

病毒促成出血型胰腺炎的发生及 大黄的防治作用

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内容提要 本研究将麻疹活疫苗注入家兔主胰管及耳缘静脉, 14 及 48 小时血清淀粉酶明显升高, 血小板聚集率显著增强, 与两个对照组相比均有显著差异($P < 0.05 \sim 0.01$)。胰腺可见明显瘀血及点片状出血。大黄治疗组 24 及 48 小时血清淀粉酶及血小板聚集升高均受到阻抑, 胰腺瘀血、出血亦减轻。结果提示病毒对胰腺的侵袭是发生出血型胰腺炎的因素之一; 大黄是治疗出血型胰腺炎的有效药物。

关键词 麻疹活疫苗 胰腺炎 大黄

临床已报道急性胰腺炎可并发于流行性腮腺炎等病毒性感染, 以大黄为主要药物的通腑法治出血坏死性胰腺炎有明显疗效^①。本研究从实验医学角度探讨病毒是否是出血型胰腺炎发生的因素之一, 大黄对此型胰腺炎是否有防治作用, 结果报告于下。

材料与方法

一、分组: 实验用日本大耳白家兔(中国医学科学院动物中心提供)27 只, 体重 1.5~2.2kg, 雌雄不拘, 分为 4 组。

1. 疫苗组(8 只): 局麻开腹, 将溶于 5ml 注射用水的 10 人份麻疹活疫苗(北京生物制品研究所生产)注入主胰导管, 注毕于针孔近胰端结扎。关腹后再将同量麻疹活疫苗注入耳缘静脉。术毕及术后 24 小时胃管注入温水 10ml/kg。术后 48 小时取血样后气枪处死, 取胰腺标本。

2. 生理盐水组(6 只): 将上组之麻疹活疫苗改为等量生理盐水。

3. 开腹组(5 只): 开腹后不做胰管注液及结扎, 仅将 5ml 生理盐水注于主胰管及胰腺表面, 其余同生理盐水组。

4. 大黄组(8 只): 将疫苗组之胃管注温水改为大黄液(唐古特大黄饮片制成 7g/10ml 水煎剂)。

二、观测指标

1. 血清淀粉酶: 术前、术后 24 及 48 小时, 颈外静脉取血, 采用 Winslow 法测血清淀粉酶。

2. 血小板聚集率: 术前、术后 24 及 48 小时, 采用美国 CHRONO-LOG 全血血小板聚集仪(阻抗法, ADP 激发)测全血血小板聚集率。

3. 胰腺标本的显微镜观察: 处死动物后取胰腺, 观察记录肉眼改变后, 置于放大 500 倍的微循环显微镜下, 用落射光观察胰腺表面小血管及出血状况, 部分录像记录。

结 果

一、各组不同时间血清淀粉酶变化(见表 1): 疫苗组术后 24 小时血清淀粉酶上升 $450.0 \pm 207.0\%$ ($\bar{x} \pm S$, 下同), 而生理盐水、开腹及大黄组分别上升 $66.7 \pm 121.1\%$ 、 $140.0 \pm 151.7\%$ 及 $87.5 \pm 35.4\%$, 疫苗组与后三组相比 P 值分别 < 0.001 、 < 0.01 、 < 0.001 。疫苗组术后 48 小时血清淀粉酶上升 $471.4 \pm 495.7\%$, 而生理盐水、开腹及大黄组分别上升 $-20.0 \pm 27.4\%$ 、 $-10.0 \pm 22.4\%$ 及 $68.8 \pm 110.0\%$, 疫苗组与后三组比较 P 值均 < 0.05 。24、48 小时生理盐水与开腹组比较均无显著差异。

表 1 各组血清淀粉酶变化 ($\bar{x} \pm S$)

组 别	血清淀粉酶(u/L)		
	术 前	术后 24 小时	术后 48 小时
疫 苗	28000 \pm 7400	14000 \pm 45300	128000 \pm 64000
生理盐水	26706 \pm 8300	37300 \pm 13100	24000 \pm 8800
开 腹	25600 \pm 8800	51200 \pm 17500	22400 \pm 8800
大 黄	30000 \pm 5700	56000 \pm 14800	52000 \pm 3700

二、血小板聚集率: 术后 24 及 48 小时疫苗组血小板最大聚集率均明显上升, 24 小时与生理盐水、开腹、大黄组相比较 P 值均 < 0.01 ; 与 48 小时相比较 P 值分别 < 0.01 、 < 0.05 、 < 0.05 。各组上升百分数见表 2。

表2 各组血小板最大聚集率上升百分数($\bar{x} \pm S$)

组 别	血小板最大聚集率上升率(%)	
	24小时	48小时
疫 苗	200.0 \pm 114.9	708.2 \pm 657.5
生理盐水	-25.9 \pm 21.2	-14.8 \pm 44.6
开 腹	-29.3 \pm 47.1	-13.5 \pm 120.0
大 黄	-4.5 \pm 48.7	50.6 \pm 116.0

三、胰腺肉眼及显微镜下改变：疫苗组8只肉眼均可见胰腺点状出血，其中4只并有融合的片状出血；生理盐水及开腹组胰腺未见出血；大黄组2只未见出血，6只可见出血，但出血程度较轻，仅为点状，无片状融合。镜下疫苗组可见出血主要发生在小血管明显瘀滞扩张基础上；大黄组瘀滞扩张程度较轻；生理盐水及开腹组未见瘀血及出血。

讨 论

1984年我们已观察到，将一定量麻疹活疫苗注入家兔胰腺包膜内，24小时静脉注射去甲肾上腺素，可造成胰腺明显肉眼可见的出血，该组胰腺病理切片镜下可见微循环停滞、小血管扩张瘀血、淋巴及胰腺导管高度扩张、间质水肿等⁽²⁾。提示病毒可通过提高胰腺小血管对儿茶酚胺类物质反应性，而促成胰腺微循环瘀滞及出血。通过肝微循环障碍在病毒所致肝损伤中作用的研究⁽³⁾，我们观察到，将一定量麻疹活疫苗注入家兔门脉，24小时可见肝小血管收缩反应性明显上升；注入耳缘静脉，24小时可见血小板聚集、粘附功能显著增强；同时注入门脉和耳缘静脉，则24小时可见肝微循环障碍及肝功能损伤。提示病毒对某靶器官

的侵袭及病毒血症同时存在，一定时间后当聚集反应性增强的血小板循环至收缩反应性升高的小血管分布器官，就可在该器官发生微循环障碍及器官功能异常。本研究沿相同途径，仅将病毒侵袭器官改为胰腺，亦观察到了胰腺瘀血、出血、血小板聚集功能增强、血清淀粉酶升高。结果不仅支持病毒对胰腺的侵袭可通过促发胰腺微循环障碍造成出血型胰腺炎，亦再次提示病毒侵袭某器官及病毒血症的同时或短期内前后存在，可能是病毒感染时器官功能障碍的机理之一。本研究观察到胰腺导管阻塞不是出血型胰腺炎发生的主要因素。

国外有人观察到内毒素侵袭家兔胰腺24小时，再静注一次内毒素可造成出血坏死性胰腺炎模型⁽⁴⁾，支持细菌或病毒可通过类似途径促成出血型胰腺炎。

本研究大黄治疗组同时可观察到血小板聚集及血清淀粉酶的升高受到阻抑，胰腺瘀血、出血亦较轻，说明大黄是治疗出血性胰腺炎的有效药物，并提示大黄抑制血小板聚集、减轻胰腺微循环障碍是其有效机理之一。

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erythrocyte deformability, the blood viscosity, Hb, Ht, MCV, MCH levels indicate that there was a significant correlation between them and the fetal average birth weight respectively. This study indicates that blood stasis is one of the pathogenetic mechanisms of asymmetrical IUGR and that the PBCRS recipe could improve intrauterine growth environment of fetal which could treat and prevent IUGR in obstetrics. (Original article on page 157)

Effects of *Ligusticum wallichii* on the Plasma and CSF Levels of Dynorphin A1-13 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 radioimmunoassays to measure the levels of dynorphin A1-13-like immunoreactivity (ir-Dyn A1-13) in plasma and cerebrospinal fluid (CSF), the authors find that the levels of ir-Dyn A1-13 in plasma and CSF have significantly increased ($P < 0.01$) after cerebral ischemia appears. The result of the *Ligusticum wallichii* Franch (*Ligusticum*) pretreatment to the test-group shows a definite improvement of the changes of ir-Dyn A1-13 levels in plasma and CSF. The severity of brain ischemic damage and neurologic dysfunction in *Ligusticum*-treated animals is lighter than that of saline-treated group, too. In this study, some new approaches are explored to explain the pathophysiology of cerebral ischemia and the mechanisms by which *Ligusticum* prevents and treats cerebral ischemia. (Original article on page 160)

The Role of Virus in Hemorrhagic Pancreatitis and the Therapeutic Effect of Rhubarb

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The living measles vaccine was injected into both of the main pancreatic duct and the ear vein of the rabbits in the model group. The serum amylase was significantly higher than that of the control saline group ($P < 0.001$ after 24h; $P < 0.05$ after 48h). The aggregation function of platelets were increased after 24h ($P < 0.01$, $P < 0.01$) and 48h ($P < 0.01$, $P < 0.05$) as compared with both two control groups. The blood stasis and hemorrhage of pancreases were observed in the model group. In the treatment group with Rhubarb the increase of serum amylase was much less marked than the control ($P < 0.001$ after 24h, $P < 0.05$ after 48h). The platelet aggregation reactivity was inhibited ($P < 0.01$ after 24h, $P < 0.05$ after 48h). The blood stasis and hemorrhage of pancreases were less evident. The results suggested that: (1) the virus may be one of pathogenetic factor of the hemorrhagic pancreatitis; (2) the rhubarb was effective in the treatment of hemorrhagic pancreatitis under our experimental conditions. (Original article on page 162)

Effect of Licorzine on Extracorporeal Fibroblast Culture

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This paper reports the experimental study of the effect of licorzine on the extracorporeal fibroblast culture. When each milliliter of the nutrient fluid contains 50 μ g, 75 μ g, 100 μ g of licorzine respectively, the rate of cellular growth and the coefficient of karyokinesis were much higher than those of the control group. There was a significant change in cell morphology. In the experimental group, the cells grew vigorously, and they appeared large, flat, branching, with fusiform or spindle shape in profile. The ratio of fibroblasts and fibrocytes was 5:2. In young fibroblasts processes interwove with each other, the cytoplasm became plump, and the cell nucleolus could be seen clearly. They were actively engaged in protein synthesis for the production of intercellular substance, the cytoplasm appeared relatively homogeneous and was basophilic because of high concentration of granular endoplasmic reticulum. Fibroblasts are considered to be responsible for the formation of the fibers and synthesize most of the amorphous components of the matrix. In the normal control group, the ratio of fibroblasts and fibrocytes was 5:3. In relatively static fibrocytes, the cytoplasm was sparse and slightly acidphilic since the endoplasmic reticulum was scanty. As licorzine has the function of increasing fibroblasts' synthesis of fibers and matrix, it can promote the healing of the gastric ulcer. (Original article on page 164)