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平肝熄风汤联合硫酸镁对肝肾阴虚型妊娠期高血压患者血液动力学、糖脂代谢及妊娠结局的影响 *

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摘要 目的:探讨平肝熄风汤联合硫酸镁对肝肾阴虚型妊娠期高血压(GH)患者血液动力学、糖脂代谢及妊娠结局的影响。**方法:**选取2018年3月~2019年10月期间兰州市第二人民医院收治的GH患者119例随机分为对照组(n=59)和研究组(n=60),对照组给予硫酸镁治疗,研究组在对照组的基础上联合平肝熄风汤治疗,比较两组患者疗效、血液动力学、糖脂代谢、血压、心率、中医证候积分及妊娠结局。**结果:**研究组治疗7d后的临床总有效率为91.67%(55/60),明显高于对照组的77.97%(46/59)($P<0.05$)。两组治疗7d后收缩压、舒张压、平均动脉压、心率均下降,且研究组低于对照组($P<0.05$)。两组治疗7d后心输出量(CO)、心脏指数(CI)均下降,且研究组低于对照组($P<0.05$)。两组治疗7d后甘油三酯(TG)、低密度脂蛋白(LDL-C)、空腹血糖、总胆固醇(TC)水平降低,高密度脂蛋白(HDL-C)水平升高($P<0.05$),且研究组变化程度大于对照组($P<0.05$)。两组治疗7d后视物模糊、手足心热、脉弦细数、口干便秘、舌红苔少等症评分均下降,且研究组低于对照组($P<0.05$)。研究组不良妊娠结局发生率低于对照组($P<0.05$)。**结论:**平肝熄风汤联合硫酸镁治疗肝肾阴虚型GH,疗效显著,可有效改善患者临床症状、血液动力学、糖脂代谢,同时还可减少不良妊娠结局发生率,临床应用价值较高。

关键词:平肝熄风汤;硫酸镁;肝肾阴虚型;妊娠期高血压;血液动力学;糖脂代谢;妊娠结局

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Effect of Pingganxifeng Decoction Combined with Magnesium Sulfate on Hemodynamics, Glucose and Lipid Metabolism and Pregnancy Outcome in Patients with Gestational Hypertension with Deficiency of Liver and Kidney Yin*

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ABSTRACT Objective: To investigate the effect of pingganxifeng decoction combined with magnesium sulfate on hemodynamics, glucose and lipid metabolism and pregnancy outcome in patients with pregnancy induced hypertension (GH) with deficiency of liver and kidney yin. **Methods:** 119 patients with GH who were admitted to Lanzhou Second People's Hospital from March 2018 to October 2019 were selected, and they were randomly divided into control group (n=59) and study group (n=60). The control group was treated with magnesium sulfate. The study group was treated with pingganxifeng decoction on the basis of the control group. The efficacy, hemodynamics, glycolipid metabolism, blood pressure, heart rate and TCM Syndromes scores and pregnancy outcome of the two groups were compared. **Results:** The total clinical effective rate of the study group was 91.67% (55/60), which was significantly higher than that of the control group 77.97% (46/59) ($P<0.05$). The systolic pressure, diastolic pressure, mean arterial pressure and heart rate of the two groups decreased at 7 days after treatment, and those in the study group were lower than those in the control group ($P<0.05$). 7 days after treatment, the cardiac output (CO) and cardiac index (CI) of the two groups decreased, and those of the study group were lower than those of the control group ($P<0.05$). Triglyceride (TG), low-density lipoprotein (LDL-C), fasting glucose, total cholesterol (TC) decreased and high-density lipoprotein (HDL-C) increased in the two groups at 7 days after treatment ($P<0.05$), and the change degree of the above indexes in the study group was greater than that in the control group ($P<0.05$). 7 days after treatment, the symptom scores of blurred vision, hot hands and feet, fine pulse, dry mouth and constipation, and little red tongue and moss of the two groups decreased, and those in the study group were lower than those in the control group ($P<0.05$). The incidence of adverse pregnancy outcome in the study group was

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lower than that in the control group ($P<0.05$). **Conclusion:** Pingganxifeng decoction combined with magnesium sulfate is effective in the treatment of GH with deficiency of liver and kidney yin. It can effectively improve the clinical symptoms, hemodynamics, glucose and lipid metabolism of the patients, and reduce the incidence of adverse pregnancy outcomes, the clinical application value is higher.

Key words: Pingganxifeng Decoction; Magnesium sulfate; Deficiency of liver and kidney yin; Pregnancy hypertension; Hemodynamics; Glycolipid metabolism; Pregnancy outcome

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前言

妊娠期高血压(Gestational hypertension, GH)属于妊娠期的常见并发症,主要指孕妇在妊娠前未确诊高血压,而在妊娠20周后出现的高血压^[1-3]。本病是导致流产、胎盘早剥、大出血及早产的主要原因,严重威胁母婴健康^[4,5]。降压是临床治疗该病的主要原则,传统西医治疗的目标主要为降低血压、预防并发症及减少靶器官损伤等^[6]。硫酸镁是治疗GH的常见药物,虽可在一定程度上阻止疾病进展,但存在停药后易复发、长期用药不良反应大等不足^[7],尚需优化治疗方案。中医学认为GH属"子晕"、"子痫"的范畴,其发病本质在于肝肾阴虚,故中医治疗主张滋养肝肾、养血活血为宜^[8]。平肝熄风汤是一种中药方剂,以清肝热、养肝血、平肝阳、熄肝风为主要疗效^[9]。本研究结合兰州市第二人民医院近期收治的相关目标患者,临床实践中在硫酸镁的基础上增加平肝熄风汤治疗,收效良好,报道如下。

1 对象与方法

1.1 对象

选取2018年3月~2019年10月兰州市第二人民医院收治的119例GH患者展开研究,并随机分为对照组($n=59$)和研究组($n=60$),其中对照组年龄22~36岁,平均(28.38 ± 2.16)岁;孕周31~39周,平均(35.62 ± 1.73)周;体质指数 $21.9\sim 27.8\text{ kg/m}^2$,平均(24.35 ± 1.46) kg/m^2 ;初产妇38例,经产妇21例;高血压严重程度:中度32例,重度27例。研究组年龄20~37岁,平均(28.71 ± 1.49)岁;孕周30~40周,平均(36.67 ± 1.83)周;体质指数 $21.5\sim 27.6\text{ kg/m}^2$,平均(24.63 ± 1.42) kg/m^2 ;初产妇40例,经产妇20例;高血压严重程度:中度34例,重度26例。两组基线资料对比,无统计学差异($P>0.05$),具有可比性。

1.2 诊断标准

西医诊断标准:参考《妇产科学》^[10]中:患者舒张压 $\geq 90\text{ mmHg}$,收缩压 $\geq 140\text{ mmHg}$,两次或两次以上测量结果均升高。中医诊断标准:参考《中医妇科学》^[11]中的相关标准,辨证分型为肝肾阴虚型,视物模糊、手足心热、脉弦细数、口干便结、舌红苔少。

1.3 纳入/排除标准

纳入标准:(1)符合肝肾阴虚型GH诊断标准;(2)妊娠前无高血压病史,均为妊娠首次出现高血压;(3)符合继续妊娠及治疗适应证者;(4)对本研究中使用药物无过敏性反应;(5)知情同意本研究并接受检查治疗者。排除标准:(1)由于甲亢等疾病继发性的血压升高;(2)近1个月内服用过相关药物治疗者;(3)合并心肺肝肾等脏器功能不全者;(4)合并急慢性感染、恶性肿瘤、免疫缺陷者;(5)虽符合纳入标准,但未按规定用药,无

法判断其疗效及安全者;(6)合并精神疾患等无法配合者。

1.4 治疗方法

对照组患者给予硫酸镁注射液(河北天成药业股份有限公司,国药准字H20033861,规格:10 mL:2.5 g)治疗,将20 mL的硫酸镁溶入100 mL的5%葡萄糖,静脉滴注,30 min内滴完,此方法为首次冲击治疗剂量;随后采用60 mL的硫酸镁溶入500 mL的5%葡萄糖,静脉滴注,30 min内滴完,1次/d,治疗7 d。在对照组基础上,研究组患者联合平肝熄风汤治疗,汤方组成如下:天麻、全蝎各6 g,川芎、红花、蔓荆子、竹茹各12 g,蜈蚣2条,僵蚕、钩藤、地龙各9 g,丹参10 g,酸枣仁2 g。上述药材加水400 mL煎至200 mL,制成汤剂内服,1剂/d,连续服药7 d。两组治疗期间均密切注意患者血清内镁离子水平,以避免镁过量而中毒。

1.5 疗效判定

观察并记录两组患者治疗7 d后的临床疗效。具体标准^[12]如下:显效:体征、症状减轻或消失,血压降至正常;有效:体征、症状、血压有所改善;无效:患者效果未达到以上情况。总有效率=显效率+有效率。

1.6 观察指标

(1)记录GH患者治疗前、治疗7 d后收缩压、舒张压、平均动脉压及心率的变化情况。测量前避免剧烈运动,安静状态维持5 min后开始测量,采用北京康宏兴业科技发展有限公司生产的多功能心电监护仪进行测量,连测两次,取平均值。(2)参考《中药新药临床研究指导原则》^[12],于治疗前、治疗7 d后对患者中医证候进行评分,包括视物模糊、手足心热、脉弦细数、口干便结、舌红苔少这几个症状,根据无~重评分0~3分。(3)于治疗前、治疗7 d后采用无创GH血液动力学监测系统测量患者的血液动力学指标,计算血液动力学指标:心输出量(Cardiac output, CO)、心脏指数(Cardiac index, CI)。(4)分别于治疗前、治疗7 d后采集患者空腹静脉血3 mL,离心分离的血清样本采用日本OLYMPUS-AU600型全自动生化分析仪检测空腹血糖以及血脂指标[甘油三酯(TG)、高密度脂蛋白(HDL-C)、总胆固醇(TC)、低密度脂蛋白(LDL-C)]水平。(5)记录两组患者的妊娠结局。

1.7 统计学方法

应用SPSS 23.0分析数据。计量资料以均数 $\pm$ 标准差表示,开展t检验。计数资料以例数及率表示,采用 χ^2 检验或Fishers精确概率法。检验水准 $\alpha=0.05$ 。

2 结果

2.1 疗效比较

研究组治疗总有效率为91.67%(55/60)高于对照组的77.97%(46/59)($P<0.05$)。详见表1。

表 1 临床疗效比较 [例(%)]

Table 1 Comparison of clinical efficacy [n(%)]

Groups	Remarkable effect	Effective	Invalid	Total effective rate
Control group(n=59)	17(28.81)	29(49.15)	13(22.03)	46(77.97)
Study group(n=60)	23(38.33)	32(53.33)	5(8.33)	55(91.67)
χ^2				4.354
P				0.037

2.2 两组血压、心率比较

统计学意义($P>0.05$);两组治疗 7 d 后收缩压、舒张压、平均动两组治疗前收缩压、舒张压、平均动脉压、心率比较差异无 脉压、心率均下降,且研究组低于对照组($P<0.05$)。详见表 2。表 2 两组血压、心率比较($\bar{x}\pm s$)Table 2 Comparison of blood pressure and heart rate between the two groups ($\bar{x}\pm s$)

Groups	Time point	Systolic pressure (mmHg)	Diastolic pressure (mmHg)	Mean arterial pressure (mmHg)	Heart rate(times/min)
Control group(n=59)	Before treatment	174.22± 10.19	114.67± 9.36	142.44± 9.63	89.47± 4.41
	After 7 days of treatment	139.95± 8.26*	88.13± 8.39*	114.97± 10.54*	84.98± 6.39*
Study group(n=60)	Before treatment	172.90± 9.13	116.22± 8.13	140.56± 9.32	89.82± 5.27
	After 7 days of treatment	121.92± 11.12**	78.61± 7.12**	98.27± 8.41**	78.56± 5.25**

Note: Compared with the same group before treatment, * $P<0.05$; Compared with the control group, ** $P<0.05$.

2.3 两组血液动力学指标比较

组($P<0.05$)。详见表 3。

经过治疗,两组患者的 CO、CI 均下降,且研究组低于对照

表 3 两组血液动力学指标比较($\bar{x}\pm s$)Table 3 Comparison of hemodynamic indexes between the two groups ($\bar{x}\pm s$)

Groups	CO(L/min)		CI(L/min·m ²)	
	Before treatment	After 7 days of treatment	Before treatment	After 7 days of treatment
Control group(n=59)	5.89± 0.96	5.52± 0.73*	3.38± 0.21	3.14± 0.17*
Study group(n=60)	5.81± 0.87	5.06± 0.68*	3.42± 0.19	2.93± 0.15*
t	0.476	3.558	1.090	7.148
P	0.635	0.001	0.278	0.000

Note: Compared with the same group before treatment, * $P<0.05$.

2.4 两组糖脂代谢指标比较

照组,HDL-C 水平则高于对照组($P<0.05$)。详见表 4。

研究组治疗 7 d 后 TC、空腹血糖、TG、LDL-C 水平低于对

表 4 两组糖脂代谢指标比较($\bar{x}\pm s$,mmol/L)Table 4 Comparison of glucose and lipid metabolism indexes between the two groups ($\bar{x}\pm s$, mmol/L)

Groups	Time point	Fasting blood glucose	TC	TG	LDL-C	HDL-C
Control group (n=59)	Before treatment	7.64± 0.29	6.55± 0.39	2.42± 0.29	3.41± 0.46	1.13± 0.26
	After 7 days of treatment	7.03± 0.28*	5.13± 0.28*	1.83± 0.27*	2.81± 0.38*	1.48± 0.22*
Study group(n=60)	Before treatment	7.72± 0.33	6.51± 0.45	2.48± 0.36	3.49± 0.37	1.16± 0.31
	After 7 days of treatment	6.52± 0.21**	4.35± 0.36**	1.26± 0.24**	2.07± 0.34**	1.82± 0.33*

Note: Compared with the same group before treatment, * $P<0.05$; Compared with the control group, ** $P<0.05$.

2.5 两组中医证候积分比较

两组治疗前视物模糊、手足心热、脉弦细数、口干便结、舌红苔少等症评分比较差异无统计学意义($P>0.05$);两组治疗

7 d 后视物模糊、手足心热、脉弦细数、口干便结、舌红苔少等症评分均下降,且研究组低于对照组($P<0.05$)。详见表 5。

表 5 两组中医证候积分比较($\bar{x} \pm s$, 分)

Table 5 Comparison of TCM syndrome scores between the two groups ($\bar{x} \pm s$, score)

Groups	Time point	Blurred vision	Hand foot heart heat	Pulse string number	Dry mouth and constipation	Red tongue with little moss
Control group (n=59)	Before treatment	2.37± 0.25	2.38± 0.26	2.39± 0.24	2.41± 0.28	2.27± 0.24
	After 7 days of treatment	1.78± 0.23*	1.61± 0.15*	1.52± 0.15*	1.49± 0.13*	1.42± 0.19*
Study group (n=60)	Before treatment	2.31± 0.24	2.31± 0.22	2.31± 0.26	2.34± 0.23	2.23± 0.27
	After 7 days of treatment	1.07± 0.18**	1.18± 0.16**	0.96± 0.14**	0.88± 0.16**	0.86± 0.12**

Note: Compared with the same group before treatment, * $P<0.05$; Compared with the control group, ** $P<0.05$.

2.6 两组妊娠结局比较

研究组出现 1 例产后出血,1 例新生儿窒息,不良妊娠结局总发生率为 3.33%(2/60);对照组出现 2 例胎盘早剥,2 例低体质量儿,3 例新生儿窒息,1 例产后出血,不良妊娠结局总发生率为 13.56%(8/59)。研究组不良妊娠结局发生率低于对照组($\chi^2=3.938, P=0.047$)。

3 讨论

GH 的发病机制十分复杂,主要是由于患者正常的生理性血液动力学自我平衡失调,血管收缩舒张系统失衡,继而引起相应的临床症状,严重时可使孕妇心力衰竭、昏迷、早产、胎盘早剥、产后出血等,严重危害了母婴的健康与生命安全^[13-15]。因此,如何治疗 GH 成为临床亟待解决的难题之一。现临床针对 GH 的主要治疗原则在于卧床休息、降压利尿、镇静解痉、合理扩容、适时终止妊娠等。硫酸镁作为 GH 的常用药物之一,可获得一定的治疗效果^[16-18],但不少临床实践发现其疗效仍有所欠缺,且长时间的用药易诱发多种并发症,降低患者依从性^[19,20]。近年来,中医治疗 GH 取得了较大进展,王雁等学者^[21]采用黄芪党参葛根汤加减联合硫酸镁治疗 GH,在改善患者产前、产后等危险指标方面效果显著。中医认为, GH 为本虚标实指征,本虚以肝肾阴虚为主,标实以痰阻、血瘀多见。GH 患者发病初期其肾、脾、肺虚弱,水湿转运不畅,聚于肌理,精血下聚于胎,则肝阳上亢,阴血不足,扰于清窍,引发患者眩晕状;而至发病中期,痰浊内生,脾虚受损,则可能累积于心肺,加重病情。《内经》中有云:"阴虚而阳盛,肝气上从",故其治疗症候靶位主要在于肝肾,常以滋肾阴、平抑肝阳为主^[22]。平肝熄风汤主要由天麻、全蝎、川芎、红花、蔓荆子、竹茹、蜈蚣、僵蚕、钩藤、地龙、丹参、酸枣仁等中药材组方而成^[23,24],具有养血熄风、平肝潜阳之效。

研究组治疗后中医证候积分、临床总有效率、血压、心率等指标的改善情况均优于对照组,提示平肝熄风汤联合硫酸镁治疗肝肾阴虚型 GH 疗效显著。究其原因,硫酸镁作为解痉药物之一,其药效作用机制主要在于以下几点:可通过抑制血管神经肌肉来减少运动神经末梢乙酰胆碱的释放,进而松弛骨骼肌平滑肌,舒张动脉痉挛,有助于增加胎儿和孕妇的血红蛋白亲

和力,改善机体代谢功能,减少疾病对母婴的影响^[25,26]。平肝熄风汤方中的竹茹清热化痰;酸枣仁补肝血,敛肝阴,宁心安神;川芎、蔓荆子散风通络止痛,天麻、僵蚕息风止痉,平抑肝阳;全蝎、蜈蚣息风镇痉、攻毒散结、通络止痛,红花活血通经、散瘀止痛,钩藤、地龙、丹参平肝熄风,同时辨证加减,诸药配伍,共奏清肝潜阳,养血熄风之效^[27]。以往研究结果显示^[28],糖脂代谢异常可增加 GH 患者并发心血管事件的危险性。此外, GH 患者除了常见的血压升高症状外,伴有不同程度的血流动力学异常。因此,调节糖脂代谢、血液动力学异常对于改善 GH 患者的预后具有积极的促进作用。本次研究中两组患者糖脂代谢、血液动力学指标均有所改善,且平肝熄风汤联合硫酸镁治疗者的改善效果更好。现代药理研究结果显示^[29,30],天麻中的天麻素、天麻微粉还具有明显的降低血清 TC、TG、LDL-C 和血糖的作用;同时天麻素还具有降低血压和外周血管阻力,增加动脉血管中血流惯性及中央和外周动脉血管的顺应性等作用。全蝎、僵蚕均具有较好的抗氧化、改善血流动力学作用。钩藤、地龙、丹参均可发挥改善机体微循环、神经营养、控制血压血糖、降脂等效果。另本研究中研究组不良妊娠结局发生率低于对照组,这可能是因为联合治疗可较好地缓解疾病进展,减轻 GH 对患者各脏器的损害,从而改善母婴结局。

综上所述,平肝熄风汤联合硫酸镁治疗肝肾阴虚型 GH,疗效显著,在改善临床症状、血液动力学、糖脂代谢等方面效果显著,同时还可减少不良妊娠结局发生率。

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