

# • 实验研究 •

## 川芎对急性实验性脑缺血大白兔血浆中 $\beta$ -TG、PF<sub>4</sub> 及 TXB<sub>2</sub>、6-酮-PGF<sub>1</sub> $\alpha$ 含量的影响

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**内容摘要** 应用酶标免疫测定法及放射免疫测定法分别测定了急性实验性脑缺血大白兔脑缺血前后血浆中  $\beta$ -血栓球蛋白( $\beta$ -TG)、血小板因子4(PF<sub>4</sub>)、血栓素 B<sub>2</sub>(TXB<sub>2</sub>)、6-酮-前列腺素 F<sub>1</sub> $\alpha$ (6-酮-PGF<sub>1</sub> $\alpha$ )含量的变化。发现脑缺血后血浆中  $\beta$ -TG、PF<sub>4</sub> 及 TXB<sub>2</sub> 的含量显著升高( $P < 0.01$ ), 而 6-酮-PGF<sub>1</sub> $\alpha$  的含量无明显变化。应用中药川芎治疗能明显地抑制血浆中  $\beta$ -TG、PF<sub>4</sub> 及 TXB<sub>2</sub> 含量的变化( $P < 0.01$ ), 并使血浆中 6-酮-PGF<sub>1</sub> $\alpha$  的含量有所升高( $P < 0.05$ )。提示川芎能够有效地抑制脑缺血时体内血小板的激活, 纠正循环血中 TXA<sub>2</sub>-PGI<sub>2</sub> 平衡失调。

**关键词** 脑缺血 川芎  $\beta$ -TG PF<sub>4</sub> TXB<sub>2</sub> 6-酮-PGF<sub>1</sub> $\alpha$

近年来, 人们研究发现体内血小板激活及花生四烯酸活性代谢产物在脑缺血的病理生理过程中发挥着重要的作用。我们分别测定了急性实验性脑缺血大白兔脑缺血前后血浆中  $\beta$ -TG、PF<sub>4</sub> 及 TXB<sub>2</sub>、6-酮-PGF<sub>1</sub> $\alpha$  含量的变化, 并观察应用活血化瘀中药川芎治疗对脑缺血时血浆中  $\beta$ -TG、PF<sub>4</sub> 及 TXB<sub>2</sub>、6-酮-PGF<sub>1</sub> $\alpha$  含量的影响, 以进一步探索川芎防治脑缺血的作用机理。

### 材料与方 法

一、动物分组与模型建立, 取18只体重 2.5~3.0kg 健康无孕纯种新西兰大白兔, 雌雄不拘。在水和饲料充足条件下饲养1周。然后随机分成三组: 川芎治疗组、生理盐水治疗组和假手术组。川芎治疗组经耳静脉注射 20% 川芎注射液 1.0ml (我院药厂制备, 批号: 890226); 生理盐水治疗组经耳静脉注射生理盐水 1.0ml, 每日注射1次, 共注射14天; 对照组不使用任何药物。各组动物在完全相同的条件下饲养。

将动物固定在手术台上, 先用塑料无菌注射器分别从三组动物的右心室内抽血 4 ml, 然后在2%奴夫卡因局部麻醉下作颈正中切口, 切开皮肤和皮下组织, 分离并同时结扎双侧颈总动脉, 造成大白兔双侧大脑半球部分性脑缺血。假手术组动物只分离双侧颈总动脉, 未予结扎。手术后川芎治疗组和生理盐水治疗组动物立即再经耳静脉分别注射20%川芎注射液和生理

盐水各 1 ml。假手术组动物仍不使用任何药物。手术后1小时, 再用塑料无菌注射器分别从三组动物的右心室内抽血 4 ml。

二、标本制备与测定: 将抽取的血液标本各2ml, 分别放入预冷的装有2%EDTA-Na<sub>2</sub>抗凝剂 0.2 ml 和ETP抗凝剂0.2ml的塑料试管中, 轻轻摇动, 使其充分混匀。然后迅速在4℃条件下离心(3 000r/min)15min, 吸出上层血浆约 1 ml, 放入-40℃低温冰箱中保存, 于1周内分别应用酶标免疫测定法及放射免疫测定法测血浆中  $\beta$ -TG、PF<sub>4</sub> 及 TXB<sub>2</sub>、6-酮-PGF<sub>1</sub> $\alpha$  的含量, 用成对资料t检验比较两组之间差异的显著性。

### 结 果

一、血浆中  $\beta$ -TG、PF<sub>4</sub> 含量的变化: 生理盐水治疗组大白兔脑缺血后, 血浆中  $\beta$ -TG、PF<sub>4</sub> 的含量显著高于假手术组( $P < 0.01$ ), 其中  $\beta$ -TG 的含量升高了 36.9%, PF<sub>4</sub> 的含量升高了 170.7%, PF<sub>4</sub> 含量变化的幅度明显大于  $\beta$ -TG 含量的变化。川芎治疗组大白兔脑缺血后, 血浆中  $\beta$ -TG 和 PF<sub>4</sub> 的含量仅略高于假手术组( $P > 0.05$ ), 见表1。

二、血浆中 TXB<sub>2</sub>、6-酮-PGF<sub>1</sub> $\alpha$  含量的变化: 生理盐水治疗组大白兔脑缺血后, 血浆中 TXB<sub>2</sub>、6-酮-PGF<sub>1</sub> $\alpha$  的含量与假手术组相比, TXB<sub>2</sub> 显著升高( $P < 0.01$ ), 而 6-酮-PGF<sub>1</sub> $\alpha$  无明显变化( $P > 0.05$ ); 川芎治疗组大白兔脑缺血后, 血浆中 TXB<sub>2</sub> 的含量与假手术组相比,

表1 三组血浆中 $\beta$ -TG和PF<sub>4</sub>含量的变化 (ng/ml,  $\bar{x} \pm S$ , 下同)

组别	脑缺血前		脑缺血后	
	$\beta$ -TG	PF <sub>4</sub>	$\beta$ -TG	PF <sub>4</sub>
川芎	33.4 $\pm$ 1.3	8.6 $\pm$ 1.9	39.7 $\pm$ 8.4	10.9 $\pm$ 3.1
生理盐水	34.1 $\pm$ 2.5	10.0 $\pm$ 1.8	48.2 $\pm$ 9.5	24.9 $\pm$ 4.6
假手术	36.0 $\pm$ 5.9	10.5 $\pm$ 3.2	35.2 $\pm$ 8.7	9.2 $\pm$ 5.9

\*与假手术组相比,  $P < 0.01$

无明显差异( $P > 0.05$ ), 而6-酮-PGF<sub>1 $\alpha$</sub> 的含量显著升高( $P < 0.05$ ), 见表2。

表2 血浆中TXB<sub>2</sub>和6-酮-PGF<sub>1 $\alpha$</sub> 含量的变化 (pg/ml)

组别	脑缺血前		脑缺血后	
	TXB <sub>2</sub>	6-酮-PGF <sub>1<math>\alpha</math></sub>	TXB <sub>2</sub>	6-酮-PGF <sub>1<math>\alpha</math></sub>
川芎	148.5 $\pm$ 15.3	24.9 $\pm$ 3.9	150.7 $\pm$ 14.9	29.9 $\pm$ 4.8*
生理盐水	148.4 $\pm$ 14.1	24.4 $\pm$ 3.2	174.8 $\pm$ 15.3	24.5 $\pm$ 4.6
假手术	150.5 $\pm$ 13.0	25.5 $\pm$ 4.3	149.5 $\pm$ 14.7	24.8 $\pm$ 5.4

注: 与假手术组相比, \* $P < 0.05$ , \*\* $P < 0.01$

## 讨 论

我们在结扎大白兔双侧颈总动脉, 使其双侧大脑半球部分性脑缺血之后, 发现血浆中 $\beta$ -TG、PF<sub>4</sub>和TXB<sub>2</sub>的含量显著升高( $P < 0.01$ ), 而6-酮-PGF<sub>1 $\alpha$</sub> 的含量无明显变化。提示脑缺血时, 血小板被激活, 释放反应增强; 循环血中TXA<sub>2</sub>-PGI<sub>2</sub>的平衡失调。在血小板中,  $\beta$ -TG和PF<sub>4</sub>的含量相等, 释放速度也相同。但由于PF<sub>4</sub>在体内从血浆中清除的速度较快, 因此我们测定血浆中 $\beta$ -TG的含量高于PF<sub>4</sub>, 而且脑缺血时血浆中PF<sub>4</sub>含量变化的幅度也明显大于 $\beta$ -TG, 说明 $\beta$ -TG和PF<sub>4</sub>的释放是由于脑缺血所致。若 $\beta$ -TG和PF<sub>4</sub>在体外发生释放, 则不会出现这种差异<sup>(1~3)</sup>。

川芎能够扩张小动、静脉, 降低红细胞和血小板的聚集性, 增加脑和微循环的血流量<sup>(4~6)</sup>, 并能明显减轻脑组织缺血性损害, 改善神经系统功能障碍<sup>(7)</sup>。本实验应用四川省灌县产川芎之干燥根茎, 由我院药厂制成20%川芎注射液, 其1ml相当于生药0.2g。结果可见大白兔血浆中 $\beta$ -TG、PF<sub>4</sub>和TXB<sub>2</sub>的含量与对照组相比无明显差异, 而血浆中6-酮-PGF<sub>1 $\alpha$</sub> 的含量显著升高( $P < 0.05$ )。说明应用川芎治疗, 能够有效地抑制脑缺血时体内血小板的激活, 纠正循环血中TXA<sub>2</sub>-

PGI<sub>2</sub>的平衡失调。

TXA<sub>2</sub>是血小板中花生四烯酸的主要代谢产物, 它是一种作用强烈的血管收缩因子, 并能促进血小板聚集和诱发血栓形成。PGI<sub>2</sub>是血管壁中花生四烯酸代谢的主要产物, 它是一种强烈的血管扩张因子, 是对血小板聚集最有效的内源性抑制剂<sup>(8)</sup>。在正常的生理状态下, 循环血中TXA<sub>2</sub>和PGI<sub>2</sub>的水平处于相对的平衡状态。但脑缺血时, 由于脑组织细胞内Ca<sup>++</sup>浓度升高, 释放出ADP、5-HT和儿茶酚胺等生物活性物质, 刺激血小板中花生四烯酸活性代谢产物TXA<sub>2</sub>大量合成, 并释放入血; 而在花生四烯酸环氧化酶和脂氧化酶代谢途径的初期, 伴有自由基产生, 其代谢产物脂质过氧化物也是自由基, 它们能抑制PGI<sub>2</sub>合成酶的活性, 使PGI<sub>2</sub>合成减少。结果循环血中TXA<sub>2</sub>-PGI<sub>2</sub>的平衡失调, 以致发生脑缺血低灌注, 血小板微血栓形成及脑微循环损害<sup>(9)</sup>。Stewart等认为血浆中 $\beta$ -TG含量超过50ng/ml的短暂性脑缺血发作患者, 在未来几年中发生脑梗塞的可能性很大<sup>(10)</sup>。应用川芎治疗, 由于能有效地抑制脑缺血时体内血小板的激活, 并能纠正循环血中TXA<sub>2</sub>-PGI<sub>2</sub>的平衡失调, 因而川芎对脑缺血具有积极的防治作用。

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**Analysis on the TCM Syndromes of the Patients with Autoimmune Thyroid Diseases****—Observation on the Change of Thyroid and Immune Functions in 109 Patients**

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Eighty-nine cases of hyperthyroidism and 20 cases of hypothyroidism caused by Hashimoto's thyroiditis were observed in order to analyse the thyroid and immune functions of the patients, and their relationship with the syndromes of TCM. The results showed that, in the patients with Yin(阴) deficiency syndrome, the contents of total  $T_4$ ,  $T_3$  were higher than normal and TSH lower than normal, while in Yang(阳) deficient patients, the contents of total  $T_4$ ,  $T_3$  were lower than normal and TSH higher than normal. This results suggested that the states of thyroid functions were closely related to the TCM syndromes. It was also found that the percentage of OKT 4<sup>+</sup> cells and the self-recognizing ability of lymphocytes were lower than normal in patients with hyperthyroidism and Yin deficiency. While in patients with hypothyroidism and Yang deficiency, they were higher than normal. These meant that the abilities of lymphocyte autoreaction in Yin deficient patients were in contrary tendency with those in Yang deficient patients. The former had the manifestation of over-inhibition while the latter, hyperaction. Besides, the contents of auto-antibodies were higher than normal in both the patients with hyperthyroidism and hypothyroidism, which manifested itself as a common character of autoimmune thyroid diseases. The results indicated that there were common characters as well as individual characters of thyroid and immune functions between hyperthyroid patients and hypothyroid patients, and these characters might well be the material bases of various syndromes in TCM.

(Original article on page 538)

**Investigation on Blood Stasis Syndrome of Patients with Gastric Malignant Tumor****Pre-, Post-Operation and Before Death**

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In the past three years, the authors observed substance of tongue and 5 indexes of blood coagulation (AT-III, Fn, Fa, VIII R:Ag and  $\beta$ TG) for a long time in 140 patients of gastric malignant tumor pre-operation, one month post-operation and 3 months before death. All patients were verified as gastric carcinoma by pathological section. The results showed that the positive rate of substance of tongue in patients pre-operation was as high as 58% (51/88), 5 indexes of blood coagulation in patients had obvious difference ( $P < 0.001$ ) comparing to that of healthy persons. This implied it existed relationship between gastric malignant tumor and blood stasis in TCM, and accorded with diagnosis of blood stasis syndrome. With the resection of tumor focus, the states of blood stasis in patients had been improved to a certain extent. But the positive rate of substance of tongue post-operation was still as high as 51.1% (45/88) comparing to that pre-operation ( $P > 0.05$ ). 5 indexes of blood coagulation in patients post-operation had no obvious improvement comparing to those pre-operation. This showed that the simple resection did not basically improve blood stasis in patients. The another important result was that the substance of tongue and 5 indexes of blood coagulation of 23 patients in last 3 months before death had more obvious blood stasis comparing to those post-operation even those pre-operation. This explained that blood stasis is one of the main characters of gastric malignant tumor before death. In conclusion, the extent of blood stasis syndrome can be used as an objective index to judge seriousness and prognosis of gastric malignant tumor patients' condition.

(Original article on page 540)

**Effects of *Ligusticum wallichii* on the Plasma Levels of  $\beta$ -TG, PF<sub>4</sub>, TXB<sub>2</sub> and 6-keto-PGF<sub>1 $\alpha$</sub>  in Rabbits under Acute Experimental Cerebral Ischemia**

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By occluding the bilateral carotid arteries of rabbits to produce bilateral partial cerebral ischemia, and by using RIA and ELISA to measure the levels of Beta-thromboglobulin ( $\beta$ -TG),