

益母草、赤芍、当归、三棱、莪术、泽兰 对大白鼠血液凝固作用的影响

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益母草、赤芍、当归、三棱、莪术、泽兰是临床常用的活血化瘀药。这些药物对于血液凝固作用的影响,近年有所报道,但限于体外血栓形成^(1,2)、血小板聚集^(3,4)、凝血酶时间⁽⁵⁾等几个指标,多数采用离体^(1,3~5)和动物静脉给药^(2,4)的方法。为了更全面地了解这些活血化瘀药对血液凝固的影响,并使给药方法更接近于中医的传统,我们通过胃饲中药煎剂,观察这些药物对大白鼠体外血栓形成、血小板计数和聚集、凝血和纤溶活性的影响。

材料和方法

取健康雄性、体重 200 ± 50 g 左右大白鼠,禁食(不禁水) 14~15 小时,胃饲中药煎剂 6~8 ml,连续二次,间隔 1 小时,总量相当于生药 15~20g。于胃饲后 1 小时左右,在乌拉坦腹腔麻醉下,自颈总动脉放血,作下述各种测定。对照组胃饲自来水代替药汁,余同实验组。

一、体外血栓试验:按 Chandler 氏法改良⁽⁶⁾,

包括体外血栓形成时间、血栓长度、血栓湿重和血栓干重测定。

二、血小板计数和聚集功能:包括血小板计数和血小板聚集功能(ADP 诱导,试管和玻片法)测定⁽⁷⁾。

三、凝血功能测定:包括血浆凝血酶原时间测定和白陶土部分凝血活酶时间测定⁽⁷⁾。

四、纤维蛋白(原)溶解活性试验:包括血浆纤维蛋白原含量(酚试剂比色法),优球蛋白溶解时间测定⁽⁷⁾。

实验结果

一、药物对体外血栓形成试验的影响:益母草、赤芍、当归、三棱、莪术、泽兰均有抗体外血栓形成作用,唯益母草、赤芍、当归、三棱、莪术抗血栓形成作用较强,可同时使血栓形成时间延长,血栓长度缩短,血栓重量减轻(湿重、干重),泽兰抗血栓形成作用较弱,仅血栓干重减轻(表 1)。

表 1 药物对体外血栓形成试验的影响 ($\bar{x} \pm S\bar{x}$)

组 别	动物数	血栓形成时间 (sec)	血栓长度 (cm)	血栓湿重 (mg)	血栓干重 (mg)
对 照 组	18	179.2 ± 46.1	5.7 ± 0.6	152.6 ± 18.7	41.9 ± 5.6
益母草组	18	$432.4 \pm 58.4^{**}$	$3.9 \pm 0.7^*$	$79.0 \pm 18.1^{**}$	$22.9 \pm 4.4^{**}$
赤 芍 组	15	$398.3 \pm 66.3^{**}$	$3.8 \pm 0.7^{**}$	$80.4 \pm 20.9^*$	$20.3 \pm 5.4^{**}$
当 归 组	14	$350.4 \pm 63.7^*$	$4.3 \pm 1.3^*$	$91.4 \pm 17.5^*$	$25.1 \pm 4.7^*$
三 棱 组	12	$418.8 \pm 75.5^{**}$	$3.4 \pm 1.0^*$	$75.4 \pm 23.4^*$	$21.9 \pm 5.9^*$
莪 术 组	8	$455.6 \pm 135.4^*$	$2.5 \pm 0.9^*$	$51.6 \pm 17.4^{**}$	$15.4 \pm 4.4^{**}$
泽 兰 组	10	285.0 ± 95.0	5.1 ± 0.4	119.3 ± 25.2	$34.0 \pm 6.9^*$

与对照组比较 ** $p < 0.01$ * $p < 0.05$

二、药物对血小板计数及血小板聚集功能的影响:益母草、当归、三棱、莪术可使血小板计数减少,血小板聚集功能减弱。赤芍及泽兰不降低外周血小板计数,但能使血小板聚集功能减弱(表 2)。

三、药物对凝血功能的影响:益母草、赤芍、当

归、三棱能使凝血酶原时间及白陶土部分凝血活酶时间延长,泽兰不能使凝血酶原时间延长,但能使白陶土部分凝血活酶时间延长,莪术对凝血酶原时间及白陶土部分凝血活酶时间均无作用(表 3)。

四、药物对纤维蛋白(原)溶解活性的影响:益母

表2 药物对血小板计数及聚集功能的影响 ($\bar{x} \pm S\bar{x}$)

组 别	动物数	血小板计数 0.2万/mm ³	血小板聚集功能 (ADP诱导) $\mu\text{g/ml}$
对 照 组	18	269.8 \pm 11.8	7.3 \pm 0.5
益母草组	17	220.4 \pm 9.9**	55.1 \pm 17.2**
赤 芍 组	14	260.4 \pm 15.3	174.9 \pm 94.2**
当 归 组	12	222.0 \pm 13.4*	208.0 \pm 42.3*
三 棱 组	10	220.0 \pm 6.6**	19.2 \pm 6.1**
莪 术 组	10	213.8 \pm 7.7**	33.6 \pm 19.0*
泽 兰 组	8	222.4 \pm 26.8	52.8 \pm 37.4*

与对照组比较 **p<0.01 *p<0.05

表3 药物对凝血功能的影响 ($\bar{x} \pm S\bar{x}$)

组 别	动物数	血浆凝血酶原时间 (sec)	白陶土部分凝血 活酶时间 (sec)
对 照 组	18	14.6 \pm 0.3	20.7 \pm 0.2
益母草组	17	15.5 \pm 0.2*	27.8 \pm 0.3**
赤 芍 组	14	16.8 \pm 0.5**	23.2 \pm 0.9**
当 归 组	12	16.4 \pm 0.5**	23.7 \pm 0.9**
三 棱 组	8	15.4 \pm 0.2**	22.2 \pm 0.5**
莪 术 组	10	15.0 \pm 0.2	21.5 \pm 0.4
泽 兰 组	8	15.2 \pm 0.4	29.9 \pm 0.6*

与对照组比较 **p<0.01 *p<0.05

草能使血浆纤维蛋白原减少, 优球蛋白溶解时间缩短。赤芍及三棱能使优球蛋白溶解时间缩短。当归、莪术及泽兰对纤维蛋白原及优球蛋白溶解时间无明显作用(表4)。

表4 药物对纤维蛋白(原)溶解活性的影响 ($\bar{x} \pm S\bar{x}$)

组 别	纤维蛋白原 (mg%)	优球蛋白溶解时间 (min)
对 照 组	340.9 \pm 11.6 (18)	393.9 \pm 47.3 (18)
益母草组	311.2 \pm 9.2* (17)	216.0 \pm 18.3* (15)
赤 芍 组	319.4 \pm 9.0 (11)	235.0 \pm 9.5* (9)
当 归 组	316.0 \pm 12.0 (12)	283.9 \pm 32.9 (9)
三 棱 组	306.8 \pm 16.9 (5)	189.4 \pm 17.5* (8)
莪 术 组	347.8 \pm 10.9 (5)	305.6 \pm 39.7 (9)
泽 兰 组	356.8 \pm 10.5 (6)	300.0 \pm 42.9 (7)

与对照组比较 *p<0.05

()内为动物数

讨 论

本文报道益母草、赤芍、当归、三棱、莪术、泽兰等六味中药对体外血栓形成的时间、长度、和重量、血小板计数和聚集功能、凝血酶原时间、白陶土部分凝血活酶时间, 血浆纤维蛋白原以及优球蛋白溶解时间的影响。实验表明这六味活血化瘀中药也是通过: (1)减少血小板计数、抑制血小板功能; (2)抑制内、外凝血功能; (3)促进纤溶活性这三个环节, 对体外血栓形成有所抑制, 但是每种药物的主要作用环节及其强度并不完全相同。本实验结果重复性强, 所用不同产地的药物均有作用, 从而为这些药物活血化瘀的临床疗效提供了理论根据。

迄今为止, 文献报道研究活血化瘀中药对血液凝固作用的影响, 有的用离体实验的方法。由于血液化学的特点, 血液凝固, 血小板聚集及纤维蛋白溶解等与离子性质、离子强度、酸硷度等有关, 在试管内测得的药物对血凝等影响, 可能存在一定差异, 用整体动物实验方法者则都为静脉给药。由于药物制成注射液, 在制作过程中有效成份可能丧失, 阴性结果往往不能说明问题。中药传统给药方法是口服, 研究中药不通过口服, 最终是难以说明问题的。因此, 我们采用中药煎剂胃饲大白鼠, 然后从颈总动脉放血进行血液凝固性测定的方法, 实验说明这个方法是可行的。

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A Preliminary Study on the Change in Pathology and Histochemistry of Affected Limbs in Filarial Elephantiasis after the Treatment with the Baking-Bandage Method and Hetrazan

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Relatively satisfactory results have been obtained in the treatment of 17 patients with advanced filarial elephantiasis with both the baking-bandage method and hetrazan, and changes in morphology and histochemistry in sections have also been observed with the following results.

1. The effects on the local: After treatment, the inflammation in the patients' affected limbs disappeared, the nutritional condition of tissue was improved. As a result, the sweat glands and hair follicles began to regenerate, the secreting function of the sweat glands gradually restored and elastic fibers in dermis reappeared too. It was found that the amount of acid mucopolysaccharides in the base is related to the formation of elastic fibers. As the nutrition of extracellular environment has been improved, the cell metabolism and mitosis were restored shortly. Glycogen plays an important role during the cell division and is also an energy donor. After treatment, glycogen disappeared in the epidermis, which then resembled the normal. The above-mentioned reduction of the size of affected limbs was due to following reasons. First, the inflammation caused by filarias was suppressed. Second, the edema and inflammation in the dermis disappeared. A pressure by means of the baking-bandage method was added to affected limbs instead of the action of the elastic fibers in the dermis.

2. The effects on organism: The clinical practice has demonstrated that inflammation might be temporarily suppressed after the patients were treated with the baking-bandage method. The effect probably influenced the organism through the local, and strengthened the defensive function of the whole body. Besides, the method could also raise the ability to defend the pathogenic agents, but the baking-bandage method does not kill the filarias in the body. So long as the patients' health worsens, inflammation will reoccur immediately. During the period, the IgG in the patients' sera increased. A lot of Ig granules could be seen below the endothelium of vessels, demonstrable with the immunoenzymatic technique. The Ig granules could stimulate the complements which attract the white cells to release various enzymes that will produce the inflammatory reactions, so the permeability of vessels increases. That is why the limb swells. After the patients had taken Hetrazan, the pathogenic agents were controlled. Subsequently, the frequency of inflammatory attacks decreased. The deposited Ig in the vessel walls disappeared too, so the permeability of vessels was restored to normal again. On the other hand, as the elastic fibers in vessels remarkably increased, the backflow of liquid was promoted. With the help of the baking-bandage method, the vicious circle turned into the benign circle.

3. Evaluation of the therapy: According to clinical experiences in our province, the size of the affected limbs of the patients who only took Hetrazan could not be reduced. The mere use of the baking-bandage method was also ineffective. In order to achieve a good efficiency in the treatment of elephantiasis, one must apply the integration of traditional and western medicine, for it has manifested a remarkably effective result. Both baking and bandage are necessary, but the filarias could not be killed. Furthermore, they have a disadvantage, that is, it took longer time to treat the patients, so a few patients could not follow the treatment to the end. However, the therapy still remains the best one in the treatment of elephantiasis at present.

(Original article on page 106)

An Experimental Study of the Segmental Sensory Innervation of Point Yanglingquan of Rabbits by Means of Axonal Retrograde Transport of Horseradish Peroxidase

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The segmental sensory innervation of the point yanglingquan of rabbits were studied with the method of retrograde transport of horseradish peroxidase (HRP).

Experiments were made in a series of adult rabbits. Under pentobarbital sodium, 2 or 3 mg of HRP were embedded in the point yanglingquan. After a survival time of 6-7 days or 6-8 days, the animals were perfused with fixative solution (2.0% paraformaldehyde in 0.1 M phosphate buffer, at pH 7.4).

The lumbosacral spinal ganglia were removed and then postfixed in the same fixative at 4°C for one hour. The frozen sections were incubated in a medium containing 3,3'-diaminobenzidine tetrahydrochloride and hydrogen peroxide. The sections were examined microscopically under both bright-field and dark-field illumination.

Labelled neurons were found only in the embedded aspect of ganglia (L₅-S₂) of those animals, in which 3 mg of HRP were embedded in point yanglingquan and their survival time was 6-8 days. Statistical examination showed that labelled neurons were mainly large ones.

(Original article on page 109)

The Influence of Yimucao, Chishao, Danggui, Sanleng, Erzhu and Zelan* upon the Blood Coagulation of Rats

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Male rats weighing 200 ± 50 gm each were fed with 6-8 ml of testing herb decoctions twice at an interval of 1½ hours, after 14-15 hours of fasting. The total amount of decoction given to one rat corresponded to 15-20 gm of crude drugs. Instead of decoction, fresh water was used in control animals. At 1½ to 2 hours after the second feed the rats' blood was let out from the carotid artery under urethane for the determination of the coagulative function and the fibrinolytic activity in comparison with those of the control group. The results were as follows: (1) Yimucao, Danggui, Chishao, Sanleng and Erzhu prolonged the time for thrombus formation in vitro, shortened the length of thrombus and decreased the weight (both dry and wet) of thrombus, while Zelan lessened the dry weight only. (2) Yimucao, Danggui, Sanleng and Erzhu decreased the platelet count and lowered the platelet aggregation function, while Chishao and Zelan had no effect on the platelet count but inhibited the aggregation function. (3) Yimucao, Danggui, Chishao and Sanleng prolonged the prothrombin time as well as the partial thromboplastin time, i.e. both the extrinsic and the intrinsic coagulation systems were inhibited, while Zelan prolonged only the partial thromboplastin time, i.e. the intrinsic system was involved. There was no effect on the coagulation system was involved. There was no effect on the coagulation system in the case of Erzhu. (4) The serum fibrinogen level was decreased by Yimucao and the euglobulin lysis time was shortened by Yimucao, Chishao and Sanleng, which indicated that fibrinolysis was promoted by these drugs.

* Yimucao (益母草) motherwort, *Leonurus heterophyllus* Sweet. Chishao (赤芍) *Paeonia lactiflora* Pali. Danggui (当归) *Angelica sinensis* (Oliv.) Diels. Sanleng (三棱) *Sparganium stoloniferum* Buch-Ham. Erzhu (莪术) *Curcuma zedoaria* (Berg.) Rosc. Zelan (泽兰) *Lycopus lucidus* Turcz.

(Original article on page 111)