

症瘕口服液治疗子宫内位症实验研究

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摘要 用种植内膜的方法造成子宫内位症动物模型,观察症瘕口服液的疗效并与丹那唑比较。采用放射免疫法测定大鼠血浆前列腺素 $F_{2\alpha}$ ($PGF_{2\alpha}$) 水平;酶联免疫吸附法 (ELISA) 测定血清抗子宫内膜抗体 (EMAb);双抗体放免法测定血清雌二醇 (E_2) 与孕酮 (P) 水平。结果症瘕口服液能降低大鼠血浆 $PGF_{2\alpha}$ 水平、血清 E_2 及 P 水平;EMAb 均无阳性;各用药组与模型组比较,差异有显著性 ($P < 0.05$ 或 $P < 0.01$)。证明症瘕口服液是治疗子宫内位症 (EMT) 的有效药物,血浆和血清 $PGF_{2\alpha}$ 、EMAb、 E_2 和 P 水平的变化,可作为 EMT 诊断和治疗的监测指标。

主题词 子宫内位症/中医药疗法 @ 症瘕口服液

子宫内位症 (Endometriosis, EMT) 是妇科常见病,近年来发病率有上升的趋势,因常与不孕同时存在,已引起医学界的普遍关注。目前对 EMT 尚缺乏敏感的实验室诊断及监测方法,本文应用放射免疫方法及酶联免疫吸附法 (ELISA) 分别测定大鼠血浆前列腺素 $F_{2\alpha}$ ($PGF_{2\alpha}$) 水平;血清雌二醇 (E_2)、孕酮 (P) 水平和血清中抗子宫内膜抗体 (EMAb) 水平,探讨 4 者在 EMT 诊断和治疗中的应用价值,并观察症瘕口服液在改善这些指标方面的作用。现报告如下。

1 材料与方法

1.1 试剂与药品: $PGF_{2\alpha}$ 放免试剂盒由中国医学科学院基础所药理室提供;EMAb 试剂盒 (ELISA 法) 由南京军区总医院临床免疫科提供;血清 E_2 和 P 放免试剂盒均由中美合资天津九鼎医学生物工程有限公司提供;丹那唑胶囊,上海市华联制药公司生产,批号 950302;口服液由丹参、水蛭、土鳖虫、生大黄、莪术、菟丝子、淫羊藿、生牡蛎等中药组成,安徽中医学院药剂教研室提供。

1.2 仪器: FJ-2107 液体闪烁计数器和 ^{125}I -放免测定仪,西安 262 厂生产。

1.3 动物: 健康未孕 Wistar 大鼠,体重 $135 \pm 15g$,由安徽医科大学实验动物中心提供。

2 方法

2.1 子宫内位症动物模型制作: 于造模前连续 2

天在大鼠皮下注射己烯雌酚 $0.1mg/kg$,腹部脱毛。用 $30mg/kg$ 戊巴比妥钠腹腔注射麻醉,腹部皮肤常规消毒,沿腹中线剪开腹壁和腹膜 (切口大约为 $3cm$),找到子宫左侧,在离卵巢约 $1cm$ 处,分离附着于子宫肌壁的脂肪和结缔组织后,两头分别用手术线结扎,剪取中间约 $1.5cm$ 一段子宫体置于盛生理盐水的培养皿中,剥去其外膜,缝在右侧子宫距卵巢 $1cm$ 处,缝时缝针不得穿透子宫右侧浆膜层,然后剪开筒状子宫,使之内膜暴露,最后缝合切口,术后将动物分笼单放,让其自然苏醒。每鼠每天腹腔注射庆大霉素 $0.1ml$,连续 1 周,假手术对照组的大鼠只用镊子牵拉子宫,其余处理同上。

2.2 分组及给药: 3 周后,将大鼠随机分为 5 组: 假手术对照组,症瘕口服液低剂量组 $3.9g/kg$,高剂量组 $14g/kg$,治疗对照药丹那唑组 $0.18g/kg$ 和 EMT 模型组,按 $1.2ml/100g$ 体重灌胃给药,每日 1 次。假手术对照组与 EMT 模型组给等容量溶媒 ($1ml$ 丙二醇,加 $0.06g$ 苯甲酸钠,加 $62ml$ 蒸馏水),连续 3 周。末次给药后用 20% 乌拉坦 $1.5g/kg$ 腹腔注射麻醉^[1],腹主动脉抽血检测各项指标,取异位内膜组织送病理组织学检查。

2.3 测定方法: 血浆 $PGF_{2\alpha}$ 测定采用放射免疫法;血清 EMAb 测定采用 ELISA 法,试验在聚苯乙烯反应板上进行,终止反应后测 $492nm$ 波长吸光度 A 值;血清 E_2 、P 测定采用双抗体放射免疫法,用 γ -计数器测定各管沉淀物的放射性强度。具体操作按试剂盒要求进行。

2.4 病理组织学检查: 取上述抽血后的大鼠,立即解剖观察其异位内膜及周围子宫,取其标本,经常规制片,HE 染色,光镜观察。

3 结果

3.1 对大鼠血浆 $PGF_{2\alpha}$ 水平的影响: EMT 模型组大鼠血浆中 $PGF_{2\alpha}$ 水平明显高于假手术对照组,而症瘕口服液的高、低剂量组和丹那唑组 $PGF_{2\alpha}$ 水平明显低于假手术对照组 (P 均 < 0.01)。见附表。

3.2 对大鼠血清 EMAb 影响: EMT 模型组大鼠血清 EMAb 阳性率为 90.91% ($10/11$),假手术对照组与症瘕口服液高剂量组、丹那唑组均无 EMAb 阳性者,症瘕口服液低剂量组阳性率为 20% ($2/10$)。说明症瘕口

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服液能降低 EMAB 水平,随剂量增加作用增强。

3.3 对大鼠血清 E_2 、P 水平的影响:EMT 模型组大鼠血清 E_2 和 P 水平明显高于假手术对照组,而用药各组均能降低 EMT 模型大鼠血清中 E_2 和 P 水平($P < 0.05$ 或 $P < 0.01$)。见附表。

附表 各组大鼠血浆 $PGF_{2\alpha}$ 、血清 EMAB、 E_2 、P 水平比较($\bar{x} \pm s$)

组别	$PGF_{2\alpha}(pg/ml)$	$E_2(pg/ml)$	P(ng/ml)
假手术对照组	$288.57 \pm 22.48(8)^{**}$	$12.90 \pm 0.27(8)^{**}$	$29.53 \pm 4.04(8)^{**}$
EMT 模型	$637.77 \pm 44.59(8)$	$14.42 \pm 0.32(8)$	$44.18 \pm 8.62(8)$
症瘕口服液			
低剂量组	$406.52 \pm 23.83(9)^{**}$	$13.56 \pm 0.76(8)^{**}$	$33.97 \pm 6.91(8)^{*}$
高剂量组	$344.33 \pm 29.17(9)^{**}$	$13.28 \pm 0.43(8)^{**}$	$31.59 \pm 2.74(8)^{**}$
丹那唑组	$317.08 \pm 29.55(8)^{**}$	$13.11 \pm 0.40(8)^{**}$	$32.63 \pm 5.64(8)^{**}$

与 EMT 模型组比较, $^{*}P < 0.05$, $^{**}P < 0.01$; 括号中数字为鼠数

3.4 病理组织学检查:EMT 模型组的异位内膜中腺腔极度扩大,有乳头状突起,腺上皮呈柱状或立方形。假手术对照组无异常病变。症瘕口服液高剂量组异位内膜组织中内膜腺体数减少,腺上皮萎缩,在萎缩程度上与丹那唑组相比,差异不明显。说明用药组具有抑制内膜腺体生长的作用。

4 讨论

用大鼠制作 EMT 模型的同时,用药物治疗并检测上述各项指标,作为评价药物疗效的方法。探讨了这 4 项指标 EMT 诊断与治疗中的应用价值。EMT 患者腹腔内大量的子宫内膜蛋白质可能导致体液或细胞介质的自身免疫反应,已经发现在 EMT 患者的血清及腹腔液中有 EMAB 存在^[2],EMAB 与其它自身抗体不同,是 EMT 患者的标志抗体,用于 EMT 的诊断特异性较高,同时 ELISA 方法敏感性较高,既可作为诊断 EMT 的客观指标之一,也可作为治疗观察^[3]。

DAN(17 α -乙炔睾酮异构衍生物)20 世纪 70 年

代开始在国外用于治疗 EMT,它能降低血清 E_2 和 P 水平,造成低雌激素状态,使异位内膜失去激素周期性变化,导致内膜萎缩^[4]。其消退异位病变效果肯定,但因肝功能等方面的不良反应^[5],已影响了该药在临床上的进一步使用。

症瘕口服液是由水蛭、土鳖虫、生大黄、莪术、菟丝子、淫羊藿、丹参、生牡蛎等中药组成。水蛭的主要成分水蛭素有抗凝作用,能使体内瘀血分解消散,土鳖虫具有活血化瘀止痛及抗缺氧作用^[6],淫羊藿对异常升高的血浆前列腺素有一定的降解作用。该药治疗 EMT,在于对异常升高的 $PGF_{2\alpha}$ 的降解,中和 EMAB 及降低 E_2 、P 水平,从而抑制了异位内膜的生长。丹参、莪术可通经、消瘀;生牡蛎消症散结。由于子宫内膜异位症属中医“痛经”、“症瘕”、“月经不调”及“不孕”范畴。中医认为,若七情抑郁,劳伤气血或风寒相搏,使瘀血阻滞,离经之血积聚日久成为症瘕。此方集化瘀、通络、消症于一体,共同达到疏肝解郁、行气止痛、祛瘀、消症之功,能有效地治疗 EMT。

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清热解毒、化痰祛瘀、软坚散结、消肿定痛等作用,用以治疗本类疾病颇为合拍,经本组病例临床验证,疗效确切。根据近几年对活血化瘀方药的研究,已经证实活血化瘀药物能有效地降低血液粘度,改善微循环,增加有效循环量,并能降低毛细血管通透性,调节免疫功能^[2]。治疗处方中穿山甲、皂角刺搜风消肿、软坚散结,除有抑制血小板粘附及聚集作用,增强纤维蛋白溶解活性外,还有抗凝血作用;当归、赤芍功能活血化瘀,均有抑制血小板和红细胞聚集、抗血栓形成,改善微循环,并有抗炎及抑制免疫反应等作用^[3];浙贝母化痰散

结;生地黄、牡丹皮清热凉血,能降低毛细血管通透性,减少炎性渗出;金银花、黄芩、白芷、甘草等清热解毒,具有抗菌、消炎、抗过敏、调节免疫等功能,用以消除瘀结形成之原因。诸药配伍、标本兼顾,从而取得了较好的治疗效果。

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ABSTRACTS FROM ORIGINAL ARTICLES

Effect of Acupoint—Injection of PSN in hot summer days on Immunologic Function in Patients of Bronchial Asthma

Shen Lihua

Acupoint—Injection of bacille Calmette—guerin polysaccharide nucleic acid (BCG—PSN) injection at Zusanli (ST 36), Dingchuan (EX—B 1) and Feishu (BL 13) points were used for treatment of 32 cases of bronchial asthma in hot summer days and T—lymphocyte subgroups and serum IgA, IgG, IgM and C₃ contents were detected before and after treatment. Results indicated that the total effective rate was 84.37%: acupoint—Injection of PSN at Zusanli (ST 36), Dingchuan (EX—B 1) and Feishu (BL 13) points could increase the lowered CD₄⁺ ($P < 0.01$): decrease the increased CD₄⁺/CD₈⁺ ratio ($P < 0.01$): obviously lower IgG content ($P < 0.01$) and increase C₃ content ($P < 0.05$). It is suggested that this method can regulate immunologic function of the organism. The method of acupoint—Injection provides a simple and effective therapy for patients of bronchial asthma.

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Key words: Asthma/acupoint injection Asthma/immunology Hydro—acupuncture therapy

(Original article on page 343)

Effect of Hua Yu Tong Mai Injectio on Hemorheologic Indexes and Thrombase in the Patient of Cerebral Infarcion

Han Ai

360 cases of cerebral infarcion were assigned to Hua Yu Tong Mai Liquid group (Treatment group, 270 cases) and Fu Fang Dan Shen Liquid group (Control group, 90 cases), and changes of blood rheologic indexes and thrombase activity were investigated before and after treatment. The result indicated that blood rheological indexes and thrombase activity in both groups had obvious improvement after treatemnt. The improvement extent of high spear of whole blood viscosity, plasma viscosity, fibrinogen, time value of activating partial thrombogen was superior to that of the control group, and the clinical symptoms, signs in the two groups were all improved to a certain degree, however, the treatment group was superior to that of the control group.

Author's address: The First Affiliated Hospital of Tianjin College of Traditional Chinese Medicine

Key words: Cerebral infarcion and thrombosis/TCM therapy @Hua Yu Tong Mai Injectio

(Original article on page 353)

Significance of Control Observation of Inspection of the Tongue in TCM and Colonoscopy in Diagnosis of Colonopathies

Yang Hanhui, Su Ruose, Lin Ruifu, et al

From the data of inspection of the tongue and colonoscopy in 1121 cases it was found that in changes of tongue coating and tongue proper, and colonoscopy were significant differences ($P < 0.05$ $P < 0.01$). Among them, most tongue coating was thick and greasy with yellow, thick and greasy tongue coating as majority; in the inflammation group it was as high as 81.1%. In the polyp group and malignant tumor group, most patients' tongue proper were dark—red and green—purple color, with significant difference ($P < 0.05$ or $P < 0.01$) as compared with the normal group. It is suggested that inspection of the tongue in TCM has a certain significance in colonoscope diagnosis of colonopathies.

Author's address: Second Affiliated Hospital of Fujian Medical University

Key words: Colonopathy/diagnosis Inspection of the tongue Colonoscopy

(Original article on page 365)

Experimental Study on Treatment of Endometriosis with Zheng Jia Oral Liquid

Yang Yaofang, Wang Qinmao, Fang Xueming, et al

Implanted tunica intima method was used to develop animal model of endometriosis, and therapeutic effect of Zheng Jia Oral liquid was observed and compared with that of danazol. Radioimmunoassay was adopted for determination of plasma prostaglandin F_{2a} (PGF_{2a}) level and enzyme linked immunosorbent assay (ELISA) was used for detection of serum endometrium antibody (EMAb), double antibody radioimmunoassay for determination of estradiol (E₂) and pregnendione (P) levels in rats. Results indicated that Zheng Jia Oral Liquid could decrease plasma PGF_{2a}, serum E₂ and P levels; positive rate of EMAb was 0%. There were significant differences ($P < 0.05$ or $P < 0.01$) as the drug treatment groups compared with the model group. It is suggested that Zheng Jia Oral Liquid is effective for treatment of endometriosis (EMT), and changes of plasma and serum PGF_{2a}, EMAb, E₂ and P levels can be served as monitoring indexes of EMT diagnosis and treatment.

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Key words: Endometriosis/TCM therapy @Zheng Jia Oral Liquid

(Original article on page 371)