

脑梗死患者 PGI₂、TXA₂异常的性别差异及临床意义的探讨^①

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提 要 对40例脑梗死(脑梗塞)患者及53例正常对照的血浆 PGI₂(前列腺环素)、TXA₂(血栓素 A₂)水平进行了分析,发现男女患者体内均存在 PGI₂-TXA₂平衡紊乱,但是造成这种平衡紊乱的因素随性别不同而不同:男性患者主要是由于 TXA₂增高引起,而女性患者主要是由于 PGI₂降低引起。这结果可以从另一角度解释阿斯匹林抗栓作用仅限于男性脑梗塞患者的现象。

主题词 依前列醇/血液;血栓素 A₂/血液;脑梗塞/病理生理学;脑梗塞/药物治疗;阿期匹林/治疗应用;性别因素

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80年代以来,国内外研究表明,脑梗塞患者血浆中 PGI₂水平降低和/或 TXA₂水平增高,患者体内存在 PGI₂-TXA₂平衡紊乱^[1~5],但 PGI₂和 TXA₂的改变在性别方面有无差异却未见报道。本文对40例脑梗死患者(男25例,女15例)及53例正常对照的 PGI₂、TXA₂进行了分析,以了解它们有无性别差异,并探讨阿斯匹林抗栓作用仅限于男性脑梗死患者的机理。

1 材料与方 法

1.1 研究对象

1.1.1 患者组 选择起病48h之内的血栓性脑梗死患者40例,年龄47~79岁,平均64.5岁。男性25例,年龄47~79岁,平均69.2岁;女性15例,年龄50~70岁,平均60.3岁。诊断标准按照1986年“第2次全国脑血管病学术会议”第3次修订的诊断要点^[6]。均排除各类动脉炎、血液病、变态反应等原因引起的脑梗死,排除脑栓塞、蛛网膜下腔出血、颅内感染及占位性病变,排除存在 PGI₂、TXA₂水平异

常的疾病,如偏头痛、糖尿病、冠心病、肺动脉高压、血小板减少性紫癜、溶血性尿毒症以及雷诺病等周围性血管病。所有病人均经过头颅 CT 检查确诊。

1.1.2 正常对照组 选择与患者年龄、性别匹配的健康人53例,年龄45~70岁,平均62.3岁。其中男性30例,年龄45~70岁,平均57.5岁,女性23例,年龄49~68岁,平均58.2岁。

1.2 研究方法

上述检测对象均在检测前2周内未服用阿斯匹林、消炎痛、潘生丁等药物。于清晨空腹抽取肘静脉血。用放射免疫分析法测定血浆的 TXB₂(血栓素 B₂)、6-keto-PGF_{1α}(6-酮-PGF_{1α})含量,它们分别代表 TXA₂、PGI₂水平。

1.3 统计学处理

采用 *t* 检验进行组间比较。

2 结 果

2.1 患者组与对照组比较

脑梗死患者的6-keto-PGF_{1α}水平较正常

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对照组显著性降低, TXB₂水平显著性增高, 反映 PGI₂-TXA₂平衡的 T/K 值亦较对照组显著性增高(表1)。

2.2 男女性别比较

将男、女患者分开进行比较, 结果发现:

男、女患者的 T/K 值均较正常对照组显著性增高, 但是男性患者的 TXB₂增高显著, 而6-keto-PGF_{1α}水平较对照组降低, 差异具有高度显著性, 而 TXB₂也较对照组增高, 但差异仅具有显著性(表2)。

表1 脑梗死患者组与对照组的6-keto-PGF_{1α}、TXB₂、T/K 比较 ($\bar{x} \pm s$)(ng/L)

组别	例数	6-keto-PGF _{1α}	TXB ₂	T/K
患者组	40	78.30±59.9	236.27±149.26	7.61±9.76
对照组	53	123.42±84.74	155.15±58.48	1.93±1.57
<i>t</i> 值		3.012	3.254	3.646

注:3项患者组与对照组相比分别为 $P < 0.01$ 、 $P < 0.01$ 、 $P < 0.001$

表2 男、女性患者组与对照组的6-keto-PGF_{1α}、TXB₂、T/K 比较 ($\bar{x} \pm s$)(ng/L)

性别	组别	例数	6-keto-PGF _{1α}	TXB ₂	T/K
男	患者组	25	85.46±67.26	221.99±135.41	7.28±9.53
	对照组	30	97.79±36.43	146.26±54.08	2.32±1.73
	<i>t</i> 值		0.928 ¹⁾	2.784 ²⁾	2.916 ²⁾
女	患者组	15	66.37±44.66	260.08±172.2	8.13±10.44
	对照组	23	154.88±95.46	166.75±63.07	1.51±1.22
	<i>t</i> 值		3.348 ²⁾	2.378 ³⁾	3.031 ²⁾

注:与对照组相比 1) $P > 0.05$; 2) $P < 0.001$; 3) $P < 0.05$

3 讨论

PGI₂-TXA₂的动态平稳对于维持血管(包括脑血管)和血小板的正常功能具有重要作用^[1~5,7]。国内外许多研究的结果表明, 脑梗死患者的血浆 TXA₂水平增高和/或 PGI₂水平降低, PGI₂-TXA₂平衡紊乱。本文对40例脑梗死患者及对照组的6-keto-PGF_{1α}、TXB₂水平研究的结果与上述结果相吻合。

有关脑梗死患者血浆 PGI₂、TXA₂改变的性别差异, 至今未见报道。通过本组研究, 我们发现, 虽然男女患者体内均存在 PGI₂-TXA₂平衡紊乱, 但是造成这种平衡紊乱的因素随性别不同而不同: 男性患者主要是由于 TXA₂增高引起, 而女性患者主要是由于

PGI₂降低引起。这一发现目前尚属首见。

近年来, 对于阿斯匹林抗栓作用仅限于男性患者这一现象, 不少研究者进行了探索^[8,9]。有学者认为阿斯匹林抗栓作用在男性患者有效可能与下列因素有关^[8]: ①由于男性体内睾丸酮较高而致环氧化酶活性偏高; ②在女性体内, 环氧化酶不易发生乙酰化作用。

阿斯匹林能使脂肪酸环氧化酶活性中心的丝氨酸乙酰化, 从而使其丧失活性, 阻断环氧化酶通路, 使花生四烯酸向前列腺素内过氧化物的转化受到抑制, 最终使 PGI₂、TXA₂的合成受到抑制。根据本研究所发现的结果, 对于脑梗死患者来说, 由于男性患者的 PGI₂-TXA₂平衡失调主要由于 TXA₂水平增高引起, 应用阿斯匹林后可使 TXA₂水平降低, PGI₂-TXA₂失衡得到纠正, 因而

有效。而女性患者的 PGI₂-TXA₂平衡失调的原因,以 PGI₂水平降低为主,应用阿斯匹林后,虽然能使 TXA₂水平有所降低,但是作为矛盾主要方面的 PGI₂水平降低则无法得到纠正,因此无效。

因此,根据本研究的结果,至少可以部分地认为,阿斯匹林抗栓作用的性别差异不仅与性激素有关,而且还与花生四烯酸的代谢(即 PGI₂-TXA₂动态平衡)有关。

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ABNORMALITIES OF PGI₂ AND TXA₂ IN SEX DIFFERENCE IN CEREBRAL INFARCTION: AN APPROACH OF ITS CLINICAL SIGNIFICANCE

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The plasma levels of prostacyclin (PGI₂) and thromboxane A₂ (TXA₂) were studied in 40 patients (male 25, female 15) with cerebral thrombotic infarction and 53 normal controls. The results shown that there was a disturbed balance between TXA₂ and PGI₂ in all patients. But the factor resulting in the disturbed balance has sex difference: high concentration of

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THE CLINICAL OBSERVATION OF HPD ENHANCING RADIATION EFFECT ON NASOPHARYNGEAL CARCINOMA RADIOTHERAPY

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In order to observe whether hematoporphyrin derivatives (HPD) may have a radiosensitive enhancement effect on nasopharyngeal carcinoma (NPC), the authors selected 98 consecutive cases which were diagnosed as NPC in I-IV_a stages pathologically. Based on similar TNM staging and sex, these patients were equally distributed into HPD plus radiation group (experimental group) and radiation group (control group). All received continuous conventional fractionation of radiotherapy by ⁶⁰Co γ -ray. The result revealed that the total remission rates of primary NPC lesion, determined by the finding of indirect nasopharyngoscopy and CT scanning, were 100% and 65.3% respectively in the experimental combined group as a whole, whereas those in the control group were 73.5% and 32.7% respectively. These differences between the two groups were of statistical significance, particularly in the remission rates of tumors in stages T_{3,4}. The remission rate of metastatic neck tumor was 92.3% in the experimental group, a rate much higher than that 59% in the control group ($P < 0.01$). The radiosensitive enhancement ratio of HPD was calculated as 1.4~1.5. The acute radiation and toxic reaction did not differ significantly in these two groups. It shows that HPD may improve the short-term effect of radiotherapy of NPC and its use as a supplementary treatment has to be further investigated.

Subject headings nasopharyngeal neoplasms/radiotherapy; hematoporphyrin derivatives/therapeutic use

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TXA<sub>2</sub> was essentially demonstrated in the male patients, and low concentration of PGI<sub>2</sub> in female patients. It can explain the phenomenon that antithrombotic effect of aspirin is effective only on the male patients with cerebral thrombotic infarction.

**Subject headings** epoprostenol/blood; thromboxane A<sub>2</sub>/blood; cerebral infarction/physiopathology; cerebral infarction/drug therapy; aspirin/therapeutic use; sex factors