

麝香心脑乐治疗345例冠心病的 临床观察及实验研究

白求恩医科大学第三临床学院内科

刘忠铭 戴绍东 林国珍 卢尔滨 何敏 魏大愚 孙晶

内容提要 用麝香心脑乐治疗冠心病345例,缓解心绞痛总有效率为88.1%,改善心电图心肌缺血总有效率为72.9%。实验证实该药有改善急性心肌缺血作用,能增加心肌营养性血流量,降低全血及血浆粘度,改善血小板最大聚集率,是一种安全有效治疗冠心病的新药。

1983年1月~1985年9月我们应用麝香心脑乐治疗冠心病345例,取得了较满意效果,同时进行了动物实验观察,现总结报道如下。

临床资料

一、诊断、分级及疗效评定标准:冠心病诊断采用世界卫生组织命名及诊断标准^①。心绞痛分级及疗效评定,按1974年冠心病及高血压病普查预防座谈会修订的“心绞痛症状疗效评定标准”^②。心绞痛症状分级:(1)轻度:不是每天发作,每次发作持续数分钟,有时需含硝酸甘油片。(2)中度:每天发作数次,每次持续时间数分钟至10分钟左右,一般需口含硝酸甘油片;或不是每天发作,但疼痛较剧烈可伴有出汗,需口含硝酸甘油片。(3)重度:每天发作多次,影响日常活动,每次发作持续时间较长,疼痛难忍伴有出汗,需多次口含硝酸甘油片。

二、病例选择:治疗组及对照组患者皆住院治疗观察。

1. 治疗组345例,其中男230例,女115例;年龄24~81岁,平均52.5岁。本组皆为劳力型心绞痛^③,其中轻度112例,中度180例,重度53例。心电图有S-T段下降或T波倒置呈缺血性改变者277例(80.3%)。患者合并高血压病115例,其中一期48例(41.7%),

二期67例(58.3%);高脂血症161例,其中胆固醇增高者161例,甘油三酯增高者119例, β 脂蛋白增高者88例(数据均见附表);高血糖者35例。心电图检查显示心律失常者108例,其中室性早搏40例,房性早搏22例,心房颤动21例,窦性心动过缓18例,束支传导阻滞5例及二度房室传导阻滞2例。

2. 对照组220例,男140例,女80例;年龄28~68岁,平均50.5岁。本组皆为劳力型心绞痛,轻度88例,中度118例,重度14例。心电图S-T、T有缺血改变者168例(76.4%)。患者合并高血压病61例,高脂血症88例,高血糖17例。心电图显示心律失常者共63例。

三、观察指标:(1)治疗前后心绞痛发作程度、次数、持续时间、诱因及用硝酸甘油药物增减情况等。(2)治疗前后作心电图或二级梯运动试验,观察S-T、T异常及/或心律失常变化。(3)全血比粘度、血浆比粘度、红细胞压积、血沉、红细胞电泳率、血小板聚集率及血脂的改变。(4)治疗期间患者症状,心、肝、肾功能的改变。

治疗方法

一、治疗组用麝香心脑乐,由麝香、冰片、人参皂甙、三七、丹参、淫羊藿等中药组成(每片含生药1.6g,由白求恩医科大学第三临床

学院研制, 吉林省抚松制药厂生产)。

二、对照组用心舒乐[®], 由葛根、丹参、桃仁、红花、郁金 5 味中药组成 (每片含生药 1.3g, 由白求恩医科大学第三临床学院研制, 吉林省四平制药厂生产)。

三、用药方法: 治疗组与对照组皆每日 3 次, 每次 4 片, 3 周为 1 个疗程。本组病例皆进行 1 个疗程后观察疗效, 治疗期间除应用维生素类药物外, 停用其它治疗冠心病药物。疗程中心绞痛发作时, 临时给硝酸甘油药物治疗。

结 果

一、改善心绞痛疗效分析: 治疗组治疗后 304 例有效, 总有效率为 88.1%。轻度 112 例中显效 83 例, 无效 29 例; 中度 180 例中, 显效 81 例, 改善 91 例, 无效 8 例; 重度 53 例中, 显效 16 例, 改善 33 例, 无效 4 例。轻度与重、中度疗效比较有显著和非常显著差异 ($P < 0.05 \sim 0.01$)。

对照组 220 例中有效 168 例, 总有效率 76.4%, 两组比较差异有非常显著性意义 ($P < 0.01$)。

二、对心电图的影响

1. S-T、T 改变情况: 治疗组治疗前 277 例有缺血性改变 (平静心电图 S-T、T 改变者 247 例, 双倍二级梯运动试验阳性者 30 例), 治疗后平静心电图显效 109 例, 改善 73 例, 无改善 60 例, 加重 5 例; 双倍二级梯运动试验中显效 13 例, 改善 7 例, 无改善 9 例, 加重 1 例。总计: 显效 122 例 (44.0%), 改善 80 例 (28.9%), 无改善 69 例 (24.9%), 加重 6 例 (2.2%)。总有效率为 72.9%。

对照组有缺血改变者 168 例, 有效者 82 例, 总有效率 48.8%。

2. 心律失常改善情况: 治疗组 108 例心律失常患者, 治疗后有效 76 例 (70.4%), 其中室性早搏有效 34/40 例, 房性早搏 18/22 例, 心房颤动 6/21 例, 窦性心动过缓 16/18 例, 束支传导阻滞 1/5 例, 二度房室传导阻滞 1/2 例。

三、对血液流变性影响: 治疗组治疗后全血比粘度、血浆比粘度、红细胞压积分别由治疗前的 5.27 ± 0.91 ($M \pm SD$, 下同)、 1.81 ± 0.20 、 $54.12 \pm 7.40\%$ 降低为 4.41 ± 0.75 、 1.62 ± 0.18 、 $48.25 \pm 5.90\%$, P 值均 < 0.01 。红细胞电泳速度增快, 由治疗前的 0.85 ± 0.18 增至 $0.98 \pm 0.17 \mu\text{m}/\text{sec}/\text{v}/\text{cm}$ ($P < 0.01$)。血小板最大聚集率由治疗前的 $27.32 \pm 12.14\%$ 降至 $22.06 \pm 11.12\%$ ($P < 0.05$)。

四、血脂改变: 治疗组治疗后血清胆固醇、甘油三酯、 β 脂蛋白均降低, 治疗前后对比有非常显著性差异 ($P < 0.01$), 见附表。

附表 治疗前后血脂 (mg/dl) 变化对比 ($M \pm SD$)

	n	胆 固 醇	n	甘 油 三 酯	n	β 脂 蛋 白
治前	181	285.5 ± 46.6	119	226.0 ± 72.7	88	629.0 ± 111.2
治后		237.2 ± 53.6		184.7 ± 87.0		560.6 ± 160.5
t 值		3.6		3.5		3.3
P 值		< 0.01		< 0.01		< 0.01

注: n 为例数

对照组未进行治疗前后心律失常改善情况、血液流变性、血脂的观察对比。

五、副作用: 治疗组治疗期间有 2 例患者胃部不适, 但不影响用药。另有 304 例、261 例、241 例患者分别进行了治疗前后肝功能、尿常规、血常规及血小板计数检查, 实验结果均未见异常改变。

实 验 研 究

一、麝香心脑乐对家兔急性心肌缺血心电图的影响: 选择心电图正常的健康家兔 8 只, 先用蒸馏水 20ml 灌胃, 1 日 2 次, 共 7 天, 然后经耳静脉注入脑垂体后叶素 $3\text{u}/\text{kg}$, 15 秒内注完, 描记心电图作为对照组。喂养 3 天后, 再用麝香心脑乐每日 $0.15\text{g}/\text{kg}$, 加蒸馏水至 20ml 灌胃, 1 日 2 次共 7 天, 耳静脉注入脑垂体后叶素 $3\text{u}/\text{kg}$, 15 秒内注完, 描记心电图为给药组, 比较两组心电图 S-T 段、T 波、P-R 间期以及心律失常变化。实验结果将减少 S-T 段抬高程度, 降低高耸 T 波振幅, 缩短最长 P-R 间期, 减少

心律失常发生为给药组心电图改善的4项指标。结果上述4项指标对心肌缺血的抑制率为100%(8/8例), 3项指标抑制率为62.5%(5/8例)。一般认为抑制心肌缺血百分率超过20%即有意义。

二、麝香心脑乐对小鼠心肌营养血流量的影响: 选用雄性健康小鼠94只, 体重18~22g, 分成5组: (1)对照组19只, (2)给药组19只, (3)模型组20只, (4)治疗组18只, (5)硝酸甘油组18只。其中(1)、(3)组给予20%淀粉液0.4ml(4g/kg)灌胃, (2)、(4)组给予50%麝香心脑乐0.24ml(24mg/kg)灌胃, (5)组给0.1%硝酸甘油0.4ml(20mg/kg)灌胃, 并给(1)、(2)两组自尾静脉注入⁸⁶铷液0.2ml, (3)、(4)、(5)组自尾静脉注入⁸⁶铷0.2ml与脑垂体后叶素0.2ml(10u/kg), 5秒钟内注完, 30秒后断头处死, 用自动定标器测定心肌摄取⁸⁶铷放射强度, 以每只心脏放射性占总放射性的百分数为⁸⁶铷的摄取率。比较组间差异并计算放射增减率。结果表明麝香心脑乐不仅可使健康小鼠对⁸⁶铷摄取能力增加, 亦对脑垂体后叶素所致心肌⁸⁶铷摄取减少条件下, 有明显改善作用, 且作用很显著。

三、毒性试验

1. 急性毒性试验: 小白鼠20只, 体重20g, 雌雄各半, 给药前禁食12小时, 以50%麝香心脑乐水混液按15.0g/kg体重的剂量灌胃给药, 观察12小时未见不良反应, 72小时无一鼠死亡。

2. 亚急性毒性试验: 选择大鼠32只, 以50%麝香心脑乐水混液按每公斤体重2.0、4.0、8.0g连续给药4周, 对大鼠体重、血常规、肝功能、肾功能均无影响, 病理组织切片检查对心、肝、脾、肺、肾均未见药物所致病理改变。

讨 论

一、根据近年来多数中医学者认为冠心病

病机是本虚标实^[3,4], 益气活血是中医治疗本病的主要治则之一的理论, 我们组成了麝香心脑乐复方制剂。其中麝香、丹参等药, 有作者报道分别具有扩张冠脉、增加血流量、提高心肌对缺氧耐受性的能力, 降低血脂、抑制凝血等作用^[5,6]; 而人参皂甙对缺糖、缺氧的心肌细胞有保护作用^[7]。

二、麝香心脑乐复方经药理实验证明, 具有明显对抗脑垂体后叶素引起家兔急性心肌缺血作用, 可改善S-T、T改变, 缩短R-R间期, 减少心律失常的发生; 并可增加小白鼠心肌对⁸⁶铷的摄取能力, 该药不仅可增加健康小鼠心肌营养性血流量。而且对脑垂体后叶素所致心肌缺血疗效更明显, 表明该药具有较强的抗冠脉血管痉挛所致心肌损伤的作用, 为临床防治冠心病提供了依据。

三、本文临床观察麝香心脑乐对缓解心绞痛(尤其对中度、重度), 改善心肌缺血、心律失常均有较好的疗效, 且疗效优于对照组心舒乐。另外该药对血液流变性亦有明显改善作用, 可能与本方剂的益气活血作用有关。本药经急性及亚急性毒理试验证明, 是一种治疗冠心病的安全有效药物, 值得推广应用。

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seems to have the best result. The total effective rate amounted to 95%, mixed type reached 80%, and the heat type was only 73%. The longer the duration of medicated plaster lasted and the more frequently it was applied, the better the efficacy. This plaster proved to be effective not only during the attack of asthma, but it has preventive action also when applied in the remission period. The sensitivity of respiratory tract mucosa was reduced by it also. It might enhance the immunity of patients, and therefore decrease the fit of common cold. The effectiveness sustained for a long time and the recurrence rate reduced to minimum. (Original article on page 336)

A Clinical Study on 345 CHD Patients Treated with Shexiang Xinnaoie (麝香心脑乐)

Liu Zhongming (刘忠铭), et al

3rd Teaching Hospital, Norman Bethune University of Medical Sciences, Changchun

Shexiang Xinnaoie tablet is a kind of compound drug consisted of several expensive Chinese herbs including *Moschus moschiferus*, *Borneolum syntheticum*, Ginsenoside, *Panax pseudoginseng* and *Epimedium brevicornum*, etc. Each tablet weighed 0.3g, containing 1.6g of crude medicine, 4 tablets thrice per day for three weeks composed a course, orally taken. In this paper, 345 cases of CHD were treated with a good result: 88.1% of angina pectoris were relieved, 72.9% of myocardial ischemia in ECG were improved and 70.4% of cardiac arrhythmia were alleviated. It was obviously superior to that of Xinshule (心舒乐) group as previously published, decreasing blood viscosity from 5.27 ± 0.91 to 4.41 ± 0.75 ($P < 0.01$), plasma viscosity from 1.81 ± 0.20 to 1.62 ± 0.18 ($P < 0.01$), rate of RBC electrophoresis from 0.85 ± 0.18 to $0.98 \pm 0.17 \mu\text{m/sec/v/cm}$ ($P < 0.01$) and the platelet agglutination rate lowered from $27.32 \pm 12.14\%$ to $22.06 \pm 11.12\%$.

In conclusion, this drug could lower both blood and plasma viscosity, improve maximal platelet agglutination rate, it exerted also good effect in reducing myocardial ischemia, increasing nutritious blood flow to the myocardium. As to the rat myocardial uptake rate of ^{86}Rb , there is a significant difference between pre- and post-experiment ($3.30 \pm 0.39\%$ and $2.96 \pm 0.35\%$ respectively, $P < 0.01$) as well as in treated and control groups ($2.32 \pm 0.30\%$ vs $1.67 \pm 0.23\%$, $P < 0.001$).

(Original article on page 338)

Clinical Observations and Experimental Studies on Naoxuekang (脑血康)

in Treating Hypertensive Cerebral Hemorrhage

Xie Daozhen (谢道珍), et al

Xiyuan Hospital, China Academy of TCM, Beijing

This paper reports the clinical observations and experimental studies in treating hypertensive cerebral hemorrhage with Naoxuekang. 306 cases of hypertensive cerebral hemorrhage with similar conditions have been observed, of which 180 cases formed group A which has been treated with Naoxuekang for 4~6 weeks while the remaining 126 cases formed group B as control, which has been subdivided into two subgroups: 66 cases were treated by Western medicine (WM) and the other 60 cases were treated with surgical operation. Results indicated the total effective rate of group A was 90%. The rate of cure and marked improvement was 80.5%. In WM group and surgical operation group, the rates were 81.8% and 83.3%, 66.7% and 61.7% respectively. The difference was significant statistically ($X^2 = 19.11$, $P < 0.01$). Naoxuekang is an oral liquid. The remedy is composed of ingredients extracted from Chinese materia medica, which contain various kinds of amino acids, anticoagulin and other chemical substance. The clinical observations and experimental studies showed that the Naoxuekang could improve cerebral anoxia and microcirculatory disorder, reduce blood pressure, promote dissolution of fibrin and stimulate the phagocytosis of macrophages, so as to promote absorption of cerebral hematoma and benefit the recovery of neural function.

After discussion, a conclusion could be drawn that when the quantity of hemorrhage is less than 40 ml or the hematoma is an external localized one and the patient is in mild disturbance of consciousness, good curative effect could be expected. (Original article on page 341)

Alcoholic Extract Tablet of Rhubarb in Treating Acute Upper GI Hemorrhage

Jiao Donghai (焦东海), et al

Xiangshan TCM Hospital, Shanghai

Alcoholic extract tablet of rhubarb (AETR) was used in treating 182 cases of upper GI hemorrhage with total effective rate of 96.1% and hemostasis occurred in an average period of 2.8 days. The commonest cause of bleeding was peptic ulcer, and then gastritis, neoplasm of stomach, etc. Through retrospective, prospective and double blind comparative studies, it revealed that the marked effective rate of AETR was higher than that of Western medication ($P < 0.001$), and equivalent to the simple recipe of rhubarb ($P > 0.05$). The adverse side effect of rhubarb such as nausea and vomiting, as well as the unstable therapeutic effect due to the variation in species of rhubarb was avoided. The mechanism of its hemostatic effect was: contraction of local blood vessel, reduction in