

## • 实验研究 •

# 丹参注射液对实验动物同种移植心脏存活期的影响

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**内容提要** 丹参为常用活血化瘀药物。本实验表明,肌肉注射丹参注射液,可使大鼠同种异体移植心脏的存活期延长( $P<0.05$ )。在家兔心脏移植模型中,将丹参注射液与强的松龙合用,其抗排斥效果较两者单独使用时有明显的增强( $P<0.05$ )。

我们以前的研究证明,使用活血化瘀中药复方可减轻机体的移植排斥反应<sup>[1,2]</sup>,最近又探讨了单味活血化瘀中药——丹参注射液对实验动物异体移植心脏存活期的影响。现将初步结果报告如下。

## 材料与方法

一、丹参注射液:常熟制药厂产品,每毫升注射液相当于生药1.5g。

### 二、动物

1. 大鼠:雄性SD大鼠为受体,体重300~400g;Wistar大鼠为供体,雌雄不分,体重200~300g。
2. 家兔:市售杂系家兔,受体体重1.8~3.2kg;供体体重0.4~0.9kg,供、受体性别相同,毛色不同。

### 三、手术方法

1. 大鼠腹腔心脏移植术:参考Ono氏<sup>[3]</sup>和陈忠华<sup>[4]</sup>介绍的方法进行手术。即将供心的腔静脉与肺静脉结扎,而主动脉与受体的腹主动脉行端侧吻合,肺动脉与受体的下腔静脉行端侧吻合。

2. 家兔颈部心脏移植术:采用我们以前的方法<sup>[5]</sup>,将供心的腔静脉与肺静脉结扎,而主动脉与受体颈动脉行端侧吻合,肺动脉与受体颈外静脉行端侧吻合。

3. 术后观察:术后每日触诊移植心搏情况,并记录移植心电图,以移植心电活动消失作为移植排斥终点。

### 四、实验方法

大鼠分为3组进行实验:(1)空白对照组,共15只,不给药;(2)丹参1组,共11只,从移植当日起给丹参注射液每日12g/kg,肌肉注射;(3)丹参2组,共12只,从移植当日起给丹参注射液每日24g/kg,肌肉注射。

家兔分为4组进行实验:(1)空白对照组,共18只,不给药;(2)丹参组,共6只,丹参注射液每日

6g/kg,肌肉注射,当触诊移植心搏明显减弱时改为每日12g/kg剂量静脉注射;(3)西药组,共10只,术后当日、2、4、6、8、11、14、17、20日时肌肉注射强的松龙5mg/kg;(4)丹参与西药合用组,共8只,丹参注射液按第(2)组方法给药,强的松龙按第(3)组方法给药。

## 结 果

两组剂量的丹参注射液均可使大鼠移植心脏的存活明显延长(见表1)。而两种剂量之间比较,移植心脏的存活期并无明显差异。家兔同种异体心脏移植后,联合使用强的松龙与丹参注射液,其移植心存活时间较两者单独使用时均有明显延长( $P<0.05$ )(见表2)。

表1 丹参对大鼠移植心脏存活期的影响

组别	丹参 (g/kg)	大鼠 (只)	移植心存活 时间(天)	M±SE	P 值
1	—	15	7~17	10.33±0.78	
2	12	11	9~31	14.45±1.73	<0.05
3	24	12	8~24	13.33±1.12	<0.05

表2 家兔异体心脏移植模型中丹参对强的松龙抗移植排斥作用的增强效应

组别	丹参 (g/kg)	强的松龙 (mg/kg)	家兔 (只)	移植心存活 时间(天)	M±SE
1	—	—	18	9~27	15.72±1.15
2	6	—	6	7~28	19.17±3.24
3	—	5	10	16~28	22.20±1.40*
4	6	5	8	19~40	28.12±2.32**Δ

注:与第1组比较 \* $P<0.01$ , \*\* $P<0.001$ , 与第3组比较,  $\Delta P<0.05$

## 讨 论

本实验所采用的大鼠与家兔异体心脏移植模型，其移植心血管途径为：受体动脉→移植心胸主动脉→冠状动脉→心肌→冠状静脉→静脉窦→右心房→右心室→移植心肺动脉→受体静脉。当血管吻合结束后，移植心血管循环建立，恢复搏动，并可测得相应的移植心电图。通常认为，用移植心心电活动消失判定排斥反应的终点是精确可靠的<sup>(4,6,7)</sup>。

丹参为常用活血化瘀药物，具有扩张冠脉、改善血液流变性异常、抗凝、抗血栓形成、激活纤溶等作用。在临床缺血性心脏病的防治上得到广泛应用。据报道，丹参注射液对改善心脏微循环有明显的促进作用<sup>(8)</sup>，并可减轻缺血心肌间盘的损伤<sup>(9)</sup>，改善缺血心肌的情况。我们在异体心脏移植中应用丹参注射液，目的在于改善移植心脏在排斥过程中出现的微循环障碍和由此产生的心肌缺氧，以使移植心的存活期得以延长。

从本实验结果看，丹参注射液可使大鼠移植心脏的存活期较对照组明显延长，但有效剂量的丹参注射液加大1倍，移植心脏的存活并无进一步的延长，说明单独使用丹参注射液尚难控制移植排斥反应。丹参注射液也使家兔移植心脏的存活有所延长，但统计学意义不显著。我们认为这一方面可能与动物数较少及药物剂量不一定合适有关，另一方面也进一步说明丹参注射液对移植物的保护作用不够强。有必要将丹参注射液与其它药物配伍应用。

我们考虑丹参注射液作用较缓和，对移植后期改善移植物功能有一定效果，而皮质激素作用强烈，可有效地控制移植早期的排斥反应。若两者联合应用估计效果较好。故在兔心移植模型中将丹参注射液与强的松龙配伍应用。实验结果与预期相符。两者联合用药

时移植心存活时间较两药单独使用时均有明显延长( $P<0.05$ )。这说明丹参注射液确实可增强皮质激素的抗移植排斥作用。

丹参注射液毒性较低，在实验中未见明显毒性反应，动物食量、体重等一般情况与对照组均无明显差异。

已有报道指出，丹参注射液本身具有一定的免疫抑制作用<sup>(10)</sup>。因而，丹参注射液延长异体移植心脏的存活期主要是通过早期的免疫抑制，还是通过后期的改善微循环，尚需进一步研究。

## 参 考 文 献

1. 朱洪荫,等. 中西医结合治疗家兔同种肾移植排斥反应的初步观察报告. 中医杂志 1982; 23:149.
2. 朱洪荫,等. 中西医结合治疗家兔同种肾移植排斥反应的组织学及组织化学观察. 中医杂志 1983; 24:945.
3. Ono K, et al. Improved technique for heart transplantation in rats. J Thorac Cardiovasc Surg 1969; 57:225.
4. 陈忠华,等. 改进的大白鼠同种异位心脏移植术. 中华器官移植杂志 1982; 3:38.
5. 庄红明,等. 家兔同种心脏移植术. 中国病理生理杂志 (待发表).
6. Heron I. The iso-and allotransplanted rat heart, Histological, Electrocardiographic and Serological observations. Acta Pathmicrobiol Scand Section A 1972; 80:9.
7. Abbott CP, et al. The transplanted rat heart. Histologic and electrocardiographic changes. Transplantation 1965; 3:432.
8. 张 照,等. 丹参注射液对心脏微循环的影响. 病理生理学报 1985; 2:19.
9. 范世藩,等. 丹参对兔急性缺血心肌间盘损伤的作用. 药理学报 1979; 14:416.
10. 傅乃武,等. 几种活血化瘀药物对免疫功能的影响. 中国药理通讯 1985; 2:5.

## · 简 讯 ·

▲华东地区第三次中西医结合学术交流会于1987年9月22~24日在福建省漳州市召开。来自六省一市的代表117名参加了会议。会议收到论文304篇，有50篇在会上进行了交流。论文内容充分反映了近年来华东地区中西医结合临床、科研水平。

(何鸿钦)

▲全国中西医结合胆石症排石疗法学习班于1987年9月23日在辽宁省中医研究院结束。学员来自全国

17个省、市、自治区，由陈淑珍、贺瑞麟等多位教授、专家授课，并有实验室示教、临床实习。通过学习，学员们反映收效很大，纷纷表示要把学到的本领带回去，让其在胆石症的治疗中发挥更大的效益。参加学习的36名学员经考试合格，全部发给了结业证书。

(刘 杰)

▲1987年8月10日，中国中西医结合研究会第七次二届常务理事会决定成立中国中西医结合研究会眼科专业委员会。挂靠单位为中国中医研究院眼科研究所，联系人高培质。

(燕 春)

## Effect of *Salvia Miltiorrhiza* on Survival Time of Heart Allograft in Experimental Animals

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Heterotopic heart allotransplantation was performed in rats and rabbits. On the basis of successful operations, one of traditional Chinese drugs of promoting the blood circulation, *Salvia miltiorrhiza* was evaluated for its effect in increasing the survival time of cardiac allograft. We found that at the dose of 12 g/kg and 24 g/kg per day, *Salvia miltiorrhiza* prolonged the survival time of cardiac allograft significantly in rats, but there was no significant difference in allograft survival time between the two groups in which *Salvia miltiorrhiza* was used. In rabbit cardiac allograft model a dose of 6 g/kg per day of *Salvia miltiorrhiza* combined with prednisolone (5 mg/kg, administered respectively at the time of 0, 2, 4, 6, 8, 11, 14, 17, 20 days after transplantation) showed stronger anti-rejection effect than either drug used alone. No significant toxic effect was noticed in our experiment.

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## Study of *Tripterygium wilfordii* on Prolonging Survival Time of Mice Myocardial Allografts

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Myocardial tissues of new-born BALB/c mice (within 24 hrs after birth) were transplanted to adult NIH mice as free allografts. ECG activity was used to detect rejection. Three groups of mice were treated with *Tripterygium wilfordii* Hook f. in doses of 0.05g/day, 0.10 g/day and extract tablets *Tripterygium wilfordii* 0.10g/day, p. o. The control groups were treated with normal saline (NS) and azathioprine. The average survival time of grafted heart tissue for the NS group was  $12.3 \pm 2.9$  days and for the azathioprine group  $17.8 \pm 2.9$  days. The survival time of grafted heart tissue was significantly prolonged by *Tripterygium wilfordii* and its extracts. The average survival time was as follows: for 0.05 g/day  $18.5 \pm 2.7$  days, for 0.10 g/day  $19.3 \pm 2.7$  days and for extract-tablets  $20.7 \pm 1.2$  days. Comparing the above-mentioned groups with the NS group, the difference was significant,  $P < 0.001$ . The survival time for extract-tablets group was longer than that of the azathioprine group ( $P < 0.05$ ). Comparing the rejection percentage at definite times, the rate of drug administered groups decreased remarkably: Ten days after transplantation, 57% of the NS group were rejected, and none of the drug administered groups were rejected ( $P < 0.05$ ). 19 days after transplantation, 100% of the NS group were rejected, but the extract group for 0.10 g/day only 17% were rejected ( $P < 0.05$ ). A histological examination of the grafts revealed that there were large amount of lymphocytes and certain amount of monocytes infiltrated in the broken-down myocardial fibers in the control groups 12 days after transplantation. While in the drug administered groups, the myocardial fibers remained intact. All these data mentioned suggested that *Tripterygium wilfordii* can prolong the survival time of allografted myocardial tissue significantly. Its mechanism is possibly the inhibition of cell mediated and humoral immunity.

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## "Activating Blood Circulation and Relieving Stasis" in Treating Experimental Peritonitis

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The treatment of "activating blood circulation and relieving stasis" therapy (the main component of which is *Salvia miltiorrhiza*) was used alone in early experimental peritonitis in rats, with a result of acceleration in absorption of exudative fibrinogen and of the elimination of intraperitoneal infection. The mortality of the medicated group (16.7%) was significantly lower than that of the control (60%,  $P < 0.05$ ), and the severity of pathologic changes milder as well, the mean diameter of intraperitoneal abscess and the length of intestinal adhesion were shorter than that of the control ( $P < 0.001$  and  $0.005$  respectively). Hence the results provided a sound basis for the application of "activating blood circulation and relieving stasis" herbal medicines during the early and middle stages of peritonitis.

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