

doi: 10.3978/j.issn.2095-6959.2022.03.014

View this article at: <https://dx.doi.org/10.3978/j.issn.2095-6959.2022.03.014>

复方甘草酸苷治疗妊娠期肝功能异常的效果及对胎儿的影响

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[摘要] 目的: 分析妊娠期肝功能异常应用复方甘草酸苷的效果及对胎儿的影响。方法: 选择2019年1月至2020年1月于北京市通州区妇幼保健院收治的妊娠期肝功能异常患者80例, 随机分为对照组与观察组, 观察组给予复方甘草酸苷治疗, 对照组给予谷胱甘肽治疗。分别于治疗前后采集两组患者的空腹静脉血, 采用全自动生化分析仪检测丙氨酸氨基转移酶(alanine aminotransferase, ALT)、天门冬氨酸氨基转移酶(aspartate aminotransferase, AST)、总胆红素(total bilirubin, TBIL)水平。评估两者患者疗效、并发症发生情况、胎儿结局及满意度评分。结果: 两组患者年龄、孕周、产次差异无统计学意义($P>0.05$)。治疗后两组患者ALT、AST、TBIL水平明显低于治疗前, 其中观察组患者ALT、AST、TBIL水平明显低于对照组($P<0.05$)。观察组患者治疗总有效率为92.50%, 明显高于对照组的72.50%($P<0.05$)。两组患者不良反应发生率差异无统计学意义($P>0.05$)。观察组患者发生胎儿宫内窘迫及新生儿窒息的概率分别为10.00%、2.50%, 明显低于对照组的27.50%、15.00%(均 $P<0.05$)。观察组患者满意率为92.50%, 明显高于对照组的70.00%($P<0.05$)。结论: 复方甘草酸苷治疗妊娠合并肝功能异常疗效较好, 可有效改善肝功能, 安全性较高, 对胎儿影响较低, 可在临床中推广应用。

[关键词] 妊娠期; 肝功能; 复方甘草酸苷; 胎儿; 影响

Effect of compound glycyrrhizin on abnormal liver function during pregnancy and its influence on fetus

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Abstract **Objective:** To analyze the effect of compound glycyrrhizin on abnormal liver function during pregnancy and its influence on fetus. **Methods:** A total of 80 patients with abnormal liver function during pregnancy admitted to our hospital from January 2019 to January 2020 were randomly divided into a control group and an observation group. The observation group was treated with compound glycyrrhizin, and the control group was treated with glutathione. Fasting venous blood was collected before and after the treatment, and alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) levels were detected by automatic biochemical analyzer. The curative effect, complications, fetal outcome, and satisfaction score were evaluated. **Results:** There was no significant difference in age, gestational week, and delivery time between the 2 groups

收稿日期 (Date of reception): 2021-06-21

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($P>0.05$). After the treatment, ALT, AST and TBIL levels of the 2 groups were significantly lower than those before the treatment, and ALT, AST and TBIL levels in the observation group were significantly lower than those in the control group ($P<0.05$). The total effective rate of treatment in the observation group was 92.50%, which was significantly higher than that of the control group (72.50%, $P<0.05$). There was no significant difference in the incidence of adverse reactions between the 2 groups ($P>0.05$). The rate of fetal distress and neonatal asphyxia in the observation group were 10.00% and 2.50%, significantly lower than that of the control group (27.50%, 15.00%; both $P<0.05$). The satisfaction rate of the observation group was 92.50%, which was significantly higher than that of the control group ($P<0.05$). **Conclusion:** Compound glycyrrhizin has a good effect on the abnormal liver function of pregnancy. It can improve the liver function effectively with high safety and low influence on fetus, which can be widely used in clinical practice.

Keywords pregnancy; liver function; compound glycyrrhizin; fetus; influence

妊娠会增加肝的负荷, 由于肝功能损伤, 机体凝血功能出现损伤, 产后出血的概率也会大幅度升高, 可出现食欲不振、恶心呕吐、腹胀及全身乏力等表现, 还可出现肝增大, 严重可有移动性浊音、肝性脑病等^[1]。妊娠合并肝功能异常还可能引起流产、早产、死胎等, 增加围产儿死亡率, 严重威胁孕妇及胎儿的生命健康^[2]。因此, 早期治疗妊娠合并肝功能异常, 对改善患者症状、提高患者预后方面具有重要意义。由于妊娠期间用药需要考虑药物对胎儿的影响, 用药受到一定限制^[3]。复方甘草酸苷是由甘草酸苷、甘氨酸和蛋氨酸等组成的复合物, 具有调节免疫、保护肝细胞、抗炎等作用^[4]。Wang等^[5]研究表明: 复方甘草酸苷可明显降低机体转氨酶水平, 发挥一定的肝保护作用。本研究选择2019年1月至2020年1月于北京市通州区妇幼保健院收治的妊娠期肝功能异常患者80例为观察对象, 旨在分析妊娠期肝功能异常应用复方甘草酸苷的效果及对胎儿的影响。

1 对象与方法

1.1 对象

选择2019年1月至2020年1月于北京市通州区妇幼保健院收治的妊娠期肝功能异常患者80例, 纳入标准: 1) 经人绒毛膜促性腺激素(human chorionic gonadotropin, HCG)检查及多普勒超声检查明确妊娠诊断; 2) 患者于北京市通州区妇幼保健院行实验室肝功检测确诊肝功能异常; 3) 年龄20~40岁。排除标准: 1) 合并心、肝、肾、肺等重要器官存在严重功能紊乱; 2) 存在精神或神经系统疾病, 无法配合检查及治疗; 3) 合并肝癌、肝硬化等疾病; 4) 存在其他恶性肿瘤; 5) 长期服

药。本研究采用随机数字表法, 随机均分为对照组与观察组。

1.2 方法

观察组给予复方甘草酸苷治疗, 对照组给予注射用谷胱甘肽治疗。

观察组: 复方甘草酸苷胶囊(北京凯因科技股份有限公司提供, 国药准字H20080006, 规格: 复方制剂, 每粒含甘草酸苷25 mg, 甘氨酸25 mg, 蛋氨酸25 mg)2~3粒/次, 3次/d, 2周1个疗程。对照组: 注射用谷胱甘肽(山东绿叶制药有限公司提供, 国药准字H20030002, 规格0.6 g/瓶)1.2 g加入5%葡萄糖250 mL中静脉滴注, 2周为1个疗程。

治疗期间密切观察丙氨酸氨基转移酶(alanine aminotransferase, ALT)、天门冬氨酸氨基转移酶(aspartate aminotransferase, AST)、总胆红素(total bilirubin, TBIL)等肝功能指标。同时监测血压、血常规、电解质。胎心监护(non-stress test, NST)检查1周1次, 胎儿B超检查2周1次。

1.3 观察指标

血清检测: 分别于治疗前后采集两组患者的空腹静脉血5 mL, 于室温静置20 min, 以3 000 r/min的转速离心10 min, 小心分离血清, 放入-70 ℃环境冷藏备用, 避免反复冻融。采用全自动生化分析仪检测ALT、AST、TBIL水平。其中ALT>40 U/L、AST>40 U/L、TBIL>20.4 μmol/L均为异常表达。

疗效评估: 分为显效、有效及无效, 其中临床症状和体征消失, ALT、AST及TBIL降至正常1.5倍, 胎心、胎动无异常为显效; 临床症状和体征有所改善, ALT、AST及TBIL降至治疗前的50%

以下,胎心、胎动无异常为有效;临床症状和体征无改善,ALT、AST及TBIL降至治疗前的50%以上为无效。

并发症发生情况:治疗期间观察并比较两组患者的高血压、低血钾、皮疹、浮肿等并发症的发生情况。

胎儿结局:观察并比较两组患者出现早产、胎儿宫内窘迫及新生儿窒息等发生情况。

满意度评分:根据北京市通州区妇幼保健院满意度调查表进行评分,其中满分为100,90~100分为非常满意,70~90分为比较满意,<70分则为不满意。

1.4 统计学处理

采用SPSS 20.0统计学软件进行数据分析,计量资料均采用均数±标准差($\bar{x} \pm s$)表示,组间比较采用t检验;计数资料均采用频数(%)表示,组间比较采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者一般资料分析

两组患者年龄、孕周、产次差异均无统计学意义(均 $P > 0.05$,表1)。

表1 两组患者一般资料分析($n=40$)

Table 1 Analysis of general data of patients between the 2 groups ($n=40$)

组别	年龄/岁	孕周	产次
对照组	28.15 ± 5.16	33.46 ± 3.38	1.42 ± 0.30
观察组	27.51 ± 5.09	33.12 ± 3.84	1.34 ± 0.46
<i>t</i>	0.558	0.420	0.921
<i>P</i>	0.578	0.675	0.359

表2 两组患者治疗前后肝功能指标比较($n=40$)

Table 2 Comparison of liver function between the 2 groups before and after the treatment ($n=40$)

组别	时间	ALT/(U·L ⁻¹)	AST/(U·L ⁻¹)	TBIL/(μmol·L ⁻¹)
对照组	治疗前	230.16 ± 90.16	180.45 ± 84.16	40.85 ± 32.16
	治疗后	154.23 ± 52.18*	101.26 ± 62.18*	19.52 ± 15.24*
观察组	治疗前	228.64 ± 98.45	174.39 ± 82.16	37.64 ± 15.28
	治疗后	60.35 ± 54.16* [#]	52.84 ± 30.16* [#]	16.52 ± 10.35* [#]

与同组治疗前相比,* $P < 0.05$;与同时间对照组相比,[#] $P < 0.05$ 。

Compared with the same group before the treatment,* $P < 0.05$; Compared with control group at the same time,[#] $P < 0.05$.

2.2 两组患者治疗前后肝功能指标比较

治疗前两组患者ALT、AST、TBIL水平差异均无统计学意义(均 $P > 0.05$)。治疗后两组患者ALT、AST、TBIL水平均明显低于治疗前,其中观察组患者ALT、AST、TBIL水平均明显低于对照组,差异均有统计学意义(均 $P < 0.05$,表2)。

2.3 两组患者疗效比较

观察组患者治疗总有效率为92.50%,明显高于对照组的72.50%,差异有统计学意义($P < 0.05$,表3)。

2.4 两组患者不良反应发生率比较

两组患者不良反应发生率相比,差异均无统计学意义(均 $P > 0.05$,表4)。

2.5 两组新生儿胎儿结局比较

观察组患者发生胎儿宫内窘迫及新生儿窒息的概率分别为10.00%、2.50%,明显低于对照组的27.50%、15.00%,差异均有统计学意义(均 $P < 0.05$,表5)。

2.6 两组满意度比较

观察组患者满意率为92.50%,明显高于对照组的70.00%,差异有统计学意义($P < 0.05$,表6)。

表3 两组患者疗效比较($n=40$)Table 3 Comparison of curative effect between the 2 groups ($n=40$)

组别	显效/[例(%)]	有效/[例(%)]	无效/[例(%)]	总有效/[例(%)]
对照组	16 (40.00)	14 (17.50)	10 (25.00)	29 (72.50)
观察组	20 (50.00)	16 (40.00)	4 (10.00)	37 (92.50)
χ^2				5.541
P				0.018

表4 两组患者不良反应发生率比较($n=40$)Table 4 Comparison of the incidence of adverse reactions between the 2 groups ($n=40$)

组别	血压升高/[例(%)]	血钾降低/[例(%)]	皮疹/[例(%)]	浮肿/[例(%)]	总发生/[例(%)]
对照组	0 (0.00)	0 (0.00)	2 (5.00)	0 (0.00)	2 (5.00)
观察组	1 (2.50)	2 (5.00)	0 (0.00)	1 (2.50)	4 (10.00)
χ^2					0.720
P					0.395

表5 两组患者新生儿及胎儿结局比较($n=40$)Table 5 Comparison of Neonatal and fetal outcomes between the 2 groups ($n=40$)

组别	早产/[例(%)]	胎儿宫内窘迫/[例(%)]	新生儿窒息/[例(%)]
对照组	8 (20.00)	11 (27.50)	6 (15.00)
观察组	3 (7.50)	4 (10.00)	1 (2.50)
χ^2	2.635	4.020	3.913
P	0.104	0.045	0.047

表6 两组患者满意率比较($n=40$)Table 6 Comparison of satisfaction rate between the 2 groups ($n=40$)

组别	非常满意/[例(%)]	比较满意/[例(%)]	不满意/[例(%)]	满意率/%
对照组	15 (37.50)	13 (32.50)	12 (30.00)	70.00
观察组	20 (50.00)	17 (42.50)	3 (7.50)	92.50
χ^2				6.646
P				0.009

3 讨论

由于妊娠期内分泌的变化致各种甾体激素较孕前明显升高, 而诸多激素的灭活均需要在肝内进行, 因此肝负担较孕前明显增重^[6]。妊娠期发生肝功能异常的原因多种多样, 其中各种肝源性

疾病、妊娠相关的肝病、缺血性疾病及药物原因等均会导致妊娠期间出现肝功能异常。随着近年生活方式的变化及营养状态的改变, 妊娠合并肝功能异常的发病率呈现逐年升高的趋势, 成为产科及相关医护人员关注的重点^[7-10]。

谷胱甘肽可作为内源性物质维护肝细胞活动

及代谢,可清除氧自由基,保护肝细胞膜,改善肝的合成及解毒功能^[11]。目前谷胱甘肽已广泛用于各种原因导致的肝损伤。但Yu等^[12]研究表明:谷胱甘肽治疗妊娠合并肝功能异常疗效较差。注射用谷胱甘肽给药途径为静脉给药,必须住院治疗,具有一定的不安全性,同时给患者带来了不便。总之,治疗妊娠合并肝功能异常疗效不是很好。复方甘草酸苷是以甘草酸苷为主要成分的复方制剂,它以甘草酸苷为主要成分,辅以甘氨酸、蛋氨酸而制成的肝细胞膜保护剂,广泛应用于急慢性肝炎的治疗。牛素梅等^[13]研究表明:复方甘草酸苷治疗利福平所致的药物性肝损伤疗效显著、安全性较好,可作为结核病患者长期抗结核治疗的保肝药物在临床中广泛应用。Zhang等^[14]研究表明:复方甘草酸苷治疗急性中毒性肝损伤疗效较好,并发症发生率低。本研究观察组患者治疗总有效率为92.50%,明显高于对照组的72.50%,治疗后两组患者ALT、AST、TBIL水平明显低于治疗前,其中观察组患者ALT、AST、TBIL水平明显低于对照组。说明复方甘草酸苷治疗妊娠合并肝功能异常的疗效较好,可明显改善肝功能,保障孕妇及胎儿的身体健康。

既往研究^[15]发现:复方甘草酸苷具有免疫调节的作用,可预防肝纤维化及类固醇样作用。Behdad等^[16]研究表明:复方甘草酸苷在保护肝功能的同时,还具有肝解毒及抗变态反应作用,因此复方甘草酸苷的毒副作用较低。刘露等^[17]研究发现:异甘草酸镁注射液能改善肝病患者临床症状,促进肝功能的恢复,减少不良反应的发生率。由于妊娠期间用药可能对胎儿产生不同的影响,严重者还可导致早产、胎儿宫内窘迫及新生儿窒息,给患者及家庭带来沉重打击,因此评估药物对妊娠期间胎儿的影响是妊娠期用药一大评估标准^[18]。本研究中,两组患者不良反应发生率差异无统计学意义。观察组患者发生胎儿宫内窘迫及新生儿窒息的概率分别为10.00%、2.50%,明显低于对照组的27.50%、15.00%。观察组患者满意率为92.50%,明显高于对照组的70.00%。提示复方甘草酸苷治疗妊娠合并肝功能异常不良反应较少,对胎儿的影响较小,患者满意度较高,可明显改善孕妇及胎儿的生活健康及医患关系,解决患者及医师的后顾之忧。

综上,复方甘草酸苷治疗妊娠合并肝功能异常疗效较好,可有效改善肝功能,并发症较低,对胎儿影响较低,可在临床中广泛应用。

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本文引用: 支艳俊. 复方甘草酸苷治疗妊娠期肝功能异常的效果及对胎儿的影响[J]. 临床与病理杂志, 2022, 42(3): 615-620. doi: 10.3978/j.issn.2095-6959.2022.03.014

Cite this article as: ZHI Yanjun. Effect of compound glycyrrhizin on abnormal liver function during pregnancy and its influence on fetus[J]. Journal of Clinical and Pathological Research, 2022, 42(3): 615-620. doi: 10.3978/j.issn.2095-6959.2022.03.014