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丙基硫氧嘧啶影响妊娠合并甲状腺功能亢进孕妇甲状腺功能及妊娠结局的研究

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摘要 目的:探讨丙基硫氧嘧啶(PTU)影响妊娠合并甲状腺功能亢进(甲亢)孕妇甲状腺功能及妊娠结局的影响。**方法:**选择我院妇产科2010年3月至2013年1月收治的110例妊娠合并甲亢的患者作为观察对象,随机分为观察组58例,对照组52例。观察组予PTU每天300 mg口服,对照组确诊后未能定期检测甲状腺功能而自行停药,或拒绝PTU药物治疗。**结果:**观察组TT3、TT4、FT3、FT4、TSH水平均显著低于对照组,差异均具有统计学意义(均P<0.05);观察组早产或流产、剖宫产、妊娠高血压、心力衰竭、重度子痫明显低于对照组,而足月产明显高于对照组,差异均具有统计学意义(均P<0.05);观察组的围生儿发生胎儿窘迫、低体重儿、新生儿甲亢、转入NICU发生率均显著低于对照组,两组比较差异均具有统计学意义(均P<0.05)。**结论:**规范的PTU治疗能很好地改善妊娠合并甲亢患者的孕期甲状腺功能,减低甲亢对孕妇及新生儿的危害,改善妊娠结局,且对新生儿畸形率无显著的影响,是一种相对安全和有效的治疗方法。

关键词:妊娠;甲状腺功能亢进;丙基硫氧嘧啶;妊娠结局

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Study on the Influence of Thyroid Function and Pregnancy Outcome of Propylthiouracil in the Treatment of Pregnancy Combined with Hyperthyroidism Women

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ABSTRACT Objective: To investigate the influence of thyroid function and pregnancy outcome of propylthiouracil in the treatment of pregnancy combined with hyperthyroidism women. **Methods:** 110 cases of pregnancy combined with hyperthyroidism in department of gynecology and obstetrics of our hospital from March 2010 to January 2013 were selected as observation objects, and were randomly divided into observation group of 58 cases, 52 cases in control group. Observation group were given PTU 300 mg per day orally, control group after the diagnosis of thyroid function failed to regularly test their withdrawal, or refused to PTU therapy. **Results:**In the observation group, TT3, TT4, FT3, FT4, TSH levels were significantly lower than those in the control group, the differences were statistically significant (P<0.05); premature delivery or abortion, cesarean section, pregnancy induced hypertension, heart failure, and severe preeclampsia of the observation group was significantly lower than that of the control group, while the term birth was significantly higher than that of the control group, the differences were statistically significant (P<0.05); the occurrence of fetal distress, perinatal infants, low birth weight, neonatal hyperthyroidism, transferred to the incidence of NICU in observation group was significantly lower than control group, the difference between the two groups were statistically significant (P<0.05). **Conclusion:** PTU treatment specification can improve thyroid functionhyperthyroidism during pregnancy in patients with pregnancy, reduce the harm to the maternal and neonatal hyperthyroidism,improve the pregnancy outcome, and had no significant effect on neonatal malformation rate. It is a relatively safe and effective method in the therapy.

Key words: Pregnancy; Hyperthyroidism; Propylthiouracil; Pregnancy outcome

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前言

妊娠合并甲状腺功能亢进(甲亢)属于常见的高风险妊娠之一,国内发病率约为0.1%至0.2%,易引起不良妊娠结局[1],对母体和胎儿的危害较大,可造成如胎儿流产、早产、妊娠高血压等并发症,严重者会造成胎死宫中。Graves病、毒性结节性甲状腺肿、妊娠呕吐、葡萄胎等都是引起妊娠合并甲亢的原因。保持甲状腺功能正常对母婴发育有着至关重要的作用。治疗甲亢的药物主要有甲状腺药、甲硫咪唑和丙基硫氧嘧啶等,其中丙基硫氧嘧啶属于硫脲类抗甲状腺药,它可以直接影响自身免疫性甲状腺疾病患者的免疫反应[2],目前已成为治疗孕期甲亢

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的首选药物。本研究目的在于观察 PTU 对妊娠合并甲亢孕妇甲状腺功能及妊娠结局的影响,现报告如下。

1 资料与方法

1.1 临床资料

选择我院妇产科 2010 年 3 月至 2013 年 1 月收治的 110 例妊娠合并甲亢的患者作为观察对象，年龄 20~39 岁，平均(29.4±3.9)岁;初产妇 74 例,经产妇 36 例;甲亢病程 1 月 ~9 年,平均(2.9±1.6)年。所有病例均符合中国甲状腺协会 2010 年甲亢的诊断标准。随机将患者分为观察组 58 例、对照组 52 例,两组妊娠患者除甲亢外无其他并发症。观察组年龄 20~37 岁,平均(28.6±3.2)岁;初产妇 40 例,经产妇 18 例;甲亢病程 1 月 ~9 年,平均(3.1±1.7)年;对照组年龄 21~39 岁,平均(30.1±3.8)岁;初产妇 34 例,经产妇 18 例;甲亢病程 1 月 ~8 年,平均(2.8±1.6)年。两组患者在年龄、孕次、病程等一般资料方面比较无显著性差异(P>0.05),具有可比性。

1.2 方法

两组在治疗前 1 个月禁用含碘食物和药物。观察组 PTU(德国赫尔布兰德大药厂，规格:50 mg×100 片，国药准字 H20060262)每天 300 mg 口服。定期检测甲状腺功能,根据甲状腺功能及临床表现及时调整药物的剂量，并定期复查随访,以了解母婴的情况。对照组确诊后未能定期检测甲状腺功能而自行停药,或拒绝 PTU 药物治疗。

1.3 观察指标

检测并观察两组患者 TT3、TT4、FT3、FT4、TSH 等指标,并对妊娠结局、并发症及胎儿情况进行随访并记录。

1.4 统计学方法

采用 SPSS13.0 统计软件进行统计学分析，数据以均数±标准差($\bar{x}\pm s$)表示,计量资料采用 t 检验,计数资料采用卡方检验,P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组甲状腺功能指标比较

观察组 TT3、TT4、FT3、FT4、TSH 水平均显著低于对照组,差异均具有统计学意义(均 P<0.05),说明规范的 PTU 治疗能对患者激素水平有显著的改善作用。见表 1。

Table 1 Comparison of two groups of thyroid function indexes($\bar{x}\pm s$)

Group	N	TT3(nmol/L)	TT4(nmol/L)	FT3(pmol/L)	FT4(pmol/L)	TSH (μU/mL)
Observation group	58	1.89± 1.04	150.72± 28.64	5.03± 1.09	17.20± 2.95	1.12± 0.72
Control group	52	3.42± 1.20*	298.29± 29.31*	19.24± 2.23*	72.28± 6.79*	0.89± 0.01*
X^2		7.64	22.39	15.94	25.17	5.30
P		<0.05	<0.05	<0.05	<0.05	<0.05

Note:Compared with the control group, *P <0.05

2.2 两组妊娠结局和并发症情况比较

观察组早产或流产、剖宫产、妊娠高血压、心力衰竭、重度子痫明显低于对照组,而足月产明显高于对照组,差异均具有统计学意义(均 P<0.05)。见表 2。

Table 2 Comparison of pregnancy outcomes and complications of two groups (cases (%))

Cases		Observation group (n=58)	Control group (n=52)	X^2	P
Pregnancy outcomes	Premature delivery or abortion	4(6.90)	11(21.15)*	7.84	<0.05
	uterine-incision delivery	12(20.69)	27(51.92)*	10.59	<0.05
	partus maturus	42(72.41)	14(26.92)*	15.80	<0.05
Complications	hypertension of pregnancy	3(5.17)	13 (25.00) *	8.85	<0.05
	heart failure	1 (1.72)	4 (7.69)*	4.06	<0.05
	Severe preeclampsia	1(1.72)	8(15.38)*	6.93	<0.05

Note:Compared with the control group, *P <0.05

Table 3 Comparison of two groups of pregnancy and perinatal outcome of thyroid function hyperthyroidism patients (cases (%))

Cases		Observation group	Control group	X^2	P
The fetal condition	Fetal distress	2(3.45)	10(19.23)*	8.12	<0.05
	Deformity	1(1.72)	2 (3.85)	1.27	>0.05
	Infant of low-birth weight	4(6.90)	20(38.46)*	10.91	<0.05
	Neonatal hyperthyroidism	0(0.00)	3 (5.77)*	4.02	<0.05
	Into NICU	6(10.34)	13(25.00)*	7.68	<0.05

Note:Compared with the control group, *P <0.05

2.3 两组妊娠合并甲状腺功能亢进症患者围生儿结局比较

观察组的围生儿发生胎儿窘迫、低体重儿、新生儿甲亢、转入 NICU 发生率均显著低于对照组，两组比较差异均具有统计学意义(均 P<0.05)，详见表 3。

3 讨论

2010 年我国十大城市甲状腺病流行病学调查显示甲亢患病率为 1.1%，毒性弥漫性甲状腺肿(Graves 病) 占全部甲亢的 85%[3]。甲状腺功能亢进可能存在一些误导性的症状，在诊断上容易误诊，如早孕期的妊娠呕吐及晚孕期的子痫等症状[4]。还要区分妊娠合并甲亢的先后问题，如妊娠前就已经接受过甲亢药物治疗及妊娠期间首次诊断甲亢的患者[5]。因考虑到妊娠合并甲亢可能带来的严重后果以及该类疾病的可预防性，所以有专家学者提出应对妊娠期妇女进行甲状腺功能普查[6]。其中妊娠合并甲状腺功能亢进症发病率为 0.02%~0.20%[7]，也有研究证实母体孕 16–20 周的甲状腺功能的异常，对婴儿的智力、运动发育低下有关[8]。

在治疗甲亢时，药物的选择非常关键，由于现在的许多抗甲状腺药物都能通过胎盘，影响胎儿，引起胎儿甲亢及胎儿甲减[9]。已知甲状腺疾病患病情况与碘营养状况相关[10]，PTU 主要是通过阻断甲状腺中碘的氧化和有机结合，减少甲状腺中的碘量，进而使 T3/T4 的比值增加，达到抑制甲状腺激素合成的目的[11]，而且其通过胎盘量少，速度慢，与胎儿的畸形无关，其副作用与给药剂量并无直接相关性[12]。但在甲亢治疗过程中要严格控制给药剂量，要定期检测甲状腺功能[12]，剂量过大往往会造成甲状腺功能减低，如果是在治疗早期出现的甲状腺功能减低就说明给药量过大应该及时降低给药剂量[13]；但是如果甲状腺功能减低出现在治疗维持期时，则说明疾病正在缓解，属于治愈过程中的正常反应[14]。

本研究结果显示，观察组 TT3、TT4、FT3、FT4、TSH 水平均显著低于对照组，差异均具有统计学意义(均 P<0.05)；观察组早产或流产、剖宫产、妊娠高血压、心力衰竭、重度子痫明显低于对照组，而足月产明显高于对照组，差异均具有统计学意义(均 P<0.05)；观察组的围生儿发生胎儿窘迫、低体重儿、新生儿甲亢、转入 NICU 发生率均显著低于对照组，两组比较差异均具有统计学意义(均 P<0.05)。证实妊娠合并甲亢患者若未及时有效系统治疗，妊娠不良结局发生率较高。

孕妇对碘的需求较非孕期的要明显增加，甲状腺出现代偿性生理性肥大，妊娠合并甲亢患者由于体内甲状腺激素分泌过多，中枢及交感神经兴奋性增加，引起血管痉挛和宫缩加强，进而出现妊娠高血压、流产和早产等不良妊娠事件[15]。其中妊高征是发病率最高的妊娠合并症，最低的是甲状腺危象，但以上两个并发症对孕妇的危害最为严重[16]。此外，绒毛膜促性腺激素(hcG)的刺激，促甲状腺激素(TSH)水平在孕早期达到最低点，之后逐渐回升，产后恢复正常水平，如果控制不当也可诱发甲状腺机能亢进[17]。进而引起母婴发生不良事件。一旦疑诊或确诊甲亢或甲减，必须经专科医生进行时合理地诊断和治疗，以避免不良妊娠结局。

规范的 PTU 治疗能很好地改善妊娠合并甲亢患者的孕期甲状腺功能，减低甲亢对孕妇及新生儿的危害，改善妊娠结局，且对新生儿畸形率无显著的影响，是一种相对安全和有效的治疗方法。

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