血清TBA和CG检测在妊娠期肝内胆汁淤积症早期诊断及围产儿不良结局影响的临床意义*

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摘 要:目的 探讨血清总胆汁酸(TBA)、甘胆酸(CG)检测在妊娠期肝内胆汁淤积症(ICP)的早期诊断及围产儿不良结局的临床意义。**方法** 选取长安医院产科2015年6月~2017年6月诊治的ICP孕妇67例作为观察组,根据2015年《妊娠期肝内胆汁淤积症诊疗指南》的诊断标准分为轻度ICP组和重度ICP组,同时选择健康妊娠孕妇60例作为对照组。采用第五代循环酶法检测血清总胆汁酸(TBA)浓度,胶乳增强免疫比浊法检测血清甘胆酸(CG)浓度。比较各组血清TBA和CG检测结果以及结果异常率,同时比较各组间围产儿不良结局的发生率,评价血清TBA,CG检测对ICP的早期诊断及围产儿不良结局的临床价值。**结果** 血清TBA,CG检测结果在对照组、轻度ICP组、重度ICP组三组之间,差异均有统计学意义($F=267.13,201.09$,均 $P<0.01$),轻度ICP组血清TBA和CG检测结果高于对照组,差异有统计学意义($t=22.27,39.68$,$P<0.05$),重度ICP组血清TBA,CG检测结果高于轻度ICP患者组,差异有统计学意义($t=10.24,70.87$,$P<0.05$),且对照组、轻度ICP组、重度ICP组孕妇血清TBA,CG检测结果随着病情的加重而升高;血清TBA,CG异常结果在60例对照组中均未检出,在67例ICP组(轻度ICP组和重度ICP组)分别为63例和61例,两组结果异常率比较,差异有统计学意义($\chi^2=29.35,31.27$,$P<0.01$);围产儿发生早产、胎儿窘迫、围产儿死亡及死胎的不良围产儿结局发生率在对照组、轻度ICP组、重度ICP组三组之间有明显差异($\chi^2=39.17,56.31,13.02,6.92$,均 $P<0.01$)。**结论** ICP时,血清TBA和CG升高明显,可作为ICP诊断的敏感指标,提高ICP的检出率,并能有效预测围产儿结局,对ICP的早发现、早诊断具有重要的临床意义。

关键词:妊娠期肝内胆汁淤积症;血清甘胆酸;血清总胆汁酸;围产儿结局
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Clinical Significance of Detecting Serum TBA and CG in Early Diagnosis of Intrahepatic Cholestasis of Pregnancy and Perinatal Adverse Outcomes Influence

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Abstract: Objective To investigate the clinical significance of serum total bile acid (TBA) and cholyglycine (CG) detection in the early diagnosis of intrahepatic cholestasis of pregnancy (ICP) and perinatal adverse outcomes. **Methods** Chose 67 cases of ICP pregnant women diagnosed and treated in Chang'an Hospital from June 2015 to June 2017 and they were selected as observation group. According to the 2015 edition of the diagnostic guidelines for the diagnosis and treatment of intrahepatic cholestasis of pregnancy. The patients were divided into mild ICP group and severe ICP group, and 60 healthy pregnant women were selected as the control group. The serum TBA concentration was measured by fifth generation cyclic enzyme method and the concentration of serum CG was detected by latex enhanced turbidimetric immunoassay. The serum TBA, CG test results and the rate of abnormal test results, the incidence rate of perinatal adverse outcomes were compared between groups. Evaluation of serum TBA and CG detection of pregnancy early diagnosis of intrahepatic cholestasis and clinical value of perinatal adverse outcomes. **Results** The detection results of serum TBA and CG in the control group, mild ICP group and severe ICP group, there were significant differences between the three groups, the difference was statistically significant ($P<0.01$), the detection results in the CG group, serum TBA, ICP slightly higher than the control group, the difference was statistically significant ($t=22.27,39.68$, $P<0.05$). Weight of serum TBA and ICP group, the results of CG was higher than that of patients with mild ICP group, the difference was statistically significant ($t=10.24,70.87$, $P<0.05$). And in the control group, mild ICP group, severe ICP group pregnant women serum TBA, CG test results increased with the aggravation of the disease. Serum TBA and CG abnormal results in 60 cases of the control group were not detected. In 67 cases of group ICP (mild ICP group and severe ICP group) were 63 cases and 61 cases, two groups of abnormal results rate comparison, and the difference was statistically significant ($\chi^2=29.35$, 31.27, $P<0.01$). Perinatal premature labor, fetal distress, perinatal

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death and stillbirth incidence of adverse perinatal outcomes in the control group,mild ICP group and severe ICP group were significantly different between the three groups (χ^2=39.17,56.31,13.02,6.92,P<0.01). **Conclusion** Intrahepatic cholestasis of pregnancy,serum TBA and CG increased significantly,can be used as a sensitive indicator of ICP diagnosis,improve the detection rate of ICP,and effectively predict perinatal outcome. For intrahepatic cholestasis of pregnancy early detection and early diagnosis,it has important clinical significance.

Keywords:intrahepatic cholestasis of pregnancy (ICP);serum cholyglycine(CG);serum total bile acid(TBA);perinatal outcome

妊娠期肝内胆汁淤积症(intrahepatic cholestasis of pregnancy,ICP)易发生于妊娠中晚期,主要危害围产儿,有研究[1]显示,ICP孕妇发生早产、胎儿窘迫、围产儿死亡、死胎等不良围产结局依次为19.0%～60.0%,22.0%～41.0%,11.0%～20.0%和2.0%。以上数据均提示早期发现、诊断ICP并早期进行预防和治疗对胎儿发生不良结局的重要性。本文回顾性分析ICP患者血清总胆汁酸(TBA),甘胆酸(CG)检测结果变化及血清TBA,CG检测结果与围产儿不良结局发生的相关性,以期为临床ICP患者早期诊断、治疗及病情评估提供可靠依据。

1 材料与方法

1.1 研究对象 选取2015年6月～2017年6月长安医院产科诊治的ICP患者67例作为观察组,年龄19～41岁,平均年龄29.2±5.3岁,孕周20～39周。根据2015版《妊娠期肝内胆汁淤积症诊疗指南》中ICP严重程度的判定标准以及本实验室参考范围分为轻度ICP组和重度ICP,轻度ICP组:TBA为10～40 μmol/L,CG为2.7～13.5 mg/L,临床症状以皮肤瘙痒为主,无明显其他症状;重度ICP组:TBA≥40 μmol/L,CG≥13.5 mg/L,临床症状瘙痒严重、伴有其他情况。另外选择同期在长安医院进行围生期体检及分娩的健康孕妇60例作为对照组,年龄20～39岁,平均年龄28.9±3.6岁,孕周19～39周。两组孕妇年龄、孕周等一般资料比较,差异无统计学意义(P>0.05),所有孕妇均为单胎妊娠,并排除原发性肝病及其他肝脏疾病。

1.2 仪器和试剂 血清TBA,CG均采用宁波美康试剂(试剂批号:TBA 17022705,CG 16122102)在东芝-120FR全自动生化分析仪上检测。

1.3 方法 所有研究对象均于入院后次日早晨空腹采集静脉血3 ml,以3 000 r/min离心5 min,分离血清待测,标本要求无溶血、无脂血。血清TBA采用第五代循环酶法,参考范围0～10 μmol/L,超出该范围为异常;血清CG采用胶乳增强免疫比浊法,参考范围0～2.7 mg/L,超出该范围为异常。检测项目严格按照仪器和试剂说明书要求的标准操作规程操作,并进行实验室质量控制。

1.4 统计学分析 采用SPSS19.0软件对数据统计分析,计量资料以均值±标准差($\bar{x}\pm s$)表示,两样本均数比较采用t检验,组间多样本均数比较采用单因素方差分析(one-way ANOVA),阳性率比较采用卡方(χ^2)检验,均以P<0.05为差异有统计学意义。

2 结果

2.1 血清TBA,CG检测结果 见表1。血清TBA,CG检测结果在对照组、轻度ICP组、重度ICP组三组之间比较,差异有统计学意义(P<0.01),且随着病情加重而升高。血清TBA,CG异常结果在60例对照组中均未检出,在67例ICP组(轻度ICP组和重度ICP组)分别为63例和61例,对照组与ICP组异常结果检出率比较,差异有统计学意义(χ^2=29.35,31.27,P<0.01)。

2.2 围产儿不良结局发生率 见表2。在对照组、轻度ICP组、重度ICP组中随着病情加重,围产儿发生早产、胎儿窘迫、围产儿死亡及死胎的不良围产儿结局发生率均明显增加,差异有统计学意义(P<0.01)。

表1 血清TBA,CG检测结果比较($\bar{x}\pm s$)

项 目	对照组(n=60)	轻度ICP组(n=39)	重度ICP组(n=28)	F值	P值
TBA(μmol/L)	3.37±2.16	14.02±7.22[a]	59.55±15.34[b]	267.13	<0.01
CG(mg/L)	1.61±0.57	4.23±2.58[a]	26.43±12.37[b]	201.09	<0.01

注:[a] 与对照组比较t=22.27,39.68,P<0.05;[b] 与轻度ICP组比较t=10.24,70.87,P<0.05。

表2 围产儿不良结局发生率比较[n(%)]

项 目	对照组(n=60)	轻度ICP组(n=39)	重度ICP组(n=28)	χ^2值	P值
早产	3(5.00)	5(12.82)	8(28.57)	39.17	<0.01
胎儿窘迫	2(3.33)	13(33.33)	15(53.57)	56.31	<0.01
围产儿死亡	0(0)	1(2.56)	2(7.14)	13.02	<0.01
死胎	0(0)	1(2.56)	1(3.57)	6.92	<0.01

3 讨论 妊娠期肝内胆汁淤积症(ICP)是围产儿病死的主要原因之一，甚至会发生无任何预兆的流产或死胎，目前病因尚不明确，可能与女性激素、个体遗传及环境因素有关，在妊娠过程中4.5%的孕妇可能会发生ICP[2,3]，所以妊娠期ICP的早期诊断、积极治疗就显得尤为重要。

血清TBA和CG代谢受阻是引起ICP的基础，其水平在皮肤瘙痒等临床症状前即可明显升高[4]。血清TBA水平直接反映肝脏功能与肝脏损伤程度，其阳性率可作为肝病诊断的重要指标[5]，血清TBA增高可促进前列腺素释放，提高子宫肌层对缩宫素敏感度，进而诱发早产[6]。血清甘胆酸(CG)是胆酸甘氨酸的结合物，是妊娠晚期血清中最主要的胆汁酸组分，也是诊断及治疗监测ICP最主要的特异性指标[7]。本文结果显示，血清TBA,CG检测结果在对照组、轻度ICP组、重度ICP组三组之间有显著性差异，且呈递增性升高；血清TBA,CG异常结果在对照组均未检出，而在ICP组血清TBA,CG检测结果异常率分别为94.0%和91.0%，因此血清TBA,CG可作为早期ICP患者的筛查指标，这与有关报道一致[8]。

肝内胆汁淤积是ICP主要病理表现，但很少损伤正常肝脏结构，仅可在光镜下发现部分肝小管内胆汁淤积及胆栓形成，导致胆汁在肠肝循环内受阻，使胆汁酸大量停留于血液，引起皮肤瘙痒、肝酶异常[9]。孕妇血清中高胆汁酸可使绒毛间隙变狭窄，胎盘内血流灌注不足，使绒毛合体滋养层增加，出现退行性改变以及胎盘功能减弱，造成胎儿的急性缺氧，导致胎儿窘迫甚至死亡[10]。本文通过三组围产儿结局比较发现随着病情加重，发生早产、胎儿窘迫、围产儿死亡及死胎的不良围产儿结局发生率均明显增加，说明血清TBA和CG水平越高对胎儿危害越大。

综上所述，血清TBA,CG是ICP诊断敏感且可靠指标，能有效预测围产儿的结局，联合检测可提高ICP的检出率，可作为孕妇孕期特别是中、晚孕期的常规检测及动态监测项目，对预防妊娠期孕妇发生ICP及不良围产儿结局有重要临床意义。

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