

活血化瘀法治疗妊娠丢失抗心磷脂抗体阳性 38 例临床观察

李琼* 林佑武* 赖慧红* 指导:罗致强*

摘要 目的:观察中药对妊娠丢失抗心磷脂抗体阳性者的影响。方法:将 63 例患者随机分组,中药组 38 例在使用传统的补肾健脾,调理冲任基本治则同时,结合活血化瘀法治疗。对照组 25 例则用维生素 C、维生素 E 加叶酸治疗。结果:经 3~6 个月复查,中药组 38 例中 31 例转阴,对照组 25 例中 17 例转阴($P<0.01$),差异有非常显著性意义。结果显示,中药对妊娠丢失抗心磷脂抗体阳性者有较好的转阴作用。结论:提示瘀血阻滞胞脉也可能为中医堕胎、小产、滑胎的病因病机之一。

主题词 心磷脂质类/代谢 妊娠并发症/中医药疗法 活血化瘀

抗心磷脂抗体(ACA)是一种自身免疫性抗体,近年来人们从免疫学角度认识到妊娠丢失(包括习惯性流产、死胎和胚胎停止发育)与 ACA 有密切关系。1999 年以来我们对 63 例妊娠丢失 ACA 阳性者进行了治疗,现报道如下。

1 临床资料

1999 年 12 月~2001 年 6 月在中山医科大学附属第一医院专科门诊就诊的 327 名妊娠丢失患者常规筛查 ACA,检出 ACA 阳性者 63 例,其中 ACA-IgG 阳性 31 例,ACA-IgM 阳性 18 例,ACA-IgG 与 ACA-IgM 均阳性 14 例。并随机分为中药组(38 例)和对照组(25 例)。中药组 38 例中,ACA-IgG 阳性 18 例,ACA-IgM 阳性 12 例,两者均阳性 8 例,年龄 26~38 岁,平均 32.6 岁,其中胚胎停止发育 8 例,死胎 12 例(包括妊娠 28 周前死胎 8 例,28 周后死胎 4 例),习惯性流产 18 例;对照组 25 例中,ACA-IgG 阳性 13 例,ACA-IgM 阳性 6 例,两者均阳性 6 例,年龄 27~36 岁,平均 31.8 岁,其中胚胎停止发育 4 例,死胎 7 例(妊娠 28 周前死胎 5 例,28 周后死胎 2 例),习惯性流产 14 例。两组资料有可比性($P>0.05$)。

诊断标准:(1)胚胎停止发育:妊娠时间小于 8 周,B 超诊断胚胎停止发育,经刮宫组织标本检查证实^[1]。(2)死胎:至少有 1 次妊娠 20 周以后胎儿宫内死亡史,并排除感染、胎盘早剥、外观先天畸形或染色体异常等原因^[1]。(3)习惯性流产:连续发生自然流

产 2 次或 2 次以上,流产发生于孕 12 周前为早期流产,发生于孕 12~28 周者为晚期流产,并排除黄体功能不全、精神因素、垂体功能不足、染色体异常、精子缺陷、宫颈内口松弛、子宫畸形、子宫肌瘤、母儿血型不合以及弓形虫、巨细胞病毒、单纯疱疹病毒感染等因素引起的习惯性流产。

2 治疗及观察方法

2.1 治疗方法:(1)中药组:处方如下:党参 12g,茯苓 15g,白术 12g,甘草 6g,赤芍 10g,当归 6g,川芎 6g,熟地黄 15g,菟丝子 15g,桑寄生 30g,水煎 2 次,取汁 300ml,早晚各服 150ml,连续服用 3 个月为 1 个疗程,观察 1~2 个疗程;期间停服其他相关药物。(2)对照组:维生素 E 50mg、维生素 C 100mg、叶酸 10mg 口服,每日 3 次,连续服用 3 个月为 1 个疗程,观察 1~2 个疗程,停服其他相关药物。

2.2 采集及检测方法:中药组与对照组均于服药前和服药 1~2 个疗程后各抽血 1 次,空腹抽取肘静脉血 2ml。分离血清,-20℃保存,以酶联免疫吸附法(ELISA),用美国 ZEUS 公司提供的试剂同时测定 ACA-IgG 和 ACA-IgM。

2.3 统计学方法:测定结果采用 χ^2 检验,进行统计学处理。

3 治疗结果

两组 ACA-IgG、ACA-IgM 转阴例数比较:经治疗中药组中 18 例 ACA-IgG 阳性者有 16 例转阴,对照组 13 例有 6 例转阴,两组比较差异有显著性($P<0.05$)。中药组中 12 例 ACA-IgM 阳性者全部转阴,对照组 6 例中有 2 例转阴,两组比较差异有显著性($P<0.01$)。中药组中有 8 例 ACA-IgG、ACA-IgM 均阳性者,经 2 个疗程治疗有 3 例均转阴,其余 2 例 ACA-IgM 转阴,3 例 ACA-IgG 转阴,对照组 6 例 ACA-IgG 和 ACA-IgM 均阳性者,经 2 个疗程治疗只有 1 例 ACA-IgG 单项转阴。将中药组上述 8 例中两项均转阴的 3 例与前面中药组 16 例 ACA-IgG 转阴者和 12 例 ACA-IgM 转阴者合并为 ACA 阴性组(31 例),8 例中另 5 例与前面中药组 2 例 ACA-IgM 阳性者合并为 ACA 阳性组(7 例),对照组相应合并为 ACA 阳性 17 例,ACA 阴性 8 例,两组比较,中药组在

* 中山医科大学附属第一医院中医科,广东省广州市中山二路 58 号(510080)

收稿日期:2001-09-10;修回日期:2001-11-14

促使 ACA 转阴方面与对照组差异有非常显著性意义 ($P < 0.01$)。

4 讨论

ACA 对妊娠丢失的影响:已有许多相关报道妊娠丢失者中 ACA 阳性检出率显著高于正常妊娠者^[2,3],因此有必要尽早对这类患者在下次妊娠前诊断及用药,防止妊娠丢失的再发生。从生殖免疫学观点看,妊娠过程代表着机体一种特殊的免疫状态。正常妊娠时,这种状态有一系列免疫隔绝与免疫逃逸机制来保护。母体血清中 ACA 阳性时,反映了母体存在免疫功能缺陷,当妊娠开始时^[4],就可能同时伴随着不良妊娠过程的开始。关于自身抗体导致流产的机理,多数学者倾向于前列环素(PGI₂)抑制学说,即抗磷脂抗体(包括 ACA 和狼疮抗凝抗体)可能与血管内皮表面的磷脂成分结合,损伤血管内皮细胞,阻止其释放花生四烯酸,从而使前列环素合成减少,并影响蛋白质 C 系统的活化,干扰血栓调节素和纤维蛋白原激活剂的释放等。上述异常变化使胎盘血管内皮损伤,血小板粘附、聚集、释放血栓素 A₂(TXA₂),使血管收缩、血管内皮血栓形成,引起胎盘梗阻而导致胎盘供血不足,发生流产^[3]。Tulppala 等在研究流产者时还发现,早孕期 PGI₂ 的代谢并无异常改变,含量保持正常水平, TXA₂ 在妊娠的全过程中,其降解产物均显著升高。此外有学者认为可能是由于 ACA 引起胎盘磷脂发生反应导致胎盘发育不全^[5],致使妊娠丢失。愈来愈多的研究表明,ACA 与妊娠丢失密切相关。

中药对 ACA 的作用:妊娠丢失属于中医“堕胎”、“小产”、“滑胎”范畴,其病因病机多责之禀赋虚弱,肾气不盛,胎元不实;或脾胃虚弱,精亏血少;房事不慎,暗损精血,虚则提摄不固,冲任虚损,胎失荣系而致殒堕。而对气血瘀滞,冲任不畅,血运受阻而致胎失所养,引起殒堕则少见报道,教科书中也未提及气血瘀阻型。然而随着近年来人们对中医中药的微观研究,已揭示出某些中医病证的本质,对指导临床用药有一定的意义。从前面论述中可知,妊娠丢失 ACA 阳性者在微观上有着胎盘血管内皮损伤,血栓形成,引起胎盘梗阻的病理改变,提示胞宫瘀血阻滞,表明该类患者瘀血的本质。当其未孕之时,可不表现出瘀血病证,一旦受孕,则瘀血阻滞经络,冲任不畅,气血不能畅达胞宫,终致胎失所养而堕。再次怀孕前对曾发生堕胎、小产、滑胎者进行调治,使其 ACA 阳性者转阴,对预防妊娠丢失有一定的意义。在补肾健脾,调理冲任的基本治疗原则上,重视运用活血化瘀之品,既补肾填精,健脾益气,充养血海,又祛瘀消滞,使气血畅达,为日后胞宫孕育

胎儿做好准备。本临床观察提示,中药组对 ACA 阳性者有较好的促转阴作用,就单项 ACA-IgG 转阴、ACA-IgM 转阴以及合并后 ACA 转阴者,中药组与对照组相比,差异有显著性($P < 0.05$ 或 $P < 0.01$)。中药组基本方以四君子汤健脾补气,以熟地黄、菟丝子、桑寄生补肾益精,培养孕育之源,将四物汤中白芍改为赤芍,配合川芎、当归加强活血化瘀之功,同时兼调经养血。全方以补肾健脾,益气生血,调理冲任为主,又含活血养血,化瘀生新之意。现代药理研究表明,四君子汤、四物汤和菟丝子、桑寄生均有免疫调节作用,抗心磷脂抗体为一种自身免疫性抗体,中药的免疫调节作用可能使 ACA 转阴;此外,四君子汤有促进微循环和抗血小板聚集作用^[6],四物汤能抗血小板聚集和抗血栓形成^[6]。我们曾观察到 6 例 ACA 阳性者治疗转阴而妊娠,在妊娠初期的 3 个月我们仍给予上述方剂,最后胎儿均安全娩出,并未因方中川芎、赤芍活血之品而出现胎漏,该结果是否与少量活血之品改善胎盘微循环有关,尚缺乏大样本的观察,有待进一步研究。总之,中药组通过补肾健脾,益气生血、活血化瘀对 ACA 阳性者具有积极的治疗作用,其机理值得探讨。

参考文献

- 1 乐杰. 妇产科学. 第 4 版. 北京: 人民卫生出版社, 1996: 46-47, 140-141.
- 2 张新宇, 钱美伦, 刘善英, 等. 妊娠丢失与抗磷脂抗体的关系. 中华妇产科杂志, 1998, 31(1): 10-12.
- 3 李柳铭, 陈智平, 徐金霞. 抗人血清磷脂抗体与反复自然流产关系的探讨. 广西医科大学学报, 1998, 15(2): 59-60.
- 4 楠木淳一. 抗磷脂抗体综合征时的习惯性流产. 日本医学介绍, 1994, 15(4): 148-149.
- 5 黄曙光, 吴桂芳, 王兆平, 等. 抗心磷脂抗体阳性产妇胎盘的病理观察. 中华妇产科杂志, 1998, 33(2): 78.
- 6 陈奇主编. 中成药名方药理与临床. 北京: 人民卫生出版社, 1998: 424-427, 478.

• 征 文 •

中国中西医结合学会农村基层工作委员会定于 2002 年 10 月中旬在上海市召开“第七届全国农村基层中西医结合学术暨工作交流会”。会议将安排特邀报告、大会发言及专题讨论;会议还将同时举办上海市继续医学教育项目“基层中医药适宜技术学习班”,授予继续医学教育学分。现将征文有关事宜通知如下。

1. 征文内容:农村常见病、多发病的中西医结合防治经验。农村常见急重症的中西医结合抢救经验。农村开展中西医结合科研经验或科研论文。开展中西医结合工作思路与方法。农村中西医结合工作的组织管理经验。农村西医学习中医的经验等。2. 征文要求:来稿请寄全文(3000 字以内)和摘要(900 字)各 1 份。来稿请打印并附软盘。来稿请注明作者姓名、单位、邮编。稿件需单位同意并盖公章。不退稿。3. 截稿日期:2002 年 8 月 31 日。来稿请寄:上海市北京西路 1623 号上海市中西医结合学会周群,信封注明“农村基层学术会议征文”,邮编:200040,电话:021-62581714,62565939 转 1206。

ABSTRACTS FROM ORIGINAL ARTICLES

Clinical observation on 161 cases of piriformis syndrome treated with triple puncture combined with white tiger shaking head method

Wu Qi

Purpose: To approach the effects of the acupuncture manipulation method on clinical therapeutic effects. **Methods:** 161 cases of piriformis syndrome were randomized into manipulation group with 80 cases and routine acupuncture group with 81 cases, and their therapeutic effects were investigated. **Results:** In the manipulation group, 61 cases (76.25%) were cured, 13 cases (16.25%) improved, and 6 cases (7.5%) were ineffective, the effective rate being 92.5%; and in the routine acupuncture group, 46 cases (56.79%) were cured, 17 cases (20.99%) improved, 18 cases (22.22%) were ineffective, and the effective rate being 77.78% with a significant difference between the two groups ($P < 0.01$). **Conclusion:** Triple puncture combined with white tiger shaking head method has a better therapeutic effect for piriformis syndrome.

Author's address: Xuzhou City Hospital of TCM, Xuzhou 221003, Jiangsu Province

Key words: Piriformis syndrome /acup—mox ther

(Original article on page 506)

Clinical study on 202 Cases of RA treated with the method for activating blood circulation and clearing away heat

Wang Zhenqing

Purpose: To study on treatment of rheumatoid arthritis (RA) with combination of internal and external therapies. **Methods:** 322 cases of RA were randomly divided into two groups with single blind method, and they were treated respectively by the method for activating blood circulation and clearing away heat, and Fenbid and Lei Gong Teng for 6 weeks. Clinical symptoms and laboratory indexes were investigated before and after treatment. **Results:** Of 202 cases in the treatment group, 124 cases (61.38%) were markedly effective, 56 cases (27.72%) were effective, 22 cases (10.89%) were ineffective, the total effective rate being 89.10%; of 120 cases in the control group, 59 cases (49.16%) were markedly effective, 31 cases (25.83%) effective, 30 cases (25.00%) ineffective, the total effective rate being 75.00% with the treatment group being superior to the control group ($P < 0.05$). **Conclusion:** The method for activating blood circulation and clearing away heat has definite therapeutic effect on RA.

Author's address: TCM Department of Jining City Third People's Hospital, Jining 272000, Shandong Province

Key words: Arthritis, rheumatoid/TCM ther activating blood circulation and clearing away heat

(Original article on page 511)

Clinical observation on 30 cases of fibrosis of liver treated with Da Ding Feng Zhu

Li Weilin, Wang Caidang, Zhang Junli

Purpose: To study on clinical effect of Da Ding Feng Zhu on fibrosis of liver. **Methods:** 56 cases of chronic fibrosis of liver were randomly divided into treatment group (30 cases) and control group (26 cases). They were treated by Da Ding Feng Zhu and colchicine, respectively. Serum hyaluronic acid (HA), type III procollagen (PC-III), type IV collagen (IV-C) and laminin (LN) levels were determined and analysed before treatment and after treatment for 3 months. **Results:** HA, PC-III, IV-C and LN levels after treatment decreased significantly as compared with those before treatment ($P < 0.01$), and in the control group, only HA decreased significantly ($P < 0.05$). There was a significant difference between the two groups in PC-III, IV-C levels ($P < 0.05$), and a very significant difference in HA ($P < 0.01$). **Conclusion:** Da Ding Feng Zhu can decrease the serum indexes of fibrosis of liver, having the action of anti-liver fibrosis.

Authors' address: Taizhou TCM Hospital, Zhejiang 318000

Key words: Fibrosis of liver/TCM ther Da Ding Feng Zhu/treatment application

(Original article on page 520)

Clinical observation on 38 cases of pregnancy loss with positive anti-cardiac phospholipid antibody treated with the method for activating blood circulation and removing blood stasis

Li Qiong, Lin Youwu, Lai Huihong, et al.

Purpose: To observe effects of Chinese medical herbs for pregnancy loss with anti-cardiac phospholipid antibody (ACA). **Methods:** 63 cases of positive ACA were randomly divided into the Chinese drug group (38 cases) treated by tonifying kidney and strengthening spleen, combined with activating blood circulation and removing blood stasis methods, and control group (25 cases) by vitamin C, E and folic acid. **Results:** After 3—6 months, 31 cases had the antibody turned into negative in the Chinese drug group, and 17 in the control group, with a very significant difference ($P < 0.01$). It is suggested that the Chinese drug has a better turning negative action for the patient. **Conclusion:** Obstruction of blood stasis in the Uterine Collaterals is possibly one of TCM pathogenesis and pathological causes for abortion and habitual abortion.

Authors' address: The First Hospital Affiliated to Guangzhou Zhongshan Medical University, Guangzhou 510080

Key words: Cardiac phospholipids/metabolism pregnancy complications/TCM ther activating blood circulation to remove blood stasis

(Original article on page 522)