

抗胆瘀汤治疗妊娠期肝内胆汁淤积症 220 例临床观察

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摘要 目的:观察抗胆瘀汤对妊娠期肝内胆汁淤积症(ICP)血清胆酸值的影响。方法:选择在本院生产的 ICP 孕妇,治疗组 220 例口服抗胆瘀汤,另设对照组 76 例,采用西药对症治疗。结果:治疗组总有效率为 85.9%,对照组为 6.85%;治疗组治疗后血清总胆汁酸(TBA)或血甘胆酸(CG)明显下降,有显著性差异($P<0.01$),且剖宫产率低于对照组,新生儿体质量优于对照组。结论:抗胆瘀汤对 ICP 有明显的治疗作用,在降低剖宫产率、早产率、增加新生儿体质量方面有明显作用。

主题词 胆汁郁积,肝内 中医药疗法 妊娠并发症/中医药疗法 @ 抗胆瘀汤

1964 年妊娠期肝内胆汁淤积症(ICP)国内首次报道。20 世纪 80 年代以来,随着不断被产科医生识别,其发病率不断上升,临床报道日渐增多,但其发病机理尚不完全清楚。ICP 的临床症状表现为妊娠中晚期全身皮肤瘙痒,或伴有黄疸,其血清甘胆酸(CG)或血清总胆汁酸(TBA)异常为较敏感的实验室指标。本研究采用前瞻性对照的方法,对中药抗胆瘀汤降低 ICP 血胆酸值进行临床观察,现将研究结果报道如下。

1 临床资料

1.1 病例选择标准:(1)妊娠期出现皮肤瘙痒;(2)或伴有黄疸;(3)血清总胆汁酸(TBA)或血甘胆酸(CG)异常;(4)或伴有肝功能损害;(5)血清乙肝表面抗原(一)。除外妊娠合并有肝硬化、急性妊娠期脂肪肝及门诊治疗后不在本院生产的孕妇。

1.2 一般资料:观察对象为 1999 年 1 月~2001 年 10 月在安徽省合肥市第一、二、三人民医院,合肥市妇幼保健院住院生产的产妇。治疗组 220 例,年龄 19~37 岁,胎次 1~4 胎。其中 153 例治疗后测 TBA 值评定疗效,67 例治疗后测 CG 值评定疗效。对照组 76 例,年龄 22~35 岁,胎次 1~4 胎,其中 46 例治疗后测 TBA 值评定疗效,30 例治疗后测 CG 值评定疗效。治疗组与对照组年龄、胎次无统计学差异,具有可比性。

1.3 观察项目:(1)TBA 测定:采用日本第一化学试剂厂试剂盒,酶法,正常值 $<10\mu\text{mol}$;(2)CG 测定:

采用放射免疫法,中国原子能科学研究院试剂盒,正常值 $<6.4\mu\text{mol}$;(3)肝功能检查:用美国产康宁 560 型全自动生化分析仪,速率法;(4)皮肤瘙痒改善情况;(5)胎心监护、肝脾 B 超、产科 B 超、尿常规、肝肾功能;(6)分娩结局:孕周、分娩方式、产后出血量、新生儿评分及体质量。

1.4 统计学方法:计量资料用配对 t 检验,计数资料用卡方检验。

2 治疗及观察方法

治疗组用抗胆瘀汤。药物组成:茵陈、柴胡、炒黄芩、制大黄、地肤子等。使用韩国 HANSLINE 公司产快速煎药机及自动包装机、韩国产包装材料,取上药 30 剂量,浸泡,加水 11L,煮沸至 117℃,得药汁 7.8L,分装 60 袋,每袋 130ml,含生药 22.5g。每日早晚各服 1 袋,2 周为 1 个疗程,可用 1~2 个疗程。

对照组用苯巴比妥 0.03g,口服,每日 3 次;维生素 K_1 10mg、维生素 C 2.0g,静脉滴注,每日 1 次,5~7 日为 1 个疗程。分娩前用地塞米松 10mg,肌肉注射,每日 1 次,共 3 日。

3 治疗结果

3.1 疗效标准:痊愈:瘙痒消失,血清 TBA $<10\mu\text{mol}$,或 CG $<6.4\mu\text{mol}$;显效:瘙痒消失,TBA 或 CG 比原值降低 2/3 以上,但未恢复至正常;有效:瘙痒消失或明显减轻,TBA 或 CG 比原值降低 1/2 以上,不及 2/3;无效:瘙痒无改善,TBA 或 CG 值降低不明显,无降低或升高。

3.2 治疗结果

两组临床疗效比较:治疗组 220 例,痊愈 102 例,显效 38 例,有效 49 例,无效 31 例,总有效率 85.9%;对照组 76 例,无痊愈及显效者,有效 5 例,无效 71 例,总有效率 6.58%,两组总有效率比较,差异有显著性($P<0.01$)。

两组实验室指标比较:表 1 示,两组治疗前 TBA 和 CG 值差异无显著性,治疗组治疗后 TBA 或 CG 明显下降($P<0.01$),而对照组无改善($P>0.05$)。

两组分娩结局比较:表 2 示,治疗组剖宫产率显著低于对照组($P<0.01$),此外,治疗组新生儿体质量平均值为 $3.27\pm0.07\text{kg}$,对照组平均为 $3.11\pm0.08\text{kg}$,两组新生儿体质量差异有显著性意义($P<0.01$)。

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表1 两组 TBA 或 CG 值比较($\mu\text{mol/L}$, $\bar{x} \pm s$)

组 别	TBA		CG	
	治前	治后	治前	治后
治疗组	19.14 $\pm$ 11.68(153)	7.64 $\pm$ 4.96(153)*	22.26 $\pm$ 14.86(67)	13.24 $\pm$ 8.25(67)*
对照组	18.28 $\pm$ 10.85(46)	21.91 $\pm$ 9.44(46)	21.16 $\pm$ 12.33(30)	20.76 $\pm$ 13.22(30)

* 与本组治疗前比较, $P < 0.01$ 。括号内为例数

表2 两组分娩结局比较[例(%)]

组 别	例数	早产	剖宫产	Apgar 评分			产后出血
				<4	4~7	>7	
治疗组	220	8(3.6)	84(38.2)*	6(2.7)	7(3.2)	207(94.1)	14(6.4)
对照组	76	4(5.3)	45(59.2)	2(2.6)	6(7.9)	68(89.5)	6(7.9)

* 与对照组比较, $P < 0.01$

4 讨论

ICP 目前尚未见诸教科书,但近年来临床报道增多。本症可造成多种并发症,如产后出血(19.0%~22.2%)、胎儿宫内窘迫(22%~27%)、早产(22%~36%)、围产儿死亡(6.3%~13%)^[1],严重影响母婴妊娠中末期及围产期健康。ICP 临床表现并不复杂,主要是妊娠中末期皮肤瘙痒(我们在临床观察中发现,也有皮肤瘙痒不明显者),或伴有黄疸、肝功能损害,或伴有血胆红素、碱性磷酸酶增高。通常认为,血清胆酸值是诊断 ICP 的重要指标。张坚、江明礼等报道 TBA 或 CG 为灵敏度较高的指标^[2,3]。我们通过合肥市 4 家医院 220 例观察,其中两家医院检验 TBA,两家医院检验 CG,结果表明,血清 TBA、CG 测定确实为最灵敏、最确切的指标。

ICP 中医无对应病名,其证候分见于“黄疸”、“皮肤病”、“胎前病”等病证。通过临床治疗观察,我们认为,其基本病机为肝郁素体不足,孕后月经闭止,胞宫内实,冲脉气盛,而致肝气郁结故罹此症。肝郁而致肝失疏泄,水湿不行,郁而化热而见黄疸;肝与胆相表里,肝失疏泄,胆汁溢于肌肤而见瘙痒。抗胆瘀汤是在张仲景《伤寒论》经方茵陈蒿汤基础上化裁而成。其功用为清热利湿、退黄,主治湿热黄疸。现代药理研究表明,茵陈蒿汤可降低丙氨酸氨基转移酶,促进胆囊收缩。抗胆瘀汤在茵陈蒿汤基础上去栀子,加柴胡、炒黄芩、地肤子。茵陈、柴胡清热利湿、疏肝解郁,为君药;黄芩清热利胆、安胎为臣药;制大黄助茵陈退黄利胆,助柴胡疏肝泄瘀热,导瘀热从大便而下,为佐药;地肤子清热燥湿,止痒,为使药。全方主旨突出,组药精当,功效疏肝解郁,退黄止痒。主治妊娠期肝内胆汁淤积症引起的黄疸、皮肤瘙痒。

通常认为大黄为孕妇禁忌药,本方中用制大黄,且

用量为 6g,取其助柴胡疏肝泻热,使热从下行的作用,我们临床运用中未发现不良反应。茵陈主要含有香豆素类、黄酮类及挥发油等活性成分,具有利胆、保肝、降转氨酶作用;柴胡主要含皂甙、甾醇、挥发油、脂肪油和多糖等,此外,尚含生物碱、葡萄糖、氨基酸等,具有明显的保肝、降血脂和利胆作用;黄芩的主要活性成分为黄酮类化合物,具有利胆、解毒、调节免疫作用;大黄主要成分有蒽醌衍生物及二蒽醌类衍生物及大量鞣质,能促使胆红素及胆汁酸分泌,使奥狄括约肌舒张、胆囊收缩,减轻肝细胞变性与坏死;地肤子主要活性成分为三萜类、挥发油等,具有抗菌、利尿、止痒等作用^[4,5]。

西医对 ICP 的治疗多采用对症处理,或采用终止妊娠,而缺少降低血胆酸值的方法。中药治疗疗效明显,且未见不良反应。我们还对抗胆瘀汤进行了急、慢性毒理实验,结果表明,抗胆瘀汤对大鼠行动、毛色、体重、血象、肝肾功能、血糖、血脂等指标均无明显影响。抗胆瘀汤治疗 ICP 较对照组剖宫产率平均减少 21%,新生儿体质量平均增加 159.4g,对母婴均有益处。

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ABSTRACTS FROM ORIGINAL ARTICLES

Clinical study on treatment of 60 cases of arteriosclerosis obliterans by supplementing Qi and activating blood circulation method

Zhou Tao, Rong Wenping, Chen Bonan, et al.

Purpose: To explore therapeutic action of the formula for supplementing Qi and activating blood circulation on early arteriosclerosis obliterans (ASO). **Methods:** 90 cases of ASO were randomly divided into 2 groups and treated for 2 months, and changes of their clinical manifests, blood lipids, hemorheology, vascular endotheliocyte function and hemodynamics were investigated before and after treatment. **Results:** The clinical cured rate and the total effective rate in the treatment group were 61.67% and 100% respectively, and 36.67% and 93.33% in the control group. The treatment group in therapeutic effect for main symptoms and signs was superior to the control group ($P < 0.01$). There were significant differences in triglyceride (TG), high density lipoprotein-cholesterol (HDL-C), lower density lipoprotein-cholesterol (LDL-C) ($P < 0.01$) and serum total cholesterol (TC), very lower density lipoprotein-cholesterol (VLDL-C), apoprotein A₁ (ApoA₁) and apoprotein B₁₀₀ (ApoB₁₀₀) ($P < 0.05$) before and after treatment. After treatment, the various indexes of hemorheology decreased significantly ($P < 0.01$), and plasma thromboxane B₂ (TXB₂) and 6-keto-prostaglandin F_{1α} (6-keto-PGF_{1α}) restored to normal; plasma endothelin (ET-1) level decreased, nitric oxide (NO) increased ($P < 0.05$) in the treatment group. TXB₂ in the both groups and 6-keto-PGF_{1α} in the control group were significantly different from those of the normal group ($P < 0.01$). After treatment, in the treatment group the width of lumen and volume of blood flow in the posterior femoral and popliteal arteries increased, and the ankle/humeral index increased significantly ($P < 0.01$). **Conclusion:** Huang Qi Tong Mai Mixture can obviously improve clinical symptoms of early ASO, and also can regulate lipid metabolism, antagonize thrombosis and protect vascular endotheliocyte function.

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Key words: Arteriosclerosis obliterans/TCM therapy supplementing Qi and activating blood circulation method @Huang Qi Tong Mai Mixture

(Original article on page 907)

Clinical observation on Ren Zhu Jian Wei Granules for treatment of 88 cases of precancerous lesion of stomach

Li Chunting, Wang Aiyun, Shan Zhaowei, et al.

Purpose: To observe clinical therapeutic effect of Ren Zhu Jian

Wei Granules on precancerous lesion of stomach. **Methods:** 130 cases of precancerous lesion of stomach were randomly divided into two groups, the treatment group (88 cases) treated with Ren Zhu Jian Wei capsules and the control group (42 cases) treated with Wei Fu Chun Tablets, and clinical data were analyzed. **Results:** The comprehensive therapeutic effect was 92.0% in the treatment group and 73.8% in the control group; and the clinical therapeutic effect was 94.3% in the treatment group and 78.6% in the control group with a significant difference ($P < 0.01$). The effective rate for gastroscopy was 73.9% in the treatment group and 59.5% in the control group; 79.5% for gastric atrophy in the treatment group and 59.5% in the control group; 80.8% for intestinal metaplasia in the treatment group and 62.5% in the control group with significant difference between the two groups ($P < 0.01$ or $P < 0.05$). Improving rate for helicobacter pylori (HP) infection was 65.4% in the treatment group and 48.3% in the control group. **Conclusion:** Ren Zhu Jian Wei Granules exerts therapeutic action through improving HP infection and blood circulation of gastric mucosa.

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Key words: Gastric tumor/TCM therapy precancerous condition/TCM therapy @ Ren Zhu Jian Wei Granules

(Original article on page 910)

Clinical observation on Kang Dan Yu Decoction for treatment of 220 cases of intrahepatic cholestasis syndrome in pregnancy

Zhang Wenjia, Xie Sui, Zhang Yijuan, et al.

Purpose: To observe effect of Kang Dan Yu Decoction on serum cholic acid in the patient of intrahepatic cholestasis syndrome in pregnancy. **Methods:** 220 pregnant women with intrahepatic cholestasis syndrome were treated with oral administration of Kang Dan Yu Decoction as treatment group and 76 cases treated with western medicine as control group. **Results:** The total effective rate was 85.9% in the treatment group and 6.85% in the control group. After treatment, serum total bile acid (TBA) or CG in the treatment group decreased significantly ($P < 0.01$), and the cesarean rate was lower and the constitution of the newborn was better than that in the control group. **Conclusion:** Kang Dan Yu Decoction has obvious therapeutic action on intrahepatic cholestasis syndrome, decreasing the cesarean rate and the rate of premature birth, and increasing the constitution of newborn.

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Key words: Cholestasis, intrahepatic/TCM therapy pregnancy complication/TCM therapy @Kang Dan Yu Decoction

(Original article on page 919)