·论 著·

妊娠期肝内胆汁淤积症血清甘胆酸水平与妊娠结局的关系

张慧芳， 王高莹， 邹萍， 王晶， 董蕊锐， 张婷， 孟西娜
南京医科大学附属无锡妇幼保健院检验科，江苏 无锡 214002

摘要：目的 探讨妊娠期肝内胆汁淤积症（ICP）血清甘胆酸水平对妊娠结局的影响。**方法** 采用回顾性研究方法，选取无锡妇幼保健院 2020 年 1 月至 12 月就诊的 73 例 ICP 患者为 ICP 组，以同期 73 例正常孕妇作为对照组。采用电化学发光法检测血清甘胆酸水平，并分析血清甘胆酸与妊娠结局的关系。**结果** ICP 患者血清甘胆酸水平为（15.50±9.01）μg/ml，显著高于对照组的（1.15±0.64）μg/ml（P<0.05）。ICP 组围生结局发生率如产后出血（10.96%）、胎儿宫内窘迫（16.44%）、新生儿窒息（10.96%）、早产（26.03%）、羊水污染（24.66%）明显高于对照组（1.37%，4.11%，1.37%，6.85%，5.48%），差异均有统计学意义（P<0.05，P<0.01）；ICP 组新生儿 Apgar 评分明显低于对照组（7.95±1.52 *vs* 9.02±1.45，P<0.01）。将 ICP 组孕妇按血清甘胆酸水平分为低（≤10 μg/ml）、中（>10~15 μg/ml）、高（≥15 μg/ml）三组，随着孕妇血清甘胆酸水平的升高，胎儿宫内窘迫发生率随之升高（P<0.05），而新生儿 Apgar 评分伴随降低（P<0.01）。**结论** ICP 对妊娠结局影响显著，血清甘胆酸的升高对妊娠结局有一定预警作用，监测血清甘胆酸有利于尽早实施临床治疗，降低不良结局的发生率。

关键词： 妊娠期肝内胆汁淤积症；甘胆酸；妊娠结局；围产结局；胎儿宫内窘迫；新生儿 Apgar 评分
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Relationship between serum cholyglycine level and pregnancy outcome in intrahepatic cholestasis of pregnancy

ZHANG Hui-fang, WANG Gao-ying, ZOU Ping, WANG Jing, DONG Rui-rui, ZHANG Ting, MENG Xi-na
Department of Laboratory Medicine, The Affiliated Wuxi Maternity and Child Health Care Hospital of Nanjing Medical University, Wuxi, Jiangsu 214002, China
Corresponding author: ZOU Ping, E-mail: zouping20191211@126.com

Abstract: Objective To investigate the relationship between serum cholyglycine level and pregnancy outcome in intrahepatic cholestasis of pregnancy (ICP). **Methods** A retrospective analysis was performed on 73 patients with ICP admitted to Wuxi Maternal and Child Health Hospital from January to December 2020 (ICP group), and 73 normal pregnant women at the same period were served as control group. Cholyglycine level was detected by electrochemiluminescence (ECL), and the relationship between serum cholyglycine level and pregnancy outcome was analyzed. **Results** The serum cholyglycine level in ICP group was significantly higher than that in control group [(15.50±9.01) μg/ml *vs* (1.15±0.64) μg/ml, P<0.05]. The incidences of postpartum hemorrhage (10.96% *vs* 1.37%), fetal distress (16.44% *vs* 4.11%), neonatal asphyxia (10.96% *vs* 1.37%), preterm delivery (26.03% *vs* 6.85%) and amniotic fluid contamination (24.66% *vs* 5.48%) in ICP group were significantly higher than those in control group (P<0.05, P<0.01). The Apgar score of newborns in ICP group was significantly lower than that in control group (7.95±1.52 *vs* 9.02±1.45, P<0.01). In ICP group, the pregnant women were divided into low (≤10 μg/ml), middle (>10-15 μg/ml) and high (≥15 μg/ml) cholyglycine level groups, and the incidence of fetal distress increased with the increase of serum cholyglycine level (P<0.05), while the neonatal Apgar score decreased with the increase of serum cholyglycine level (P<0.01). **Conclusion** ICP has a significant impact on pregnancy outcome. The increased

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通信作者： 邹萍，E-mail：zouping20191211@126.com
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serum cholyglycine level has a certain value in predicting pregnancy outcome. Monitoring serum glycocholic acid is conducive to the early clinical treatment and the decreased incidence of adverse outcomes.

Keywords: Intrahepatic cholestasis of pregnancy; Cholyglycine; Pregnancy outcome; Perinatal outcome; Intrauterine fetal distress; Neonatal Apgar score

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妊娠期肝内胆汁淤积症(intrahepatic cholestasis of pregnancy,ICP)是一种妊娠期特有临床综合征,以皮肤瘙痒和黄疸为主要临床症状[1-3],在妊娠中晚期有着较高的发病率,且会引起胎儿生长受限、早产、胎儿宫内窘迫等一系列不良的妊娠结局,对孕妇及胎儿的身心健康极为不利,对整个家庭乃至社会造成危害[4-6]。目前,ICP 的发病原因尚不十分清楚。因此,对 ICP 及时准确的诊断、监测以及有效的治疗是改善预后、降低不良结局发生率的重点。有研究表明,ICP 产妇血清甘胆酸水平显著高于正常产妇,血清甘胆酸水平是临床判断产妇肝功能损伤的重要指标[7-9]。为了探讨 ICP 患者血清甘胆酸对妊娠结局的影响,本研究对 ICP 患者和正常孕妇的血清甘胆酸水平及妊娠结局进行对比分析。报道如下。

1　资料与方法

1.1　一般资料　采用临床对照回顾性研究方法,选取 2020 年 1 月至 12 月在南京医科大学附属无锡妇幼保健院妇产科就诊的 ICP 孕妇 73 例为 ICP 组。纳入标准:符合中华医学会制订的 ICP 诊疗指南的标准(2015 版)[10]的患者。排除标准:合并皮肤瘙痒病、病毒性肝炎、药物过敏史、多胎妊娠、妊娠急性脂肪肝、其他妊娠合并症、精神认知功能障碍、HELLP 综合征及胎儿宫内发育异常的孕妇。随机选取同期 73 例正常孕妇作为对照组。ICP 组年龄(28.90±5.29)岁,采血时孕周(36.65±1.75)周,对照组年龄(27.95±2.99)岁,采血时孕周(37.31±2.66)周,两组年龄孕周比较差异无统计学意义(P>0.05)。收集两组孕妇的新鲜血液标本,且标本收集前均未做过任何治疗。本研究经医院伦理委员会同意(2019 伦审<384>号),两组孕妇均签署知情同意书。

1.2　方法　孕妇于清晨空腹状态下抽取肘静脉血 3 ml,3 000 r/min 离心 10 min,分离血清于-80 ℃保存,用于检测血清甘胆酸水平,检测仪器为新产业 MAGLUMI 1000,方法为电化学发光法,甘胆酸水平正常参考值为≤2.7 μg/ml,所涉及的操作需严格按照仪器操作说明书以及试剂盒参数设计说明来实施。宫内窘迫、新生儿窒息、羊水粪染、新生儿早产等诊断根据临床判断。

1.3　观察指标　比较两组孕妇血清甘胆酸水平,观察并记录孕妇的妊娠结局,包括胎儿窘迫、羊水污染、新生儿窒息、新生儿早产。

1.4　统计学方法　所有研究数据均采用 SPSS 16.0 进行统计分析。计量资料以 $\bar{x}\pm s$ 表示,采用 t 检验;计数资料以例(%) 表示,采用 χ^2 检验。以 P<0.05 为差异有统计学意义。

2　结　果

2.1　两组血清甘胆酸水平比较　ICP 组孕妇血清甘胆酸水平为(15.50±9.01)μg/ml,明显高于对照组的(1.15±0.64),差异有统计学意义(t = 13.574,P<0.01)。

2.2　ICP 组与对照组孕妇妊娠结局及围产结局的情况比较　ICP 组新生儿宫内窘迫、新生儿窒息、羊水粪染、新生儿早产产后出血的发生率均显著高于对照组(P<0.05),新生儿 Apgar 评分显著低于对照组(7.95±1.52 *vs* 9.02±1.45,t = 4.352,P<0.05)。见表 1。

表 1　两组对象妊娠结局及围产结局的情况比较　[n=73,例(%)]

Tab. 1　Comparison of pregnancy outcome and perinatal outcome between the two groups [n=73, case (%)]

组别	产后出血	胎儿宫内窘迫	新生儿窒息	羊水粪染	新生儿早产
ICP 组	8(10.96)	12(16.44)	8(10.96)	18(24.66)	19(26.03)
对照组	1(1.37)	3(4.11)	1(1.37)	4(5.48)	5(6.85)
χ^2/t 值	4.263	6.018	4.263	10.490	9.773
P 值	0.039	0.014	0.039	0.001	0.002

2.3　ICP 组孕妇不同血清甘胆酸水平与妊娠结局的关系　将 ICP 组孕妇按血清甘胆酸水平分为低(≤10 μg/ml)、中(>10~15 μg/ml)、高(≥15 μg/ml)水平组,随着孕妇甘胆酸水平的升高,新生儿宫内窘迫、新生儿窒息、羊水粪染、新生儿早产、产后出血等的发生率有伴随升高趋势,但仅胎儿宫内窘迫发生率差异有统计学意义(P<0.05),而新生儿 Apgar 评分伴随降低(P<0.01)。见表 2。

表 2　不同血清甘胆酸水平的 ICP 组孕妇妊娠结局比较　[例(%)]

Tab. 2　Comparison of pregnancy outcomes in ICP group with different serum cholyglycine levels　[case (%)]

组别	例数	产后出血	胎儿宫内窘迫	新生儿窒息	羊水粪染	新生儿早产	Apgar 评分($\bar{x}\pm s$)
低水平组	20	0	0	0	2(10.00)	2(10.00)	8.93±1.67
中水平组	18	1(5.56)	3(16.67)	1(5.56)	4(22.22)	4(22.22)	7.56±1.33
高水平组	35	7(20.00)	9(25.71)	7(20.00)	12(34.29)	13(37.14)	6.98±1.57
χ^2/F 值		5.932	6.127	5.932	4.117	5.050	10.198
P 值		0.052	0.047	0.052	0.127	0.080	<0.001

3　讨　论

ICP 是目前妇产科一种常见的临床疑难、高危疾病,临床上以甘胆酸升高、肝功能异常及皮肤瘙痒为特征,对孕妇及新生儿均有着显著的影响,易引起多种不良妊娠结局,尤其对围产儿危害极大,母体发生 ICP 若得不到及时有效的干预,将会导致围产儿一系列严重全身性症状,影响正常生长发育,甚至造成脑损伤,是围产儿死亡的主要原因之一[11-13]。据流行病学调查显示,随着人们饮食习惯的改变以及生活环境的变化,ICP 的患病率呈现出逐年上升的状态,其病因还未完全明确,研究显示其发生可能和遗传因素、性激素、免疫失衡及环境因素等有关[14-16]。目前临床治疗只能缓解孕妇的瘙痒等症状,并不能减轻对胎儿的危害。因此早诊断、早治疗不仅对妊娠结局有着积极的影响,还能有效降低新生儿发病率、改善预后,对减少母婴并发症等均具有十分重要的意义。

甘胆酸是胆酸与甘氨酸在肝细胞上结合形成的结合胆酸,正常状态下外周血中甘胆酸含量甚微,当机体中出现肝细胞损伤或胆汁淤积时,肝脏对甘胆酸摄取能力降低,导致血清甘胆酸水平增高,其水平过高时可对胎儿产生直接细胞毒性,导致胎儿肺表面活性物质等合成分泌改变[17],可能是围生期缺氧的重要机制之一。多项研究显示甘胆酸升高除了会促进释放前列腺素,从而促进子宫收缩引发早产,还能导致胎盘功能减退,增加胎儿窘迫、窒息、羊水粪染及死亡的发生率[18-19]。本研究发现,研究组孕妇血清甘胆酸水平显著高于对照组;ICP 组胎儿宫内窘迫、新生儿窒息、羊水粪染、新生儿早产等的发生率均显著高于对照组,新生儿 Apgar 评分显著低于对照组。并且,ICP 患者中随着甘胆酸水平的升高,胎儿宫内窘迫发生率伴随升高。提示血清甘胆酸水平的高低对妊娠结局预后有显著影响,及时监测甘胆酸的变化水平对降低不良妊娠结局有一定的临床价值。本研究中 ICP 患者不良妊娠结局中除胎儿宫内窘迫外其他发生率也有伴随血清甘胆酸水平而升高的趋势,但差异无统计学意义,不排除样本量较小的局限,故今后应扩大样本量继续观察。

综上所述,ICP 对妊娠结局有着重要的影响,血清甘胆酸水平的升高可能对不良妊娠结局有一定预警作用。监测血清甘胆酸有利于尽早实施临床治疗,降低不良结局的发生率。

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