon Rinsho, 2016, 74(4): 666-670
- [7] Olivato S, Nizzoli S, Cavazzuti M, et al. e-NIHSS: an Expanded National Institutes of Health Stroke Scale Weighted for Anterior and Posterior Circulation Strokes [J]. J Stroke Cerebrovasc Dis, 2016, 25(12): 2953-2957
- [8] Askim T, Bernhardt J, Churilov L, et al. The Scandinavian Stroke Scale is equally as good as The National Institutes of Health Stroke Scale in identifying 3-month outcome [J]. J Rehabil Med, 2016, 48(10): 909-912
- [9] Lee MH, Kim SU, Lee DH, et al. Evaluation and Treatment of the Acute Cerebral Infarction with Convexal Subarachnoid Hemorrhage [J]. J Cerebrovasc Endovasc Neurosurg, 2016, 18(3): 271-275
- [10] Okamura K, Tsubokawa T, Johshita H, et al. Edaravone, a free radical scavenger, attenuates cerebral infarction and hemorrhagic infarction in rats with hyperglycemia[J]. Neurol Res, 2014, 36(1): 65-69
- [11] He J, Kwon Y, Li C, et al. Several considerations in using traditional Chinese patent medicine for cerebral infarction[J]. Chin J Integr Med, 2012, 18(8): 571-574
- [12] Li J, Cao R, Zhu HX, et al. A study of traditional Chinese medicine syndromes correlated to neurologic function or to coagulation function in patients with acute cerebral infarction[J]. Chinese critical care medicine, 2011, 23(6): 329-332
- [13] Zhong MC, Tang NY, Liu CH, et al. Relationship between Chinese medicine pattern types, clinical severity, and prognosis in patients with acute cerebral infarct[J]. Explore (NY), 2013, 9(4): 226-231
- [14] Li GH, Jiang HY, Xie YM, et al. Analysis of traditional Chinese medicine syndrome, traditional Chinese medicine and western-medicine in 84 697 patients with coronary heart disease based on big data [J]. China Journal of Chinese Materia Medica, 2014, 39(18): 3462-3468
- [15] Padilla-Quirarte HO, Trejo-Moreno C, Fierros-Zarate G, et al. Interferon-Tau has Antiproliferative effects, Represses the Expression of E6 and E7 Oncogenes, Induces Apoptosis in Cell Lines Transformed with HPV16 and Inhibits Tumor Growth *In Vivo* [J]. J Cancer, 2016, 7(15): 2231-2240
- [16] Lai T, Li M, Zheng L, et al. Over-expression of VEGF in marrow stromal cells promotes angiogenesis in rats with cerebral infarction via the synergistic effects of VEGF and Ang-2[J]. J Huazhong Univ Sci Technol Med Sci, 2012, 32(5): 724-731

总之,西黄胶囊联合 GP 方案较单用 GP 方案能更有效降低中晚期乳腺癌患者血清 TNF- α 、VEGF、MMP-2、MMP-9 水平,临床疗效更好,安全性更高。

参考文献(References)

- [1] Zhang Chong-jian, Qin Li, Wang Lu, et al. Effects and prognostic factors of neoadjuvant chemotherapy in breast cancer[J]. Chinese Journal of Geriatrics, 2016, 36(3): 636-637
- [2] Liu Zhi-yong, Li Bao-jiang. Breast cancer neoadjuvant chemotherapy in the dynamic changes of circulating tumor cells and the efficacy[J]. Chinese Journal of Clinical Oncology, 2013, 11(23): 1431-1435
- [3] Xu Zhi-jun, Liu Rong-feng, Wang Xiao-xiang, et al. Yang Zhengxiao capsule combined with chemotherapy in the treatment of metastatic breast cancer clinical efficacy and safety[J]. Journal of Shandong University (Medicine Edition), 2016, 54(5): 79-83
- [4] Hong Ri, Wu Yong-qiang, Wu Yue, et al. Xihuang pill adjuvant treatment of advanced breast cancer [J]. Chinese Journal of Traditional Chinese Medicine, 2014, 39(6): 1120-1123
- [5] Jonathan SB. Berek & Novak gynecology [M]. 14 version. Beijing: People's Medical Publishing House, 2008: 201-202
- [6] China Anti-Cancer Association. Breast cancer diagnosis and treatment guidelines and norms: 2011 version [J]. Chinese Journal of Cancer, 2011, 21(5): 2371
- [7] Liang Xu, Li Hui-ping, Di Li-jun, et al. Albumin-binding paclitaxel in the treatment of advanced refractory breast cancer efficacy and safety analysis[J]. Chinese Journal of Cancer, 2014, 12(11): 836-845
- [8] Zhang Lin, Hao Jie, Wang Li-ping, et al. Breast contrast-enhanced ultrasound, color Doppler ultrasound and magnetic resonance perfusion imaging in evaluating the efficacy of neoadjuvant chemotherapy in breast cancer contrast [J]. Huazhong University of Science and Technology (Medical Sciences), 2014, 14(4): 449-452
- [9] Dai Xing, Li Xiang-ke, Wu Hai-bo, et al. Clinical efficacy and safety of Tirogao monotherapy in the treatment of elderly patients with advanced breast cancer[J]. Cancer Research, 2013, 40(5): 481-484
- [10] Conceição LL, Dias MM, Pessoa MC, et al. Difference in fatty acids composition of breast adipose tissue in women with breast cancer and benign breast disease[J]. Nutr Hosp, 2016, 33(6): 1354-1360
- [11] Zhang Xiao-ling, Xing Rong-ge, Miao Zhi-gang, et al. Xihuang capsule adjuvant chemotherapy in the treatment of postoperative liver metastasis of colon cancer efficacy and peripheral blood IL-17 and IL-6[J]. Chinese herbal medicine, 2015, 46(6): 871-874
- [12] Li Jing-ran, Wang Lian-you, Wang Zhen, et al. Efficacy and Safety Evaluation of Red and Blue Light Irradiation Combined with Xihuang Capsule in Treating Facial Mild and Moderate Acne [J]. Jilin University (Medicine Edition), 2016, 42(4): 803-806
- [13] Wang Li. Xihuang capsule combined with chemotherapy in the treatment of advanced breast cancer [J]. Chinese Journal of Traditional Chinese Medicine, 2015, 13(6): 82-84
- [14] Athanasiou E, Michalopoulou-Manoloutsou E, Bobos M, et al. Coincidence of thymoma and breast cancer and in a 56-year-old female patient[J]. Ann Transl Med, 2016, 4(22): 446
- [15] Sun Q, Xu BH, Shao ZM. Chinese Expert Group on Diagnosis and Treatment of Breast Carcinoma in situ [J]. Chinese Journal of Oncology, 2016, 38(12): 942-947
- [16] Yue Jian, Ma Fei, Zhang Ling-xiao, et al. Capecitabine combined with docetaxel or vinorelbine in the treatment of breast cancer liver metastases clinical observation and efficacy analysis[J]. Chinese Journal of Clinical Oncology, 2013, 13(21): 1304-1308
- [17] Li Zhi-hua, Lei Qiu, Xiong Jian-ping, et al. Meta-analysis of the correlation between p53 expression and neoadjuvant chemotherapy in breast cancer [J]. Chinese Journal of Cancer Prevention and Treatment, 2015, 22(3): 221-226
- [18] Shi JF, Shi CL, Yue XP, et al. Economic burden of cancer in China during 1996-2014: a systematic review[J]. Chinese Journal of Oncology, 2016, 38(12): 929-941
- [19] Lu Xiang, Chen Cai-ping, Han Wen-lan, et al. Advances in the predictive factors of neoadjuvant chemotherapy in breast cancer [J]. Chinese Journal of Cancer Prevention and Treatment, 2012, 19(10): 796-800
- [20] De Gooijer MC, Zhang P, Thota N, et al. P-glycoprotein and breast cancer?resistance protein restrict the brain penetration of the CDK4/6 inhibitor palbociclib [J]. Investigational new drugs, 2015, 33(5): 1012-1019

(上接第 4505 页)

- [17] Fu HJ, Zhao LB, Xue JJ, et al. Elevated Serum Homocysteine (Hcy) Levels May Contribute to the Pathogenesis of Cerebral Infarction[J]. J Mol Neurosci, 2015, 56(3): 553-561
- [18] Ye L, Cai R, Yang M, et al. Reduction of the systemic inflammatory induced by acute cerebral infarction through ultra-early thrombolytic therapy[J]. Exp Ther Med, 2015, 10(4): 1493-1498
- [19] Wang M, Li YJ, Ding Y, et al. Silibinin Prevents Autophagic Cell Death upon Oxidative Stress in Cortical Neurons and Cerebral Ischemia-Reperfusion Injury[J]. Mol Neurobiol, 2016, 53(2): 932-943
- [20] Cao XL, Du J, Zhang Y, et al. Hyperlipidemia exacerbates cerebral injury through oxidative stress, inflammation and neuronal apoptosis in MCAO/reperfusion rats [J]. Exp Brain Res, 2015, 233(10): 2753-2765
- [21] Park SY, Kim J, Kim OJ, et al. Predictive value of circulating interleukin-6 and heart-type fatty acid binding protein for three months clinical outcome in acute cerebral infarction: multiple blood markers profiling study[J]. Crit Care, 2013, 17(2): R45
- [22] Zhang CG, Qu CH, Yang H, et al. Study on dynamic change of serum interleukin-17 and interleukin-10 levels in patients with acute cerebral infarction[J]. Chinese journal of applied physiology, 2014, 30(1): 36-37
- [23] Kumar P, Misra S, Kumar A, et al. Association between Tumor Necrosis Factor- α (-238G/A and -308G/A) Gene Polymorphisms and Risk of Ischemic Stroke: A Meta-Analysis[J]. Pulse (Basel), 2016, 3(3-4): 217-228