

doi: 10.13241/j.cnki.pmb.2014.12.028

妊娠期肝内胆汁淤积导致新生儿肺损伤的高危因素及干预对策*

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摘要 目的:探讨妊娠期肝内胆汁淤积症所致新生儿肺损伤的危险因素,并采取相应的措施以提高临床治疗水平。**方法:**选取2010年1月-2013年1月我院收治的70例妊娠肝内胆汁淤积症综合症患者作为观察组,另选取同期接受体检的65例正常晚期妊娠妇女为对照组。分析新生儿肺损伤的相关因素。**结果:**妊娠肝内胆汁淤积症综合所致新生儿肺损伤高危因素有雌激素水平、机体免疫失衡、高微量元素硒、高总胆汁酸、高甘胆酸(p 均 <0.05)。**结论:**妊娠肝内胆汁淤积症综合所致新生儿肺损伤的高危因素较多,临床上要积极采取措施,避免产后母婴并发症的发生。

关键词:肝内胆汁淤积症综合症;新生儿肺损伤;危险因素;干预对策

中图分类号:R714.7,R722 **文献标识码:**A **文章编号:**1673-6273(2014)12-2309-04

Risk Factors and Interventions of Neonatal Lung Injury Caused by Intrahepatic Cholestasis of Pregnancy*

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ABSTRACT Objective: To investigate the risk factors of syndrome of intrahepatic cholestasis of pregnancy induced lung injury in neonatal, and take corresponding measures in order to improve the level of clinical treatment. **Methods:** 70 patients with neonatal lung injury induced by intrahepatic cholestasis of pregnancy from January 2010 to January 2013 were selected as the observation group, and another 65 pregnant women who were accepted the inspection at the same time were chosen to be the control group. Then the related factors of neonatal lung injury were analyzed by regression. **Results:** The high risk factors of neonatal lung injury induced by intrahepatic cholestasis of pregnancy were high estrogen levels, immune imbalances, high-selenium, high total bile acid, high cholyglycine ($P<0.05$). **Conclusion:** Many high risk factors are related to intrahepatic cholestasis of pregnancy induced neonatal lung injury syndrome. It is suggested that the active measures should be taken to avoid the postpartum complications of maternal and infants.

Key words: Intrahepatic cholestasis syndrome; Neonatal lung injury; Risk factors; Intervention Strategies

Chinese Library Classification(CLC): R714.7, R722 **Document code:** A

Article ID:1673-6273(2014)12-2309-04

前言

妊娠期肝内胆汁淤积症是多发生在妊娠中晚期,初期临床表现主要是皮肤瘙痒和胆酸升高,后期则演变成妊娠肝内胆汁淤积症综合症,严重影响围产期孕妇和新生儿的健康。目前研究认为,妊娠期肝内胆汁淤积症是由多种共同作用形成的,各因素相互依存、相互影响。此外,据报道胆酸是造成胎儿窘迫、死胎及早产的主要原因^[1]。随着医学研究的进展,临床上对妊娠肝内胆汁淤积症的研究也更加深入,特别是对该病导致的新生儿肺损伤方面,有研究提出“胆酸性肺炎”学说,认为患有妊娠期肝内胆汁淤积症的孕妇比正常分娩导致的新生儿肺损伤的比例更高^[2]。但关于该病的发病机制尚未形成明确的理论,所以只能以预防为主。本研究通过观察妊娠肝内胆汁淤积症综合所致新生儿肺损伤的临床表现,分析其危险因素,并探讨早

期进行对症处理的意义,只在为提高临床效果,确保母婴安全,降低并发症的发生率提供依据。

1 资料与方法

1.1 临床资料

选取选取2010年1月-2013年1月70例妊娠肝内胆汁淤积症综合症患者为研究对象,作为观察组。同时选取同时期65例正常晚期妊娠妇女为对照组。两组患者在年龄、孕周、胎次上比较无显著差异性, $p>0.05$,具有可比性。详细数据见表1。妊娠肝内胆汁淤积症综合症诊断标准参考第七版人民卫生出版社《妇科学》标准进行,新生儿肺损伤诊断标准^[3]为新生儿出生后存在呼吸困难,伴有发绀、呼吸急促、呼吸浅表、呼吸暂停、三凹征、肺部湿啰音、胸片达到肺炎标准中的三项以上者。详细数据见表1。

* 基金项目:国家自然科学基金项目(81172201)

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(收稿日期:2013-11-08 接受日期:2013-11-30)

表 1 两组患者一般资料比较
Table 1 The comparison of the general information in the two groups

Category	Age (years)	Gestational age (weeks)	Production times (times)
Control group (65)	28.9± 2.6	35.9± 1.2	1.2± 0.
Observation group (70)	29.2± 2.8	35.4± 1.4	1.3± 0.3

Note: compared between two groups, P>0.05.

1.2 方法

先对 1 名全科医生进行培训,签署知情同意书,调查患者的年龄、孕龄、产次,记录产程情况、流产史等情况。追溯患者的遗传因素、胎盘因素,以放射免疫法检测孕妇甘胆酸水平、总胆汁酸、雌激素水平、微量元素等实验室指标。

1.3 统计学处理

采用 SPSS13.0 软件进行分析,将相关因素调查统计的内容作为变量,计量资料采用 t 检验,计数资料采用 χ^2 检验进行单因素分析,然后将单因素中具有差异性的单因素进行二分类

Logostic 多因素分析,均以 P<0.05 为有统计学意义。

2 结果

2.1 单因素分析结果

如表 2 所示,妊娠肝内胆汁淤积症综合症所致新生儿肺损伤的危险因素主要有:雌激素水平过高、机体免疫系统失衡、微量元素硒含量高、总胆汁酸含量高、甘胆酸含量高;而患者的年龄、孕次、遗传、胎盘因素及产程无关;差异显著且具有统计学意义(P<0.05)。

表 2 妊娠肝内胆汁淤积症综合症所致新生儿肺损伤的危险因素分析
Table 2 The risk factors of intrahepatic cholestasis of neonatal lung injury syndrome

Relevant factors	Numerical	Control group (65)	Observation group (70)	χ^2	P
Age (years)	≤ 30	47(72.31)	50(71.43)	0.794	>0.05
	> 30	18(27.69)	20(28.57)		
	High	3(4.61)	45(64.29)		
Estrogen levels	Low	4(6.15)	3(4.29)	8.584	<0.05
	Normal	58(89.24)	22(31.42)		
Pregnancy rate	Repeatedly	23(35.39)	26(37.14)	0.747	>0.05
	Single	42(64.61)	44(62.86)		
Labor situation	Stagnate	14(21.54)	17(24.29)	0.573	>0.05
	Unobstructed	51(78.46)	53(75.71)		
Abortion	Have	21(32.31)	24(34.29)	0.784	>0.05
	No	44(67.69)	46(65.71)		
Immune conditions	Balance	49(75.39)	27(38.57)	6.483	<0.05
	Imbalance	16(24.61)	43(61.43)		
Genetic factors	Have	13(20.0)	16(22.86)	0.583	>0.05
	No	52(80.0)	54(77.14)		
Placental factors	Have	6(9.23)	10(14.29)	0.639	>0.05
	No	59(90.77)	60(86.71)		
High trace elements	Selenium	3(4.61)	36(51.43)	6.893	<0.05
	Other	62(95.39)	34(48.57)		
Total bile acid (u mol / L)]	≤ 30	42(64.61)	25(35.71)	5.692	<0.05
	> 30	23(35.39)	45(64.29)		
Cholyglycine (u g / ml)	≤ 40	37(56.92)	23(32.86)	6.052	<0.05
	> 40	28(43.08)	47(67.14)		

2.2 多因素分析结果

Logostic 多因素分析显示,高雌激素水平、机体免疫失衡、高微量元素硒、高总胆汁酸、高甘胆酸是妊娠肝内胆汁淤积症综合症所致新生儿肺损伤高危因素(P<0.05)。见表 3。

3 讨论

本研究中,高雌激素水平、机体免疫失衡、高微量元素硒、

高总胆汁酸、高甘胆酸是妊娠肝内胆汁淤积症综合症所致新生儿肺损伤高危因素。这和报道^[4]的结果类似。考虑到妊娠肝内胆汁淤积症综合症是妊娠肝内胆汁淤积症的进一步防发展,故临床上发现妊娠肝内胆汁淤积症则要考虑并发综合症可能性大。国内学者^[9]称妊娠肝内胆汁淤积症患者临床症状原因是由于胆红素、转氨酶升高显著,而总胆汁酸、甘胆酸则是由以上物质结合形成的结果,是目前认为诊断妊娠肝内胆汁淤积症最

表 3 妊娠肝内胆汁淤积症综合症所致新生儿肺损伤多因素分析

Table 3 The multivariate analysis of intrahepatic cholestasis of pregnancy induced syndrome neonatal lung injury

Variable	β	S.E.	Waldalue	Palue	OR	95%CI
High levels of estrogen	2.053	0.594	5.474	0.012	6.474	1.356-13.347
Immune imbalance	1.485	0.593	5.547	0.018	8.857	1.746-26.484
High selenium	1.683	0.582	5.469	0.042	5.547	1.364-21.592
High total bile acid	1.593	0.693	5.434	0.023	8.337	1.746-25.436
High cholyglycine	1.494	0.595	5.463	0.004	5.847	1.473-21.344

敏感和有特异性指标。其高低能在一定程度上反应出妊娠肝内胆汁淤积症综合症预后情况。而研究^[6-8]通过对妊娠肝内胆汁淤积症流行性病学和诊断学研究后指出,雌激素水平是造成妊娠肝内胆汁淤积症后围生儿死亡的不良影响,但是其认为这和遗传因素、地区差异等有关。高微量元素硒能抑制氧自由基释放,会诱发围儿期缺氧缺血情况发生,诱发肺功能损伤,若治疗不及时则会造成肺损伤。研究^[9,10]指出,妊娠期间虽然患者机体免疫会升高,但对于一些本身存在基础疾病,饮食不均衡等患者来说,很容易造成机体免疫失衡情况,而胎儿是完全依靠母体营养的,故在很大程度上会受影响。

针对以上情况,我们在临床上要根据危险因素进行有效的进行干预,结合报道^[11-13]内容,我们认为以下几点是值得推荐的:①加强妊娠期间健康宣教,特别是对于妊娠肝内胆汁淤积症综合症综合症高危人群,制定相关的随访制定,如建立电话联系、门诊随访等措施确保患者的任何不适均在第一时间得到有效处理。②加强对胎儿监测,婴儿监测不仅能降低孕妇的心理负担,且研究称妊娠 36 周后常规羊膜检测对胎儿和新生儿均有良好作用^[14,15]。③积极提高机体免疫力,促进机体免疫平衡,这主要是从科学角度出发,均衡饮食是重要措施。此外,可予以干扰素等提高机体免疫力的药物。④药物应用干预,研究^[9]称维生素 K 能导致脂溶性维生素吸收不良增加,考虑带胆酸肠肝循环减少后会降低回肠末端摄入,故为了降低高总胆汁酸、高甘胆酸含量,可应用维生素 K,另外消胆胺能减轻妊娠肝内胆汁淤积症临床症状,但不能降低胆酸水平^[16]。⑤补充微量元素,虽然微量元素硒是人体不可缺少的元素,但是大量微量元素会适得其反,所以要加强监测这些指标,对于严重影响母婴安全者可考虑结束妊娠^[17-19]。

值得说明的是,妊娠肝内胆汁淤积症综合症新生儿肺损伤比正常新生儿高出 1 倍以上,据此提出了“胆酸性肺炎”学说,胆酸长时间浸润并损伤肺组织,虽然目前确切的机制不明确,但是在临床上仍要注意这些指标的变化。这也是我们在临床上可以获得的直接数据,一旦总胆汁酸 $>30 \text{ Umol/L}$,甘胆酸 $>40 \text{ Ug/mL}$,则表现存在妊娠肝内胆汁淤积症综合症所致新生儿肺损伤可能,就要采取措施早期处理。

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