

妊娠期肝内胆汁淤积症产前监测指标与围产儿预后关系的研究

卢俊玲 匡景霞 程小林

【摘要】 目的 探讨妊娠期肝内胆汁淤积症产前监测指标与围产儿预后相关性。方法 采用病例对照方法回顾性分析2011年1月至2014年1月同济医学院附属普爱医院收治的88例妊娠期肝内胆汁淤积症患者及其围产儿(研究组)的临床资料,选取同期收治的正常妊娠妇女100例及其围产儿为对照组,分析妊娠期肝内胆汁淤积症产前监测指标与围产儿预后的关系及其围产儿流行病学特点。结果 研究组围产儿羊水粪源性感染、新生儿窒息、早产儿和胎儿宫内窘迫发生率均明显高于对照组,差异有统计学意义($P<0.05$)。研究组中围产儿不良组孕妇甘胆酸(CG)、ALT、AST、总胆红素(TBIL)、直接胆红素(DBIL)和总胆汁酸(TBA)水平均明显比良好组孕妇高,差异有统计学意义($P<0.05$)。多因素回归分析显示,CG、ALT、AST、TBIL和TBA与围产儿预后不良有明显关系。围产儿疾病中以羊水粪源性感染为最多(33.3%),其次为早产儿(28.6%)、胎儿宫内窘迫(20.6%)、新生儿窒息(15.9%)和死胎(1.6%)。结论 妊娠期肝内胆汁淤积症孕妇围产儿预后不良发生率较高,其中以羊水粪源性感染为最多,产前CG、ALT、AST、TBIL和TBA水平监测可作为预测围产儿预后的指标。

【关键词】 妊娠;肝内胆汁淤积症;妊娠期;围产儿;预后

Study on the relationship between prenatal monitoring index in intrahepatic cholestasis of pregnancy and perinatal prognosis Lu Junling, Kuang Jingxia, Cheng Xiaolin. Department of Gynecology and Obstetrics, Affiliated Pu'ai Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430033, China

Corresponding author: Lu Junling, Email: lujunling@yeah.net

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【Abstract】 Objective To investigate the association between prenatal monitoring index in intrahepatic cholestasis of pregnancy and the perinatal prognosis, as well as the characteristics of perinatal situations. **Methods** A retrospective study on the clinical data of 88 cases intrahepatic cholestasis of pregnancy and prognosis that were treated in our hospital from Jan. 2011 to Jan. 2014 was carried out. Relationship between prenatal monitoring index in intrahepatic cholestasis of pregnancy and perinatal prognosis, together with the epidemiological features of infants were analyzed. **Results** The incidence rates of perinatal meconium stained amniotic fluid, asphyxia neonatorum, premature and fetal distress were significantly higher in the study group than those in the controls, with differences statistically significant ($P<0.05$). The levels of CG, ALT, AST, TBIL, DBIL and TBA in puerperant with bad perinatal situation were significantly higher than puerperant with good perinatal situation, with the difference statistically significant ($P<0.05$). Results from the multiple regression analysis indicated that close relations did exist between CG, ALT, AST, TBIL, TBA and adverse perinatal prognosis. The main perinatal risks were related to meconium stained amniotic fluid (33.3%), prematurity (28.6%), fetal distress (20.6%), asphyxia neonatorum (15.9%) and stillbirth (1.6%). **Conclusion** The rate of adverse perinatal prognosis was low in intrahepatic cholestasis of pregnancy, with most frequently seen as meconium stained amniotic fluid. It was necessary to monitor the level of prenatal CG, ALT, AST, TBIL and TBA in puerperant in predicting the perinatal prognosis.

【Key words】 Pregnancy; Intrahepatic cholestasis of pregnancy; Perinatal; Prognosis

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作者单位: 430033 武汉, 华中科技大学同济医学院附属普爱医院妇产科

通信作者: 卢俊玲, Email: lujunling@yeah.net

妊娠期肝内胆汁淤积症是孕妇妊娠中、晚期特有的并发症,以皮肤瘙痒和胆汁酸升高为主要临床特征,可危害胎儿,增加围产儿发病率和死亡率^[1]。且具有复发性,再次妊娠或口服雌激素避孕药时常引起复发^[2]。为了解妊娠期肝内胆汁淤积症产前监测指标与围产儿预后的关系,及其围产儿患病特征,以同济医学院附属普爱医院收治的88例妊娠期肝内胆汁淤积症患者为研究对象进行相关研究,结果报道如下。

对象与方法

1. 病例:选取2011年1月至2014年1月收治的88例妊娠期肝内胆汁淤积症患者及其围产儿为研究组。妊娠期肝内胆汁淤积症诊断按文献^[3,4]。患者年龄24~36岁,平均(26.4±5.4)岁;其中初产妇78例,经产妇10例;孕周20~42周,平均(32.5±4.8)周。选取同期正常妊娠100例及其围产儿为对照组,年龄22~36岁,平均(26.8±5.6)岁;其中初产妇87例,经产妇13例;孕周22~41周,平均(33.1±5.2)周。两组患者年龄、孕产次和孕周等临床资料比较,差异无统计学意义($P>0.05$),有可比性。

2. 研究内容:观察指标包括甘胆酸(CG)、ALT、AST、总胆红素(TBIL)、直接胆红素(DBIL)和总胆汁酸(TBA)水平及胎儿羊水粪源性感染(粪染)、新生儿窒息、早产儿、胎儿宫内窘迫和死胎发生情况。

3. 统计学分析:采用SPSS 12.0统计软件,计量资料采用 $\bar{x}\pm s$ 表示,组间比较采用 t 检验;计数资料采用百分率表示,组间比较采用 χ^2 检验。以 $P<0.05$ 表示差异有统计学意义。

结 果

1. 围产儿预后:研究组围产儿羊水粪染、新生儿窒息、早产儿和胎儿宫内窘迫发生率均明显高于对照组,差异有统计学意义($P<0.05$);两组围产儿死胎发生率比较,差异无统计学意义($\chi^2=1.142, P=0.285$)。见表1。

表1 两组围产儿预后比较

组别	例数	羊水粪染	新生儿窒息	早产儿	胎儿宫内窘迫	死胎
研究组	88	21(23.9)	10(11.36)	18(20.5)	13(14.8)	1(1.1)
对照组	100	2(2.0)	1(1.0)	10(10.0)	2(2.0)	0(0.0)
χ^2 值		20.839	9.126	4.036	10.401	1.142
P 值		<0.001	0.003	0.045	0.001	0.285

注:括号外数据为例数,括号内数据为发生率(%)

2. 孕妇监测指标与围产儿预后相关性:根据围产儿预后情况,将研究组又分为预后良好组(36例)和预后不良组(52例),对比分析两组孕妇CG、ALT、AST、TBIL、DBIL和TBA水平(表2)。结果显示围产儿预后不良组孕妇CG、ALT、AST、TBIL、DBIL和TBA水平均明显高于预后良好组孕妇,差异有统计学意义($P<0.05$)。

表2 围产儿预后良好组和不良组监测指标比较($\bar{x}\pm s$)

监测指标	预后不良组 (n=52)	预后良好组 (n=36)	t 值	P 值
CG(mg/L)	67.5±16.8	32.2±10.3	11.220	<0.001
ALT(U/L)	217.4±58.8	94.5±41.6	10.900	<0.001
AST(U/L)	196.7±58.3	88.6±40.5	9.625	<0.001
TBIL(μ mol/L)	35.7±7.4	19.9±5.5	10.889	<0.001
DBIL(μ mol/L)	21.1±6.4	12.9±4.8	6.518	<0.001
TBA(μ mol/L)	55.2±13.9	40.3±11.2	5.340	<0.001

3. 围产儿预后不良多因素logistic分析:以孕妇监测指标作为自变量,围产儿预后作为因变量,进行logistic多因素回归分析(表3)。结果显示CG、ALT、AST、TBIL和TBA水平与围产儿预后不良明显相关。

表3 围产儿预后不良多因素logistic分析

监测指标	OR值(95%CI)	P 值
CG	4.125(2.012~6.315)	<0.001
ALT	1.746(1.020~3.134)	<0.001
AST	1.698(0.976~2.746)	<0.001
TBIL	3.427(2.133~5.218)	<0.001
TBA	5.377(2.867~7.739)	<0.001

4. 围产儿疾病构成:分析显示,研究组围产儿疾病中以羊水粪染最多(21例,33.3%),其次为早产儿(18例,28.6%)、胎儿宫内窘迫(13例,20.6%)、新生儿窒息(10例,15.9%)和死胎(1例,1.6%)。

讨 论

妊娠期肝内胆汁淤积症是引起围产儿预后不良的严重妊娠并发症之一。目前国内外专家对其发病机制尚未明确定论,可能与孕妇机体激素水平、个体遗传基因或环境因素有关^[5,6]。研究表明,肝内胆汁淤积症对孕产妇影响并不大,但对围产儿的健康构成严重的危险,可直接影响围产儿的预后,增加围产儿发病率和死亡率^[7-9]。

本研究结果表明,相对于正常孕产妇,妊娠期肝内胆汁淤积症可明显增加羊水粪染、新生儿窒息、早产儿和胎儿宫内窘迫的发生率,与文献报道

基本一致^[10]。围产儿预后不良的孕妇CG、ALT、AST、TBIL、DBIL和TBA水平明显高于围产儿预后良好的孕妇。围产儿预后不良多因素logistic分析表明,CG、ALT、AST、TBIL和TBA水平为围产儿预后不良独立危险因素,其中以TBA危险性最高,其次为CG、TBIL、ALT和AST。妊娠期肝内胆汁淤积症,可增加胎儿体内胆红素和胆汁酸浓度,从而影响胎儿机体氧化磷酸化能力,破坏线粒体,减少三磷酸腺苷合成,降低胎儿能量供应,影响胎儿正常生理活动^[11];另外胆汁酸可促进胎盘绒毛毛细血管收缩,降低胎盘血管通透性,从而减少胎儿营养和氧气供应,导致胎儿缺氧,影响胎儿正常发育;胆汁酸还可诱导子宫释放前列腺素,诱发早产^[12,13]。妊娠期肝内胆汁淤积症致围产儿疾病分析表明,羊水粪染(33.3%)处于所有围产儿不良预后的首位,其次为早产儿、胎儿宫内窘迫、新生儿窒息和死胎。

妊娠期肝内胆汁淤积症围产儿预后不良发生率较高,产前CG、ALT、AST、TBIL和TBA水平监测可作为预测围产儿预后的指标。临床上应做好早期相关指标的监测,针对异常现象,及时给予相应的治疗和日常护理指导,加强胎儿监护,对于难以控制病情发展的患者,可建议尽早终止妊娠,减少围产儿病死率,以提高围产儿生存质量。

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