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参芪注射液对血小板环核苷酸含量及磷酸二酯酶活性的影响

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内容提要　本文用放免法测定了一次静脉给药参芪液60ml前后对冠心病心气虚或心阴虚患者血小板环核苷酸含量的变化。结果表明用药后一小时，血小板内cAMP含量由20.89±3.7增至30.0±3.0pm/10^9血小板（$P<0.02$），cGMP含量由3.3±1.0增至5.4±1.2pm/10^9血小板（$P<0.05$）。心阴虚者用药后环核苷酸含量有下降趋势。用参芪后血小板环核苷酸含量增加可能为参芪抑制血小板聚集的机理之一。环核苷酸含量增加与参芪抑制磷酸二酯酶活性有关。

临床及实验研究皆证实党参黄芪能抑制正常人和冠心病患者的血小板聚集[1,2]。为了探讨其抗血小板聚集的机理，我们就党参黄芪对血小板环核苷酸含量和磷酸二酯活性影响，进行了临床观察和实验研究。

材料和方法

一、试剂：1.参芪注射液：见前文。

2.cAMP药箱由中国医学科学院基础所生理室提供；cGMP药箱由上海第二医学院同位素室提供。

3.磷酸二酯酶：采用Mark Chasin法[3]从兔脑皮质中制备。

二、富血小板血浆制备：见前文。

三、贫血小板血浆制备：将PRP以4,000转/分离心15分钟，取上清即为贫血小板血浆(PPP)。立即对PPP进行计数。由PRP计数值减去PPP计数值即为沉淀中所含的血小板数。将沉淀中血小板用Tris-NaCl液悬浮、洗涤，制备成血小板悬液或称血小板浓缩液(PC)。

四、样品制备和测定：取PC1.0ml在37°C水浴中温育10分钟，加入15%三氯醋酸0.5ml。2小时后离心取上清液用水饱和乙醚(1:5)振荡提取三次。去水饱和乙醚后，将样品分装。cAMP样品在72°C烤干，cGMP样品在46°C水浴蒸干。然后放－20°C冰箱储备待测定。用PACKARD-460CD型液闪仪计数。血小板环核苷酸含量以picomoles/10^9血小板表示。

五、磷酸二酯酶活性测定：参照北京第二医学院生化教研组所报道方法[4]。

观察对象及分组

一、冠心病患者体内试验：

1.参芪组：根据我院气血研究室拟订虚证辨证标准（见前文），选冠心病心气虚住院患者15例，其中男8例，女7例，平均年龄59.3±7.8岁；心阴虚患者8例，其中男4例，女4例，平均年龄68.9±7.1岁。

2.葡萄糖组：冠心病心气虚患者10例，其中男4例，女6例，平均年龄61.4±8.0岁。

观察对象停药5天。实验当天禁高脂饮食，晨8时用硅化注射器采血后，分离提取血小板，制备样品测定。采血后，参芪组静点参芪注射液60ml加5%葡萄糖100ml；葡萄糖组静点5%葡萄糖160ml。静点完后1小时再次取血，制样测定，方法同前。

二、冠心病患者体外试验：冠心病心气虚住院患者16例，其中男7例，女9例，平均年龄63.3±9.0岁。本组于晨8时取血后制备PRP。在试管内，一组PRP中加入参芪液，一组PRP加等量缓冲液，在相同条件下制备样品和测定。实验对象要求条件同前。

结　果

一、参芪液、葡萄糖对血小板环核苷酸含量的影响：结果见表1。

从表1看出，心气虚患者一次静点参芪液后，血小板内cAMP含量显著升高，cGMP含量也显著升高。心阴虚患者参芪液一次静点后cAMP含量有所减少，cGMP含量有所增加，但统计学处理无意义。葡萄糖组在静点葡萄糖前后，血小板内环核苷酸含量无明显变化。在人体外实验参芪液也使血小板内环核苷酸含量增加。

在一定浓度范围内（药物终浓度在50mg/ml以下）随着参芪液浓度的增加，血小板内cAMP含量和cGMP含量都相对应地增加，呈量效一致关系。

二、参芪液对磷酸二酯酶活性影响：

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表1　参芪液、葡萄糖对冠心病患者血小板内环核苷酸含量影响　(M±SE)

	组别	例数	cAMP	t	P	cGMP	t	P	cAMP/cGMP	t	P
静点参芪液	心气虚	药前	15	20.9±3.7	2.95	P<0.02	3.3±1.0	2.22	P<0.05	9.4±2.2	0.48	P>0.5
		药后	15	30.0±3.0			5.4±1.2			8.2±1.1		
	心阴虚	药前	8	19.8±2.8	2.0	P>0.05	2.7±0.6	1.86	P>0.10	10.4±2.2	1.36	P>0.10
		药后	8	15.2±2.2			4.4±1.4			6.5±1.6		
静点葡萄糖		药前	10	18.8±2.3	1.54	P>0.10	3.5±0.4	0.8	P>0.2	6.6±0.7	0.22	P>0.5
		药后	10	20.4±2.8			3.9±0.6			6.9±1.1		
体外试验		对照	16	20.6±3.5	3.96	P<0.002	3.5±0.6	2.4	P<0.05	7.2±1.0	0.24	P>0.5
		参芪组	16	27.9±4.0			5.0±0.7			6.8±1.0		

由表2看出在一定药物浓度范围内，参芪液对磷酸二酯酶活性抑制百分率随着药物浓度增加而增加。

用不同方法测得参芪液所含离子浓度分别为K^+ 0.34mg/ml，Na^+ 0.69mg/ml，Ca^{++} 0.03mg/ml，Mg^{++} 11.4μg/ml，Zn^{++} 2.6μg/ml，Cu^{++} 0.063μg/ml。反应体系pH为7.5。参芪所含离子浓度在10^{-5}M以内，比文献报道允许值要低，故离子浓度本身不影响PDE活性。

表2　药物对cAMP-PDE及cGMP-PDE活性影响　(M±SE)

药物名称	终浓度mg/ml	cAMP-PDE抑制率%	统计学处理	cGMP-PDE抑制率%	统计学处理
参芪液	5	5.33±0.79	参芪液不同浓度间	9.95±1.17	参芪液不同浓度间
〃	10	12.75±0.78	F=111.68，P<0.01	11.89±0.83	F=9.52，P<0.01
〃	20	26.11±0.73	批间(n=5)	13.35±1.03	批间(n=5)
〃	25	27.76±1.74	F=2.74，P>0.05	16.06±0.98	F=4.36，P<0.05
氨茶碱	10	55.38±4.14		44.80±2.43	

讨　论

本文结果表明心气虚患者在静点参芪液后，血小板内cAMP含量明显增加(t=2.95，P<0.02)。体外实验也表明参芪能增加血小板内cAMP含量，和对照组相比有显著性差别(t=3.96，P<0.002)。而心阴虚患者在静点参芪液后，血小板cAMP含量有下降趋势，但无统计学意义。此外，我们以静点葡萄糖为空白对照，结果静点葡萄糖前后，血小板内cAMP含量无明显变化。这说明参芪组血小板内cAMP含量增加是药物所致，并非由于取血时间不同及其它因素所致。参芪液对血小板内cGMP含量也有不同程度增加，但不及cAMP显著。

1965年 Marcus等[5]报道cAMP是血小板聚集的抑制剂。cGMP对血小板聚集功能的影响[6]，目前尚无定论。

环核苷酸代谢受腺苷酸环化酶和磷酸二酯酶的影响。我们采用测剩余cAMP的简便方法，测定了参芪液对PDE活性影响。结果表明参芪能抑制PDE活性，从而增加血小板内cAMP含量，这可能是补气中药党参、黄芪抑制血小板聚集的机理之一。党参、黄芪对腺苷酸环化酶的影响如何，有待今后进一步研究。

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Effects of Codonopsis Pilosulae-Astragalus Injection on the Cyclic Nucleotide Levels and the Phosphodiesterase Activity in Platelets

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It has been demonstrated that ADP-induced platelet aggregation in patients with coronary heart disease (CHD) was inhibited by Codonopsis Pilosulae-Astragalus Injection (CP-A), a drug of TCM for the treatment of CHD in our laboratory recently. In order to study the mechanism responsible for the effects of CP-A on platelets, the cAMP and cGMP levels in platelets in patients with CHD (N = 15) were measured by radioimmunoassay method before and after a single dose of 60 ml CP-A (content of CP-A 30 gm each) intravenously, or 5% glucose 60 ml as control (N = 9). The results showed that the cAMP and cGMP levels were increased by CP-A, from 20.89±3.7 to 30.0±3.0 PM/10^9PLA ($P<0.02$), 3.3±1.0 to 5.4±1.2 PM/10^9 PLA ($P<0.05$). In the experiment in vitro (N = 16), the cAMP and cGMP levels were also increased, but were not so in that of glucose control group. When the cAMP level in platelets is raised, many platelet functions are inhibited. The results of the present study suggest that CP-A inhibits the platelet aggregation by increasing the cAMP level in platelets. The activity of PDE in platelet was inhibited by CP-A, which is responsible for the increase of cyclic nucleotide levels.

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The Effects of *Epimedium Sagittatum* and *Cistanche Deserticola* on DNA Synthesis in "Yang-Insufficiency" Animal model Induced by Hydroxyurea

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The effects of Yang-invigorating drugs *Epimedium sagittatum* and *Cistanche deserticola* on "Yang-insufficiency" mice were studied with a new "Yang-insufficiency" animal model induced by hydroxyurea as an inhibitor of nucleotide reductase. The animal used were divided into three groups: (1) the normal control group (8 animals), (2) the "Yang-insufficiency" group (8 animals), (3) the group with "Yang-insufficiency" treated with *Epimedium sagittatum* and *Cistanche deserticola* (9 animals). The rates of DNA synthesis in the liver and spleen (cpm/mg of DNA/minute, M±SE) of the groups were found to be 11,560±1,980, 5,600±848 and 9,900±1,660 respectively. This rate of the "Yang-insufficiency" group was significantly lowered ($P<0.05$). It can be seen that *Epimedium sagittatum* and *Cistanche deserticola* can raise the rate of DNA synthesis of the "Yang-insufficiency" animals, and thus improve the conditions of the animals.

The "Yang-insufficiency" caused by hydroxyurea is believed to be due to inhibition of the activity of nucleotide reductase, which keeps four kinds of nucleotide at the diphosphate level, unable to be reduced to DNA, and thus leads to the reduction of DNA synthesis, bringing on disturbance in metabolism of protein and fat and symptoms of "Yang-insufficiency". *Epimedium sagittatum* and *Cistanche deserticola* might contain certain biotical active agent, which could activate nucleotide reductase, counteract the inhibiting hydroxyurea and keep normal metabolism of DNA in the body.

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Five Cases of Sporadic Encephalitis Treated with Nantong Snake-Root Tablets

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The incidence of sporadic encephalitis in China has been rather high. It is usually treated with cortical hormone. This paper reports for the first time cases of sporadic encephalitis treated with Nantong Snake-Root Tablets, which are prepared by Ji Desheng, China's snake-bite doctor and expert, according to his secret prescription. All the cases were cured. The tablets began to work 3 to 6 days after administration. The patients were clinically healed 7 to 18 days after taking the medicine. Normal EEG was restored 7 to 14 days after medication. In all the five cases the tablets were administered orally, three times a day, ten tablets each time. No side-effects or remaining symptoms or signs were found when the patients were discharged from the hospital.

Compared with a group of fifty cases of the same disease treated with cortical hormone and symptomatic and palliative treatment, the cases treated with Nantong Snake-Root Tablets showed better results, with quicker and better effect, shorter course of treatment, no side-effects, less expenses and more convenience in remedy administration. As a new method to treat sporadic encephalitis, it serves a good example to integrate traditional Chinese and western medicine.

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