缩泉丸治疗氯氮平所致流涎的临床观察

南京神经精神病防治院(江苏 210029)

康 冰 刘玉成 张雅萍 韩 玉 樊禄珍 周 军

内容提要 采用双盲法观察缩泉丸治疗氯氮平所致流涎的疗效。缩泉丸治疗组 21 例,治疗后流涎症状较 19 例对照组明显减少(P<0.01)。中医辨证分型与缩泉丸治疗关系分析,表明痰湿内阻型和阳虚亏损型疗效最佳。氯氮平血浓度与流涎两者间无相关性(P>0.05)。

关键词 缩泉丸 氯氮平 流涎

流涎是氯氮平常见的副反应之一。其发生率为66.3%¹⁾。我们试用中成药缩泉丸治疗氯氮平所致的流涎,取得了较满意的疗效。现将结果报告如下。

资料和方法

一、临床资料 40 例均系确诊为精神分裂 症的住院病例;单一服用氯氮平治疗而流涎; 排除消化系统疾病。氯氮平口服量男性为 200~500 mg/d; 女性为200~300 mg/d。采 用双盲法随机分为网组。单数为缩泉丸治疗组 (甲组)21例。其中男8例,女13例;年龄 19~50 岁,平均 32.4 岁;病程 1~25 年,平 均 8.33 年。氯氮平用量平均为 312±71 mg/d $(\bar{x}\pm S, \nabla \Pi)$ 。中医辨证分型:痰火内扰型7 例, 痰湿内阻型 5 例, 气滞血瘀型 5 例, 阴虚火 旺型1例,阳虚亏损型3例。双数为对照组(乙 组)19 例。其中男性5例,女性14例,年龄 16~49 岁, 平均 28.88 岁; 病程 1~28 年, 平 均 8.21 年。氯 氮 平 用 量 平 均 为 288±69 mg/ d。中医辨证分型: 痰火内扰型 6 例, 痰湿内阻 型7例,气滞血瘀型3例,阴虚火旺型1例,阳 虚亏损型2例。其氯氮平用量经t检验, P> 0.05, 无显著性差异。两组的年龄、性别、病程基 本相似。

二、治疗方法 甲组服用缩泉 I 号,由益智仁、乌药、山药组成; 乙组服用缩泉 II 号(与缩泉丸外形、大小相等,由活性碳、淀粉组成的中性丸剂),每日2次口服,男女每次均为9g,与

氯氮平同时服下。4周为1疗程,中途不得更改药物剂量。并于治疗前后各检查一次血常规、肝功能、肾功能、心电图。部分患者检查氯氮平血浓度。

三、观察方法 流涎程度根据患者的唾液 浸润旧布枕套的范围(下衬塑料薄膜)。制定出 4 个不同程度评分标准。即:"0 分"为流涎消失 或无; "1 分"为轻度,浸润直径为 15 cm 以内, 流涎量约为10 ml 以内; "2 分"为中度,浸润 直径为16~20 cm,流涎量约为10~20 ml; "3 分"为重度,浸润直径为 20 cm 以上,流涎量 约为 20 ml 以上。两组患者服用氯氮平达到本 研究所需剂量后,一律使用内衬塑料薄膜袋,外 套旧枕套的枕头,然后开始观察夜间的流涎情 况。每夜记录 3 次, 分别于 23 时,次日1时和 4 时记录。同时记录每日大小便情况。根据前3 天的流涎范围,定出治疗前流涎分值。第4天开 始使用缩泉 I 号或 II 号至疗程结束评定疗效, 也根据流涎程度的变化,对每夜3次记录数据 之和,每周进行分析比较。疗程结束后评定疗 效。

结果

一、疗效分析 两组患者治疗前的流涎分值,分别与治疗后第1、2、3、4周末流涎分值的比较,算出各周末的差值。甲组的差值随着时间的延长,逐渐加大,而乙组则变化很小。两者比较,经t检验有显著性差异(P<0.01)。见附表。

附表 两组治疗前后的流涎评分差值比较 $(x\pm S)$

组别	例数	1周末	2 周末	3 周末	4 周末
甲	21	1.43±1.63*	2.14±1.98*	$2.33 \pm 1.62^{\bullet}$	3.00±1.67*
乙	19	0.32 ± 1.20	0.11 ± 1.14	$0.21\!\pm\!1.03$	$0.26\!\pm\! 1.33$

注。与乙组比。*P<0.01

附表说明服用氯氮平出现流涎的患者,同时加服缩泉 I 号能有效地控制流涎,并随着服药时间的延长流涎量减少更加显著。

二、中医辨证分型与缩泉丸治疗的关系根据中国中西医结合学会制定的精神分裂症辨证分型草案, 共分出五种证型。甲组流涎完全消失者13例中, 痰湿内阻型5例中占4例; 阳虚亏损型3例中占2例; 气滞血瘀型5例中占3例, 痰火内扰型7例中占3例; 阴虚火旺型1例, 流涎有减少但未消失。乙组除痰火内扰型有1例流涎完全消失, 其余各证型皆无消失者, 表明缩泉 I 号治疗氯氮平所致流涎有效, 尤以痰湿内阻型、阳虚亏损型为佳。

三、氯氮平血浓度与流涎的关系 在甲乙两组中,有 28 例治疗前测定了氯氮平血浓度。根据血药浓度的不同分为两组。一组氯氮平血浓度 $< 400 \, \mu g/ml$,共 17 例,流涎程度评分平均为 6.47 ± 1.70 。另一组氯氮平血浓度 $> 400 \, \mu g/ml$,共 11 例,流涎程度评分平均为 7.0 ± 1.55 。两者比较,经t 检验,无显著性差异(P<0.05)。提示氯氮平所致流涎的不同程度,与氯氮平血浓度的高低无明显的相关性。

四、副反应 在治疗过程中,甲乙两组均未发现验证药物所引起的副反应。两组治疗前后的大小便、血常规、肝功能、肾功能、心电图

均未见明显变化。

讨 论

宋·陈自明著《妇人良方》的缩泉丸,具有温补脾肾,固气缩泉的作用^②。现代药理学研究认为方中的益智仁具有健胃抗利尿和减少唾液分泌的作用。国内文献也曾有益智仁治疗小儿流口水的报道。

本组缩泉丸治疗氯氮平所致流涎,进行了双盲对照观察,甲组的流涎程度明显降低,而乙组则变化很小,两组治疗前和治疗后每周末流涎程度平均评分的差值比较,有非常显著性差异。提示缩泉丸对流涎有着显著的治疗相。从中医辨证论治来看,甲组中的痰湿和阳虚亏损型的疗效最佳,痰火内扰型和阳虚亏损型的疗效最佳,痰火内扰型和阴虚火旺型疗效相对较差。但由于例数不多,尚行进一步观察。初步说明缩泉丸需辨证使用。同时亦表明该辨证分型试行草案有一定的临床实用性。对部分病例治疗前氯氮平血浓度和流涎情况的比较分析,提示流涎的严重程度与氯氮平血浓度无关。因此,推测缩泉丸不是通过改变其血药浓度控制流涎,机理有待进一步研究。

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Clinical and Experimental Studies on Membranous Pulp-Capping Agent with Chinese Medicinal Herbs

Wang Zhu-ping (汪竹平), Li Zai-ren (李再仁), Li Shu-ling (李淑玲); et al Shandong Medical University, Jinan (250012)

A membranous pulp-capping agent of Chinese medicinal herbs was made by ourself prescription, and was filled in capsules for medication. Direct pulp-capping and pulpotomy were performed on 102 permanent teeth. During the observation period of more than one year, the successful rate was 82.4%. Under light microscope, the artificial exposed sites of normal sheep teeth were fully sealed after capping for 45 days. There were calcification under the exposed sites. The inner lines were preparative dentins. Experiments on dogs' teeth revealed that the pulps were normal after two month's direct pulp-capping, and the new dentins appeared. The bacteria culture test was made before and after the pulp-capping agent was used on ten deep carious teeth. It revealed that the bacteria all converted negative after medication of two weeks. Clinical and experimental studies indicated that the pulp-capping agent is valuable in clinical treatment.

Key words Chinese medicinal herb, pulpitis, pulp-capping, pulpotomy, antibacterial test (Original article on page 345)

Clinical Observation on Effect of Suo Quan Pill (縮泉丸) for Reducing Clozapine Induced Salivation

Kang Bing (康 冰), et al
Nanjing Neuropsychiatric Hospital, Nanjing (210029)

40 Schizophrenic inpatients with clozapine induced salivation were divided into two groups randomly. They were treated with Suo Quan pill and a control study of the placebo (neutral pill) for reducing clozapine induced salivation. These cases were also classified by TCM Syndrome Differentiation and laboratory examinations were performed. Results: There was a significant difference in effect on salivation between the therapeutic group (21 cases) and the controlled group (19 cases), P < 0.01. According to their TCM subtypes two subtypes (Stagnation of Phlegm-Dampness and Yin Deficiency) showed the best results. No correlation between the peripheral clozapine level and salivation was found. No side effect was recorded.

Key words Suo Quan Pill, clozapine, salivation

(Original article on page 347)

Effect of Wuzi Yanzong Liquid (五子衍宗液) on Hypothalamus, Monoamines, Sexual Hormones and Reproductivity in Male Rats

Wang Xue-mei (王学美), Xie Zhu-fan (謝竹藩), et al Institute of Integration of TCM and WM, Beijing Medical University, Beijing (100034)

About 100 male SD rats aged 2, 5, 10, 18 and 24 months (each age group for about 20 rats) were used in the antisenility experiment. The animals of each age group were further subdivided into two groups randomly: one group administered with Wuzi Yanzong Liquid (WYL) daily for 5 weeks, and the other group with normal saline. After treatment, plasma testosterone (T) and estradiol (E2), hypothalamus norepinephrine (NE), dopamine (DA) and serotonin (5-HT) levels were determined. In comparison with younger groups, the 18 and 24 months old rats administered with saline had markedly lowered plasma T, hypothalamus NE and DA levels, and elevated 5-HT, E2 levels and 5-HT/DA, E2/T ratios; while in the 18 and 24 months rats administered with WYL the above mentioned changes were much less remarkable. Since WYL only raised plasma T level in old rats