

生脉注射液对家兔体外血栓形成及凝血系统功能的影响

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内容提要 本文通过整体清醒动物实验,观察了生脉注射液对正常家兔体外血栓形成、血小板功能、凝血功能以及纤维蛋白原溶解活性的影响。结果表明:(1)生脉注射液有抑制体外血栓形成的作用;(2)抗凝血功能较强,无论对外源性和内源性凝血系统均有明显的抑制作用;(3)对纤溶功能有一定的促进作用。

生脉注射液是由传统中医古方“生脉散”研制而成的新剂型,具有益气、养阴、固脱等作用。目前临床已广泛开始应用于治疗急性心肌梗塞、冠心病心绞痛、心源性休克等疾病,并能使高凝状态的血液趋于正常。为了进一步探讨该方的作用机理,我们的实验观察了生脉注射液对正常家兔体外血栓形成、血小板功能、凝血功能以及纤维蛋白原溶解活性的影响。现将初步研究结果报告如下。

材料与方法

一、体外血栓形成实验:按李承珠等报告的方法⁽¹⁾。

二、血小板计数及功能测定:(1)血小板计数,按常规方法。(2)循环血小板聚集:按吴氏法⁽²⁾。(3)血小板聚集(ADP为诱导剂):采用PAM-2型PPP自动平衡血小板聚集仪,按比浊法测定⁽³⁾。

三、凝血功能⁽³⁾:(1)血浆凝血酶原时间测定法:Quick氏一步法。(2)凝血酶原消耗时间测定(PCT)。(3)血浆鱼精蛋白副凝试验(3P试验)。

四、纤溶功能^(4,5):(1)血浆纤维蛋白原含量。(2)优球蛋白溶解试验。(3)凝血酶时间测定。

五、实验动物:健康雄性家兔1.5~2 kg,分生理盐水及生脉注射液(实验用生脉注射液由本院附属医院制剂室提供,每支2 ml,每毫升含生药量红参0.1g、麦冬0.312g、北五味子0.156g)组。静脉注射,给药剂量均为2 ml/kg,于注射前和注射后2小时分别取血测定。

结 果

一、体外血栓形成:生脉注射液静脉注射2小时

后,体外血栓的形成时间延长,血栓重量(湿重)减轻,与注射前相比,均有显著差异($P < 0.001$),血栓长度有一定程度的缩短(见表1)。

表1 生脉注射液对正常家兔血栓形成时间、长度、重量的影响

	生脉注射液组				生理盐水组			
	n	注射前 M±SD	注射后 M±SD	P	n	注射前 M±SD	注射后 M±SD	P
血栓形成时间(s)	11	116.72 ±37	174.80 ±36	△	5	124±58	164±45	*
血栓长度(cm)	11	6.55 ±0.64	5.35 ±0.52	*	5	6.57 ±1.8	5.68 ±0.40	*
血栓重量湿重(mg)	10	107.90 ±27.32	69.50 ±16.48	△	5	162 ±10.50	120 ±10.50	*

注:n=动物数;下同;△ $P < 0.01$; * $P > 0.05$

二、血小板功能:(1)血小板计数:生脉注射液注射后,血小板总数无明显变化(见表2)。(2)循环中血小板聚集:生脉注射液注射后,非聚集血小板总数比率为0.94,比值较大,实验表明血小板解聚率大(见表2)。

表2 生脉注射液对家兔血小板功能的影响

	n	注射前 M±SD	注射后 M±SD	P 值
血小板计数(万/mm ³)	6	50.98±134.30	50.10±55.76	>0.05
血小板聚集比值	6	0.96±0.05	0.94±0.08	>0.05

(3)血小板聚集(ADP为诱导剂):ADP的浓度分别为1.25、2.5、5 μ M/ml,均可引起不同程度的聚集。生脉注射液注射前后血小板聚集率变化不大,而在ADP为2.5 μ M/ml浓度下,5分钟解聚率明显增加($P < 0.05$),见表3。

三、凝血功能:(1)血浆凝血酶原时间:注射后凝血酶原时间明显延长,实验表明,对外源性的凝血

表 3 生脉注射液对家兔由ADP诱发血小板聚集率的影响 (M±SD)

n	血小板聚集率%			5分钟解聚率%		
	5 μ M/ml	2.5 μ M/ml	1.25 μ M/ml	5 μ M/ml	2.5 μ M/ml	1.25 μ M/ml
注射前 10	34.20±10.90	24.70±13.50	11.30±7.8	49.16±20.60	22.90±3.0	100±0
注射后 8	37.50±15.40	25.53±12.0	11.50±7.6	58.60±15.40	37.30±13.0*	100±0

* 注射后与注射前相比 $P < 0.05$

功能有抑制作用(见表4)。(2)凝血酶原消耗时间:注射后凝血酶原时间明显延长,实验表明,生脉液亦能抑制内源性凝血系统(见表4)。

表 4 生脉注射液对家兔凝血功能的影响

n	注射前 M±SD	注射后 M±SD	P 值
血浆凝血酶原 6 时间(S)	19.35±5.17	69.39±22.40	<0.001
凝血酶原消耗 10 时间(S)	24.64±11.50	106.50±77.0	<0.001

(3)血浆鱼精蛋白副凝试验(3P试验):鱼精蛋白可分离纤维蛋白单体与纤维蛋白降解产物(FDP)结合成为可溶性复合物。生脉液注射后,可使血浆蛋白以外的成分纤维蛋白凝固,经非参数统计有显著的差别($P < 0.05$, 见表5)。

表 5 生脉注射液对家兔凝血功能的影响
——3P试验

n	阴性 —	+	阳性 ++	+++	P 值
注射前 11	7	2	2	0	
注射后 11	2	1	7*	1	<0.05

* 注射前后比较

四、对纤溶活性的影响:生脉注射液能使血浆纤维蛋白含量明显减少;优球蛋白溶解时间、凝血酶时间有一定程度的延长,提示生脉注射液可能有促纤溶作用(见表6)。

表 6 生脉注射液对家兔纤溶活性的影响

n	注射前 M±SD	注射后 M±SD	P 值
血浆纤维蛋白原(mg%) 10	277±64.9	209±49.0	<0.05
优球蛋白溶解时间(S) 8	225±27.8	285±69.8	>0.05
凝血酶时间(S) 8	9.16±2.10	16.6±9.5	>0.05

对照动物注射生理盐水前、后各项测定均无明显变化($P > 0.05$)

讨 论

一、生脉注射液有抑制体外血栓形成的作用,使血栓形成时间延长、重量减轻。提示生脉液对于改善血液高凝倾向,抑制血栓形成有一定的意义。也为临床运用生脉注射液治疗冠心病、脑血栓、静脉炎等病患者提供了实验的根据。

二、生脉注射液对正常血浆凝血酶原时间、凝血酶原消耗时间均有显著的延长作用,即对外源性凝血系统和内源性凝血系统均有明显的抑制作用,表明生脉注射液的抗凝血功能较强;同时生脉注射液能使纤维蛋白原含量明显减少,优球蛋白溶解时间及凝血酶时间有所延长,说明纤维蛋白原降解产物增多,而纤维蛋白原降解产物有强大的抗凝血作用,通常是当纤维蛋白原降解产物增加时,凝血酶时间延长,本实验结果与此相符,提示生脉注射液有一定的促纤溶作用。

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参 考 文 献

1. 李承珠,等。简易体外血栓形成仪装置及测定方法。上海第一医学院学报1979; 6(3): 205。
2. Wu KK et al. A new method for the quantitative detection of platelet aggregates in patients with arterial insufficiency. The Lancet 1974; 2 (7884): 924—927。
3. Born GVR. Quantitative investigation into the aggregation of blood platelets. J Physiol 1962; 162: 67。
4. 徐叔云,等。主编。药理试验方法学。第1版。北京:人民卫生出版社,1982: 834。
5. 单春文,等。人、猪、家兔、大白鼠和豚鼠优球蛋白溶解时间的正常值。中华血液学杂志1982; 3(5): 302。

Observation on TCM-WM Therapy in Treating 124 Nephrotic Syndrome Patients with Control

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From 1971 to 1981, 124 cases of children suffering from nephrotic syndrome were treated in our hospital. They were treated with corticosteroid, nitrogen mustard, cyclophosphamide combined with traditional Chinese medicine in groups of various combinations. In 80 cases treated with prednisone acetate and traditional Chinese herbs, 44 cases were cured with curative rate of 55%. In 22 cases treated with the combined therapy of nitrogen mustard, prednisone acetate and traditional herbs, 20 cases (90.91%) were cured. And finally in another 22 cases with cyclophosphamide, prednisone acetate and traditional herbs, 14 cases (63.64%) were cured. The therapeutic effect of the second group seemed to be the best one.

The combined therapy and some problems on the administration of traditional Chinese herbs with western drugs are discussed. (Original article on page 422)

Antagonistic Action of Re Du Qing Injection (热毒清注射液) on the Biological Activity of Endotoxin Induced DIC

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In this paper, an investigation was made on the therapeutic mechanism of heat-clearing and detoxifying Chinese medicinal preparation, Re Du Qing Injection, through animal experiments. According to the principle of generalized Shwartzman reaction, an animal model of DIC was established in rabbits by injecting the endotoxin of *Escherichia Coli*, and then the effect of preparation on pathophysiological process of DIC was observed. The hematological results indicated that the control group of normal saline was characterized by changes of DIC, but most of the changes of Re Du Qing treated group were not of statistical significance. Moreover, the morphological results showed that the DIC incidence and its severity were markedly lower in the Re Du Qing treated group than the control. Under electron microscope, the damage to endothelial cells of glomerular capillaries and liver cells in the Re Du Qing treated group was mild in comparison with control. These findings suggested that the preparation possess antagonistic action on the biological activity of endotoxin induced DIC.

The mechanism of the antagonistic action was also preliminarily discussed. According to the in vitro experiments, observation on morphology of Kupffer's cells with electron microscope, and other author's study, an inference was drawn that the antagonistic action may take place through degrading endotoxin directly, intensifying phagocytosis of MPS and increasing the activity of alternative complement pathway.

(Original article on page 425)

Experimental Studies on the Mechanism of Inhibition upon Thrombus Formation and Blood Coagulation in Vitro with Sheng-Mai Injection (生脉注射液)

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Sheng-Mai injection was injected intravenously into eleven rabbits with a dosage of 2ml/kg. Before and two hours after injection, blood was drawn from the rabbit heart directly for the determination of extracorporeal thrombus formation, platelet function, blood coagulation and fibrinolytic activity. The results were as follows: (1) The time of thrombus formation was prolonged ($P < 0.001$). The length of thrombus shortened and its weight decreased. All these changes indicated that the thrombus formation was inhibited by this drug. (2) The platelet count was unchanged, the ADP induced platelet aggregation rate and the ratio of peripheral platelet aggregation were not significantly influenced. (3) The prolonged prothrombin time and prothrombin consumption time indicated that the blood coagulation was inhibited. The effect of the drug may exert on both the intrinsic and extrinsic coagulation system. (4) The plasma fibrinogen was decreased, but there were no significant changes in the thrombin and the euglobulinolysis time. All these results suggest that the Sheng-Mai injection possesses an inhibitory function on extracorporeal thrombus formation and blood coagulation, it exerts a weak promotion to the fibrinolytic function, but does not influence the platelet counts and their functions. (Original article on page 428)