

附子治疗虚证病窦综合征的疗效及机理探讨

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内容提要 13 例虚证病窦综合征患者通过经食管心房调搏及心脏收缩时间间期等测定,证实附子注射液能明显缩短窦房结恢复时间及明显减小 PEP/LVET,提示附子确能提高与改善窦房结功能与心功能,尤对阳虚病例效果显著。附子温阳的机理可能是通过兴奋 β 肾上腺素能受体,促进钠、钙离子内流等多种作用途径。

病窦综合征(简称病窦)患者绝大多数表现为虚证、寒证、阴证,出现昏厥亦多属寒厥。国外至今尚无有效的药物,对严重病例则安置人工心脏起搏器。我们选用温阳中药附子注射液在临床上治疗病窦已多年^(1,2),现通过无创性经食管心房调搏方法及心脏收缩时间间期的测定,以估价附子对虚证病窦的疗效,并对其作用机理作进一步探讨。

资料与方法

一、病例选择:临床确诊病窦患者 13 例,男 7 例,女 6 例;年龄 31~69(平均 53.2 $\pm$ 5.3)岁,其中冠心病 11 例,心肌病 2 例。13 例均有胸闷、头晕、头昏、眼前发黑等心脑缺氧症状,其中 8 例有反复昏厥发作史。症状出现时间为 1 月~20 年(平均 8.5 年)。中医辨证均为虚证,其中阳虚 5 例(伴血瘀 1 例),气虚 4 例(伴血瘀 1 例),气虚伴阴虚 4 例。阿托品试验均为阳性。

二、检查项目与方法:

1. 治疗前后均作常规 12 导联心电图及 24 小时遥测心电图监护(美国 Mennen 医学公司出品),并摄胸片测心胸比例。

2. 治疗前后均抽血测定血清高密度脂蛋白—胆固醇(HDL-C),并测 24 小时尿 17 羟与 17 酮皮质类固醇。

3. 治疗前后心率比较:(1)清晨平卧位心

率;(2)活动后心率,指室内活动 10 分钟后心率;(3)固有心率,指在 3 分钟内静脉注射阿托品 2mg 和心得安 5mg,5~10 分钟时记录心电图测出最快的心率。

4. 经食管心房调搏测窦房结功能^(1,3):采用苏州电子技术研究所生产 SHB—1 型经食管心房调搏器,测出窦房结恢复时间(SNRT),计算校正后窦房结恢复时间(SNRT_C)。并通过心房连续刺激法,即给予基本心率加 10 次/分的频率,产生连续房性早搏 8 次,测定窦房传导时间(SACT)。在静脉注射阿托品和心得安阻滞植物神经 20 分钟后再重复上述心房调搏,测定植物神经阻滞下的 SNRT 与 SACT。(1)在植物神经阻滞下静脉注射 5%葡萄糖溶液 10ml,5~10 分钟后测定 SNRT 与 SACT,并计算 SNRT_C。(2)在植物神经阻滞下静脉注射附子注射液 2 支(含生药附子 8g)及 5%葡萄糖溶液 6ml,5~10 分钟后亦测定 SNRT 与 SACT,并计算 SNRT_C。(3)取治疗前心房调搏所得的最长 SNRT 与治疗 2~4 周后同一调搏频率下所得的 SNRT 作对比,并同时测植物神经阻滞前后所测的 SNRT_C 及 SACT 等作治疗前后的对比。

5. 应用上海医用电子仪器厂生产的 SJ—41 多导生理记录仪,作同步颈动脉搏动图、心音图及心电图等,以测定反映左室心功能的收缩时间间期(STI),包括射血前间期(PEP),左

室射血时间(LVET)以及两者比值(PEP/LVET)。

6. 应用上海第一医学院医学工程教研室试制XG—II型心功能综合测定仪,对8例在植物神经阻滞下静脉注射5%葡萄糖溶液或附子注射液后的PEP/LVET进行连续监测半小时,将每例在注射前后的心率及PEP/LVET值作出曲线图。

三、治疗方法:每日静脉滴注本院自制的附子注射液8g(每支2ml含生药附子4g)与5%葡萄糖溶液500ml,每日傍晚肌肉注射附子注射液4g以保持药物血浓度稳定,2周为一疗程,每例给予1~2疗程,停用其他中、西药物。

结 果

一、临床症状:13例虚证病窦患者的心脑缺氧症状除1例偶有头晕外,余均明显改善。8例反复发作昏厥者在治疗期间及治疗后均未见有昏厥再发。4例快慢交替综合征者经治疗后,1例未再发生阵发性房扑与房颤,余3例发作频度明显减少。

二、常规心电图与24小时遥测心电图监护:治疗前单纯窦缓4例,窦缓伴II度窦房阻滞及房室交界处逸搏5例,阵发性房扑与房颤(快慢交替综合征)4例。24小时遥测心电图监护在发现阵发性房扑与房颤,房性或室性早搏,以及窦性静止与窦房阻滞上均较常规心电图敏感。治疗后窦缓7例,II度窦房阻滞与房室交界处逸搏2例,余4例快慢交替综合征中2例转为正常窦性心律,2例为稳定的窦缓。

三、胸片:10例摄后前位胸片中左心增大3例,心胸比例略大4例,伴动脉硬化1例,伴肺纹理增多1例,余3例胸片正常。治疗前后胸片无明显改变。

四、血清HDL-C及24小时尿17羟与17酮皮质类固醇:治疗后血清HDL-C为 52.35 ± 12.13 (2SE)mg%,较治疗前 47.57 ± 8.56 mg%略有增高,然无显著差异($P > 0.05$);24小时尿17羟与17酮皮质类固醇在治疗后分

别为 7.58 ± 1.43 mg与 9.16 ± 2.28 mg,较治疗前分别为 6.85 ± 1.48 mg与 7.99 ± 2.74 mg有所增高,但均无显著差异($P > 0.05$)。

五、治疗前后心率变化:(见图1)。

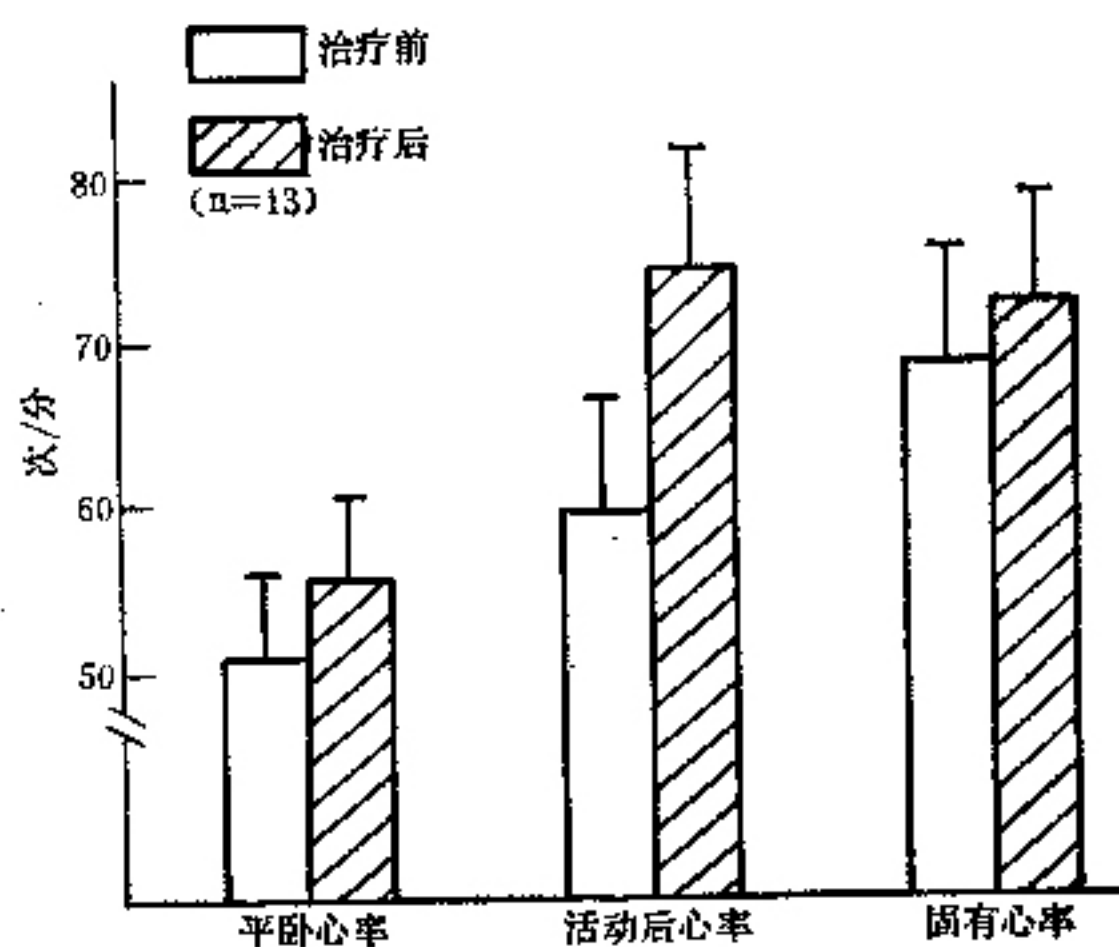


图1 治疗前后各种心率的比较

1. 平卧心率治疗后为 56.3 ± 4.5 (2SE)次/分,较治疗前 51.3 ± 5.6 次/分明显增加($P < 0.05$)。

2. 活动后心率治疗后为 74.2 ± 7.5 (2SE)次/分,与治疗前 60.9 ± 7.1 次/分相比,有极显著的差异($P < 0.001$)。

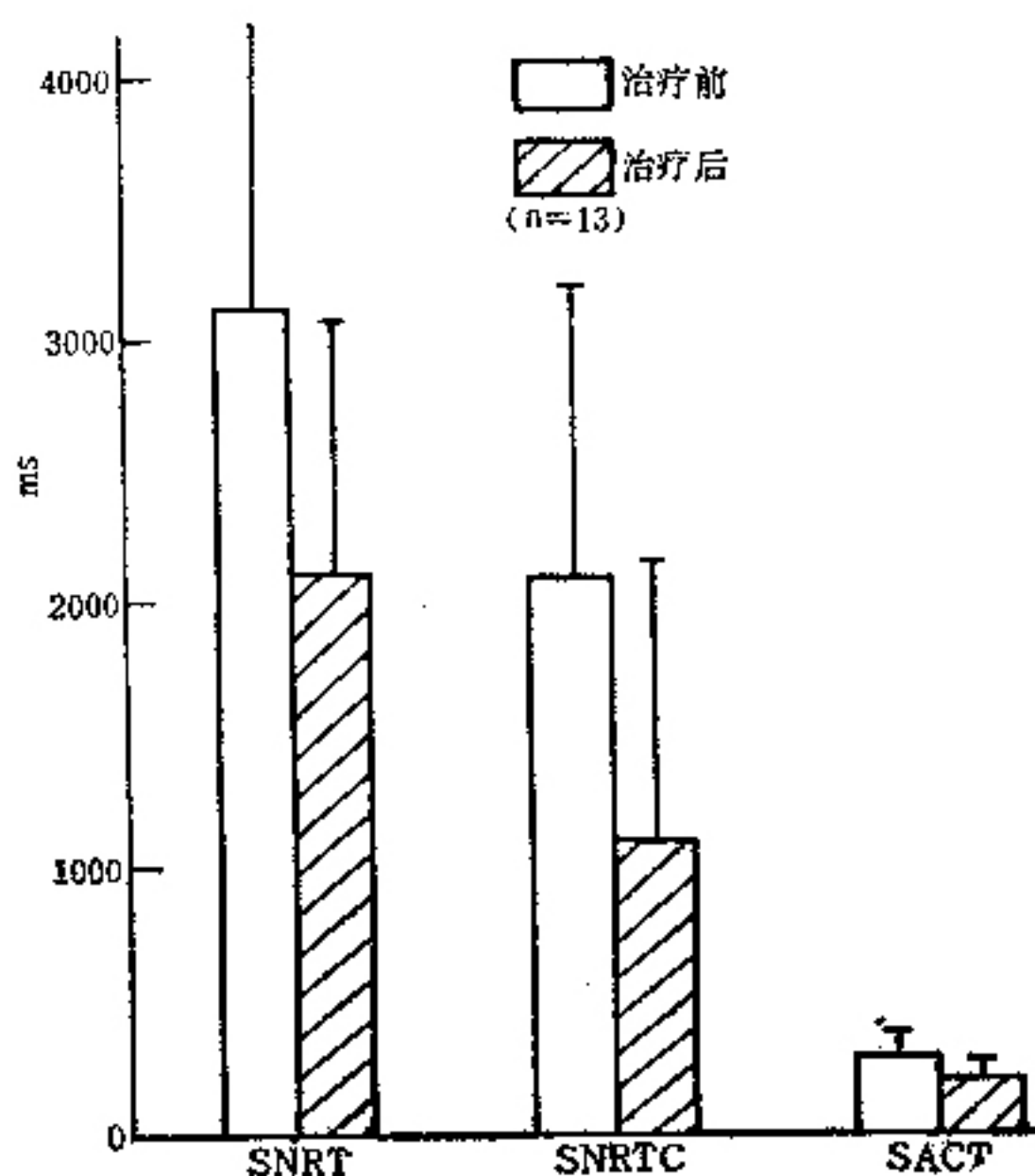


图2 植物神经阻滞前 SNRT、SNRTc、SACT 的治疗前后对比

3. 固有心率治疗后为 72.3 ± 5.4 (2SE) 次/分, 较治疗前 68.2 ± 5.9 次/分有所增加, 但无显著差异 ($0.1 > P > 0.05$)。

六、植物神经阻滞前: SNRT 治疗后为 $2,149 \pm 988$ (2SE) 毫秒 (ms), 较治疗前 $3,138 \pm 1,139$ ms 明显缩短 ($P < 0.05$); SNRT_c 治疗后为 $1,082 \pm 990$ (2SE) ms, 较治疗前 $2,119 \pm 1,188$ ms 有缩短, 但无显著差异 ($0.1 > P > 0.05$); SACT 治疗后为 202 ± 73 (2SE) ms, 较治疗前 274 ± 87 ms 有缩短, 但无显著差异 ($0.2 > P > 0.05$), (见图 2)。

七、植物神经阻滞下: SNRT 治疗后为 $2,135 \pm 947$ (2SE) ms, 较治疗前 $3,352 \pm 1,196$ ms 明显缩短 ($P < 0.01$); SNRT_c 治疗后为 $1,263 \pm 912$ (2SE) ms, 较治疗前 $2,364 \pm 1,100$ ms 明显缩短 ($P < 0.05$); SACT 治疗后为 152 ± 49 (2SE) ms, 与治疗前 147 ± 36 ms 相比无显著差异 ($P > 0.05$), (见图 3)。

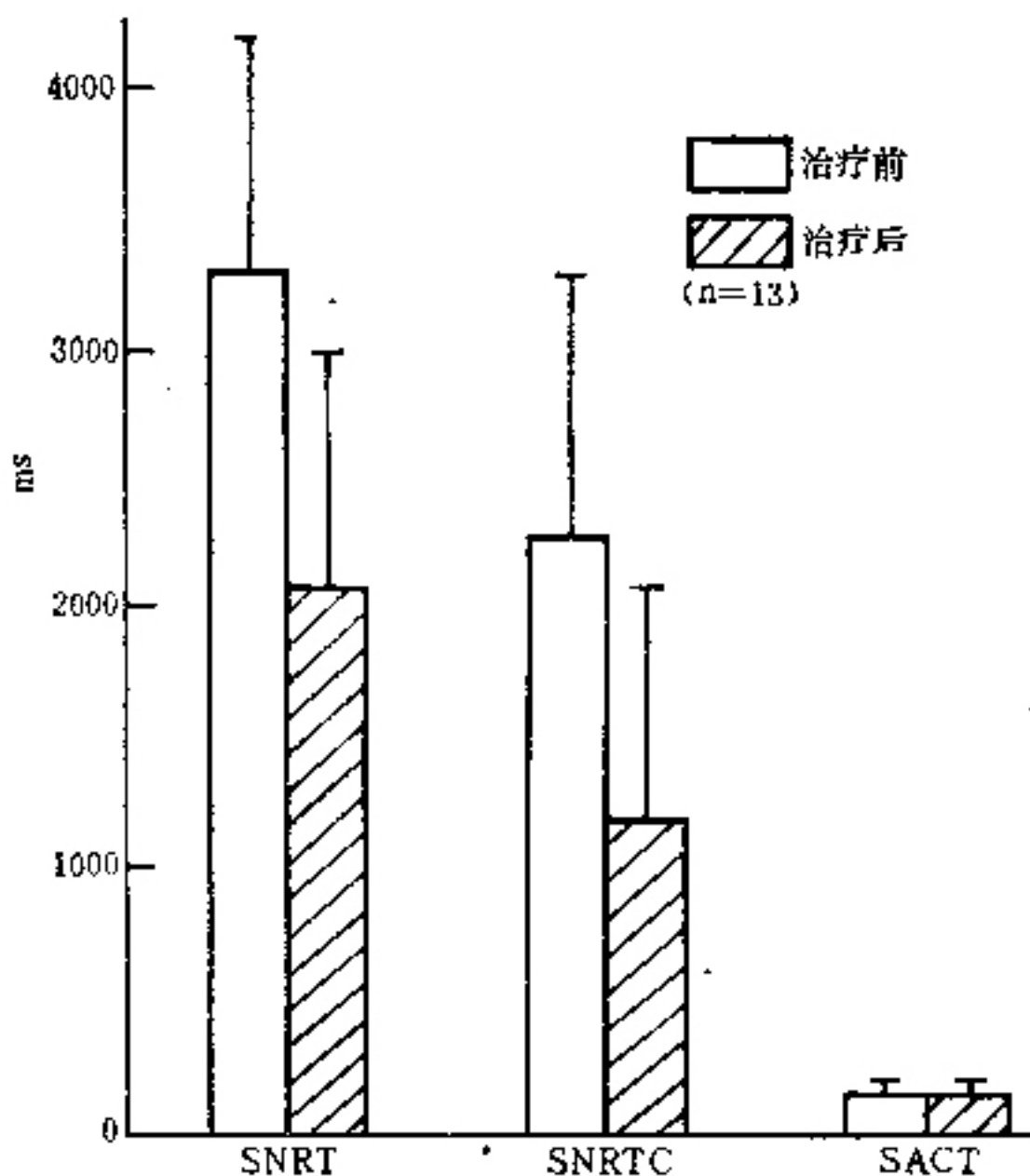


图3 植物神经阻滞下 SNRT、SNRT_c、SACT 的治疗前后对比

八、静脉注射 5% 葡萄糖溶液 10ml 后 SNRT 为 $3,234 \pm 1,102$ (2SE) ms, SNRT_c 为 $2,258 \pm 1,018$ ms, SACT 为 192 ± 86 ms, 与注射前相比均无显著差异 ($P > 0.05$); 静脉注射附子注射液 8g 后 SNRT 为 $3,386 \pm 1,359$ (2SE) ms, SNRT_c

为 $2,455 \pm 1,276$ ms, SACT 为 227 ± 78 ms, 与注射前相比亦均无显著差异 ($P > 0.05$)。

九、无创性心功能测定: 治疗后 PEP 为 93 ± 6 (2SE) ms, 较治疗前 98 ± 9 ms 有缩短, 但无显著差异 ($0.1 > P > 0.05$); 治疗后 LVET 为 313 ± 13 (2SE) ms, 较治疗前 305 ± 8 ms 有延长, 但无显著差异 ($0.2 > P > 0.05$); 治疗后 PEP/LVET 为 0.297 ± 0.024 (2SE), 较治疗前 0.320 ± 0.026 明显减小 ($P < 0.01$)。

8 例在植物神经阻滞下注射 5% 葡萄糖溶液或附子注射液前后作心率及 PEP/LVET 连续监测半小时, 结果未发现有明显改变, 8 条心率曲线及 PEP/LVET 值曲线均接近平坦, 提示在植物神经阻滞下附子与葡萄糖均不能影响左室心功能, 对 STI 无明显作用。

十、中医辨证阳虚 5 例与气阴两虚 4 例作对比, 发现阳虚型经治疗后植物神经阻滞下 SNRT 缩短值为 648 ± 408 (2SE) ms, 与气阴两虚型缩短值 310 ± 159 ms 相比有极显著差异 ($P < 0.001$), 提示附子注射液对虚证病案有效, 且阳虚者疗效优于气阴两虚者。

讨 论

由于好发于中、老年人的病案综合征多属虚证, 尤其是阳虚与气虚, 国内已报道临床上应用温阳补气法或温经扶阳法来治疗本病有较好的疗效^[4,5]。其中附子常作为主药, 通过附子此辛热之品, 达到温经祛寒、回阳救逆、温通心阳、温运脾阳及温补肾阳之功效。

一、本文研究再次证实温阳中药附子治疗虚证病案的疗效切实可靠。

通过 13 例虚证病案的自身对照, 证实经附子注射液 (每日 12g) 治疗 2~4 周后临床心脑缺氧症状明显改善; 心律失常严重程度有所减轻; 清晨平卧心率、活动后心率及固有心率均有增加, 尤以活动后心率增加为显著; 植物神经阻滞前的最长 SNRT、SNRT_c 及 SACT 均有缩短, 尤以最长 SNRT 缩短为显著; 植物神经阻滞下的最长 SNRT 及 SNRT_c 均有明显缩短。由此可见, 附子能明显提高心脏起搏点窦房结的自

律性,改善窦房结的功能,包括在植物神经阻滞下的内源性窦房结功能。同时,证实了经附子治疗2~4周后PEP有缩短,而LVET有延长,PEP/LVET值明显减小,故提示附子能改善虚证病窦病例的心功能。由于病窦病例后期常发生心功能不全,因此附子的应用具有预防心功能不全的积极意义。

通过对中医辨证5例阳虚型与4例气阴两虚型的疗效对比中发现,附子对阳虚病窦者的疗效明显超过气阴两虚病窦者,这符合中医学的辨证论治原则,温阳药适于阳虚病例,我们通过反映内源性窦房结功能的植物神经阻滞下最长SNRT的测定证实了此点。所以,温阳药附子完全适用于虚证病窦病例,是治疗虚证病窦,尤其是阳虚病窦的安全与有效的中药。

二、本文研究对温阳中药附子治疗虚证病窦的作用机理上作了进一步探讨,即对温阳的作用途径作了探索。

1. 通过 β 肾上腺素能受体兴奋作用:动物实验与临床观察均发现附子能增加心率与离体心肌收缩力,改善窦房及房室传导,希氏束电图证实附子尚能缩短A—H间期,因此类似于 β 受体兴奋剂异丙肾上腺素^[6,7]。本文研究发现在静脉注射 β 受体阻滞剂心得安及抗胆碱药阿托品后,即在植物神经阻滞下,附子与5%葡萄糖溶液一样不能立即缩短SNRT以提高窦房结功能,同时亦不能使PEP/LVET值减小以改善心功能。然而,2~4周治疗结束后附子却能明显缩短SNRT及减小PEP/LVET,提示了附子对心脏的作用部分是通过兴奋 β 肾上腺素能受体,故附子具有正性肌力与正性变时性(正性频率与传导)的作用。

本文研究未能证实附子明显改善窦房传导的功效,这是由于间接法测定的SACT有时与窦房结电图直接法测定的SACT不完全一致,且易受植物神经等因素的影响,再加上技术操作因素,因此重复性较差。在病窦病人中SACT的阳性率(37%)明显低于SNRT(95%)^[3,8]。

2. 通过促进动作电位平台期的钠与钙离子

内流:微电极技术已证实附子在较高浓度时能明显增高离体心脏中浦氏野纤维的自律性,缩短其有效不应期与动作电位时间,此可能与附子促进动作电位平台期的钠离子和钙离子内流有关^[9]。因此附子作用与钙通道阻滞剂(如异搏定)恰恰相反,能提高窦房结与房室结的自律性,加快窦房及房室传导。

3. 通过增加冠脉流量与改善微循环:从而可能改善窦房结的血供,以致提高内源性的窦房结功能。

4. 通过改善垂体—肾上腺皮质功能:阳虚病人常伴有肾上腺皮质、甲状腺及性腺等内分泌腺功能低下,本文提示了附子治疗能使虚证病窦病例的尿17羟与17酮皮质类固醇有所增加,因此附子的温阳作用可能与内分泌激素的代谢有一定的关系。

总之,温阳中药附子治疗虚证病窦的机理是复杂的,可能通过多种作用途径,包括兴奋 β 肾上腺素能受体,促进钠离子和钙离子内流,增加冠脉流量与改善微循环,以及改善垂体—肾上腺皮质功能等,这些亦反映了中医学中温阳的作用机理。

(附子注射液由本院药剂师龚志铭提供,特致谢)

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The Role of Laparoscopy in the Non-Operative Treatment of Ectopic Pregnancy by TCM-WM

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From 1980 ~ 1983, of 202 cases of suspected ectopic pregnancy examined by laparoscopy, 133 proved to be early ectopic with or without hematomas. Laparoscopy clearly showed the site of ectopic pregnancy as well as the stage of development of the disease which helped much in the clinical staging and planning of the treatment regime. All the cases that received the treatment were cured.

Twenty cases were given a follow-up examination 3 or more months after treatment. It was found that sub-acute cases of bleeding gave better results than those with hematocele — the majority of the cases showing normal pelvic findings with patent tubes belonged to the subacute cases, while all the hydrosalpinx found resulted from the cases with hematoma formation ($P < 0.01$).

Mild or filmy adhesions were separated during the laparoscopic procedure. Pregnancy followed in quite a few cases. The results showed that early diagnosis and prompt adequate treatment gave the best results. It was concluded that in a conservative treatment of ectopic pregnancy using TCM-WM, laparoscopy played a very important role: it enabled the attending gynecologist to establish the diagnosis at a very early stage of the disease, provided clear and concise documentation, helped proper treatment and protocol planning and thus gave very good prognoses to complication of pregnancy, which is sometimes very dangerous.

For those who require tuboplasty, laparoscopic assessment prior to surgery is essential. With the accumulation of more cases it is hoped that laparoscopy will also help to clarify the etiological factors of extra-uterine pregnancy.

(Original article on page 211)

TCM Treatment of Threatened Abortion — A Clinical Analysis of 62 Cases

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This paper reports the planned treatment of threatened abortion based on TCM diagnosis. Of the 62 cases under discussion, including 33 who had had case histories of abortion (28 cases of which got conceived again within one year after abortion), 31 came under the category of Pi Shen Yang Xu (PSYX 脾肾阳虚, deficiency of vital energy in the spleen and kidney), 28 under the category of Gan Shen Yin Xu (GSYX 肝肾阴虚, deficiency of essence in the liver and kidney), and 3 under the category of Qi Xue Liang Xu (QXLX 气血两虚, deficiency of both energy and blood).

As a result of the treatment, 57 cases (91.9%) proved to be successful, while 5 (8.1%) were failures. A gynecological examination disclosed that patients under the category of PSYX recovered completely or showed definite signs of recovery, with such symptoms as vaginal bleeding, lumbodynia, tenesmus, abdominal pain, abnormal pulse-manifestation and coating on the tongue either vanishing or clearly indicating a turn for the better. Furthermore, the patients in question were found without exception to have maintained their ability of normal pregnancy and delivery. The results, however, were not so satisfactory for the categories of GSYX and QXLX. In spite of the treatment, 4 (14.3%) of the 28 cases under the former category and 1 (33.3%) of the latter category met with failure, resulting unfortunately in spontaneous abortion.

The authors of this paper hold, therefore, that the planned treatment based on TCM diagnosis for threatened abortion has theoretical as well as practical value to the prophylaxis and treatment of threatened abortion and the determination of the indication of continuing pregnancy. Some suggestions were also made by the authors.

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Evaluation of Clinical Efficacy of Aconitic Injection in Asthenia Patients Suffering from Sick Sinus Syndrome and Its Mechanism

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Clinical efficacy and the mechanism of Aconitic injection were evaluated in 13 asthenia patients suffering from sick sinus syndrome. Aconitic intravenous injection was administrated at a dose of 12g per day for 2 to 4 weeks. Clinical symptoms of both cardiac and cerebral ischemia were found improved after therapy, and the severity of arrhythmias was relieved as well by EKG monitoring. The heart rate at rest increased from 51 ± 5 to 56 ± 4 beats/min ($P < 0.05$), whereas during exercise, it increased from 60 ± 7 to 74 ± 7 beats/min ($P < 0.001$).

The sinus node recovery time (SNRT) was assessed by transesophageal atrial pacing. The maximum SNRT was significantly shortened from $3,138 \pm 1,139$ ms to $2,149 \pm 988$ ms ($P < 0.05$) after therapy. The maximum SNRT after sympathetic and parasympathetic blocking was also significantly shortened from $3,352 \pm 1,196$ ms to $2,135 \pm 947$ ms ($P < 0.01$). The shortening value of patients with Yang deficiency was significantly larger than those with Ying deficiency (648 ± 408 ms vs 310 ± 159 ms, $P < 0.001$).

The value of PEP/LVET was found decreased from 0.320 ± 0.026 to 0.297 ± 0.024 ($P < 0.001$) by the measurement of STI. The results indicate that the so called warming Yang Chinese herb Aconitum appears to improve the functions of sinus node and cardiac performance in asthenia patients with sick sinus syndrome, and the stimulation of beta adrenergic receptor was considered one of the mechanisms of action.

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