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血清 SHBG 水平与妊娠期糖尿病胰岛素抵抗的关系研究

王 喆 张 倩 黎曼侬 黎 丽 李季梅 张 凤

(昆明市妇幼保健院检验科 云南 昆明 650031)

摘要 目的:探讨血清性激素结合球蛋白(SHBG)水平与妊娠期糖尿病(GDM)胰岛素抵抗(IR)的关系。**方法:**选择 2015 年 3 月~2016 年 1 月在我院收治的 90 例 GDM 孕妇为观察组,选择同期健康体检孕妇 45 例为对照组,采用化学发光法检测两组孕妇的 SHBG、胰岛素(INS)、C 肽和游离睾酮(FT),糖化血红蛋白仪检测糖化血红蛋白(HbA1c),生化分析仪检测空腹血糖(FBG),并计算胰岛素抵抗指数(HOMA-IR)和敏感性指数(ISI),分析两组孕妇各指标的关系及其与两指数的相关性。**结果:**观察组孕妇空腹及餐后 2h、3h 的 INS 水平高于对照组,差异有统计学意义($P<0.05$)。观察组孕妇餐后 1h 和 2h 的 C 肽水平低于对照组,而餐后 3h 高于对照组,差异有统计学意义($P<0.05$)。观察组孕妇 SHBG 水平、ISI 低于对照组,而 HOMA-IR、FT、FBG 和 HbA1c 水平高于对照组,差异有统计学意义($P<0.05$)。SHBG 水平与 FINS、C 肽水平、HOMA-IR 呈负相关,与 ISI 呈正相关,差异有统计学意义($P<0.05$)。**结论:**GDM 孕妇胰岛素抵抗性和敏感性下降,血清 SHBG 水平降低且与 INS 水平、IR 及敏感性相关,检测血清 SHBG 水平有助于了解 GDM 孕妇 IR 情况。

关键词:妊娠期糖尿病;性激素结合球蛋白;胰岛素抵抗;胰岛素敏感性

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Study on the Relationship between Serum SHBG Level and Insulin Resistance in Pregnant Woman with Gestational Diabetes Mellitus

WANG Zhe, ZHANG Qian, LI Man-nong, LI Li, LI Ji-mei, ZHANG Feng

(Department of Laboratory Medicine, Maternal and Child Health Care Hospital of Kunming, Kunming, Yunnan, 650031, China)

ABSTRACT Objective: To study the relationship between sex hormone-binding globulin (SHBG) and insulin resistance in pregnant woman with gestational diabetes mellitus (GDM). **Methods:** 90 pregnant woman with gestational diabetes who were treated in our hospital from March 2015 to January 2016 were selected as the observation group, and 45 cases of healthy pregnant women were selected as the control group. The content of SHBG, insulin (INS), C peptide and free testosterone (FT) of two groups were detected by chemiluminescence method. Glycosylated glycosylated hemoglobin (HbA1c) was tested by hemoglobin meter testing, and the fasting blood glucose (FBG) were tested by biochemical analyzer. The insulin resistance (HOMA-IR) and sensitivity index (ISI) were calculated. The relationship of the indexes between two groups and the relationship between the indexes and the two exponents were analyzed. **Results:** The insulin levels of limosis and postprandial 2 h and 3 h in observation group were higher than the control group, the difference was statistically significant ($P<0.05$). The C peptide value of the observation group in 1 h and 2 h after meal were lower than the control group, while the C peptide value in 3 h after meal was higher than the control group, the differences were statistically significant ($P<0.05$). The levels of SHBG and ISI in observation group were lower than the control group, and the HOMA-IR, FT, FBG and HbA1c in observation group were higher than the control group, the differences were statistically significant ($P<0.05$). SHBG were negative correlated to FINS, C peptide, HOMA-IR, and which was positively correlated to ISI, the differences were statistically significant ($P<0.05$). **Conclusion:** The pregnant woman with GDM decreases with insulin resistance and sensitivity insulin, Serum SHBG levels are decreased and correlated with INS levels, IR and sensitivity. Detecting the serum level of SHBG can help to know the insulin resistance of GMD.

Key words: Gestational diabetes mellitus; Sex hormone-binding globulin; Insulin resistance; Insulin sensitivity

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前言

妊娠期糖尿病(GDM)是妊娠前糖代谢正常或有潜在糖耐量减退,是妊娠期首次出现的糖代谢异常,可对孕妇和围生儿

产生短期和长期多种危害,严重影响孕妇及新生儿健康^[1-3]。胰岛素抵抗(IR)是 GDM 发病的主要原因,但其发病机制尚未完全明确,早发现和早干预对延缓病情和改善预后具有重要的意义^[4,5]。性激素结合球蛋白(SHBG)是一种由肝脏产生的糖蛋白,是 IR 的血清标记物,在非空腹状态下稳定且不随昼夜节律变化,糖脂代谢异常患者早期血清 SHBG 水平的下降,可作为 2 型糖尿病发病程度的预测标记物^[6,8]。本研究通过 GDM 孕妇和

作者简介:王喆(1978-),男,本科,主管技师,从事分子诊断、化学发光方面的研究,E-mail:wanggzhe@sina.com

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健康孕妇的血清 SHBG 水平和 IR 的比较,探讨血清 SHBG 水平与 GDM 孕妇 IR 的关系,为 GDM 早期诊断提供参考依据。

1 资料与方法

1.1 临床资料

选择 2015 年 3 月~2016 年 1 月我院收治的 90 例 GDM 患者为观察组,选择同期 45 例健康体检孕妇为对照组。对照组年龄 22~34 岁,平均(28.12±5.16)岁,孕期 24~28 周,平均孕期(26.14±1.42)周。观察组年龄 23~35 岁,平均(29.31±5.42)岁,孕期 24~28 周,平均孕期(26.68±1.32)周。两组孕妇在年龄、孕周等比较,差异无统计学意义($P>0.05$),具有可比性。

1.2 纳入和排除标准

纳入标准:怀孕 24~28 周孕妇,年龄 21~35 岁,宫内妊娠,空腹血糖(FBG) >6.1 mmol/L,经过口服葡萄糖耐量试验(OGTT)检测:空腹抽血后,将 75 g 无水葡萄糖粉溶于 300 mL 水中,溶解后快速将糖水喝完,期间禁食和剧烈运动,分别于 30 min、1 h 和 2 h 后采集静脉血,测定葡萄糖水平,血糖 >11.1 mmol/L 为异常^[9,10],孕前无心肝肾及其他内分泌疾病。排除标准:存在糖尿病并发症患者,合并其他内分泌疾病患者,继发性糖尿病、1 型糖尿病、继发性高血压、家族性高胆固醇血症等患者,近期内有性激素用药史。本研究方案经医院伦理委员会审批并经患者或家属签字同意。

1.3 检查方法

孕妇空腹 12 h 后于次日早晨 7:00~9:00 首次抽取肘静脉血 5 mL,餐后 1 h、2 h、3 h 抽血均在上午进行,所抽取血液分开标记,于室温下 3000 r/min 离心 10 min,分离血清,置于 -80℃ 冰箱保存。采用化学发光仪(BECKMAN COULTER DXI800)检测 SHBG、胰岛素(INS)、C 肽和游离睾酮(FT)水平,同时 EDTA-K2 管抽取全血 2 mL,采用糖化血红蛋白仪(奥迪康 AC6600)检测糖化血红蛋白(HbA1c),Olympus640 生化分析仪检测 FBG,并计算胰岛素抵抗指数(HOMA-IR)和敏感性指数(ISI)。HOMA-IR = 空腹胰岛素(FINS)×FBG/22.5,ISI=1/(FINS×FBG)。

1.4 统计学方法

采用 SPSS19.0 进行统计数据分析,计量资料以($\bar{X} \pm S$)表示,采用 t 检验,相关性分析采用 Spearman 积矩相关分析, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组孕妇 INS 释放情况比较

观察组和对照组孕妇餐后 1h 的 INS 水平比较,差异无统计学意义($P>0.05$),观察组孕妇空腹及餐后 2h、3h 的 INS 水平均高于对照组,差异有统计学意义($P<0.01$)。见表 1。

表 1 两组孕妇的 INS 释放情况比较(μ U/mL)

Table 1 Comparison of the insulin releases in the two groups(μ U/mL)

Groups	n	Fasting	Postprandial		
			1 h	2 h	3 h
Control group	45	11.24±6.13	83.71±33.04	70.71±30.28	32.47±15.83
Observation group	90	19.61±7.14	82.66±32.41	95.46±38.67	75.22±28.76
t		6.720	0.680	3.754	9.282
P		0.000	0.249	0.000	0.000

2.2 两组孕妇 C 肽释放情况比较

观察组和对照组孕妇的空腹 C 肽水平比较,差异无统计学意义($P>0.05$),观察组孕妇餐后 1h 和 2h 的 C 肽水平均低于对

照组,而餐后 3h 高于对照组,差异有统计学意义($P<0.01$)。见表 2。

表 2 两组孕妇的 C 肽释放情况(ng/mL)

Table 2 Comparison of the C-peptide releases in the two groups(ng/mL)

Groups	n	Fasting	Postprandial		
			1h	2h	3h
Control group	45	2.41±1.24	9.43±3.75	10.21±4.15	4.92±2.23
Observation group	90	2.51±1.31	5.86±2.56	8.17±3.11	7.38±2.71
t		0.425	6.504	3.203	5.261
P		0.336	0.000	0.001	0.000

2.3 两组孕妇 SHBG、ISI、HOMA-IR、FT、FBG、HbA1c 比较

观察组孕妇 SHBG 水平、ISI 低于对照组,而 HOMA-IR、FT、FBG 和 HbA1c 水平高于对照组,差异有统计学意义($P<0.01$)。见表 3。

2.4 相关性分析

观察组孕妇的 SHBG 水平与 FINS、C 肽水平、HOMA-IR 呈负相关($r=-0.611$ 、 -0.472 、 -0.714 , $P>0.05$),与 ISI 呈正相关($r=0.821$, $P<0.05$)。

表 3 两组孕妇 SHBG、ISI、HOMA-IR、FT、FBG、HbA1c 比较
Table 3 Comparison of the SHBG, ISI, HOMA-IR, FT, FBG, HbA1c in the two groups

Groups	n	SHBG(mmol/L)	FT(pg/mL)	FBG(mmol/L)	HbA1c(%)	HOMA-IR	ISI
Control group	45	136.27± 31.26	2.41± 1.16	3.65± 1.11	4.37± 0.87	1.68± 0.97	0.04± 0.02
Observation group	90	94.32± 28.57	3.54± 1.37	5.41± 1.62	5.62± 1.04	3.92± 1.44	0.02± 0.01
t		7.792	4.745	6.553	6.937	9.413	7.761
P		0.000	0.000	0.000	0.000	0.000	0.000

3 讨论

随着生活方式的改变,2型糖尿病患病率逐年增加,GDM患病率也有上升的趋势。GDM为孕妇高危疾病,孕妇持续高血糖可影响胚胎卵黄囊发育,阻断营养物质进行传输,增加胎儿畸形和巨大儿的发生率,导致围生期母儿多种合并症,对妊娠产生较大影响^[11,12]。GDM发病与IR、胰岛素分泌缺陷、自身免疫、遗传等因素相关,其诊断标准至今尚未统一,参照2013年美国糖尿病协会(ADA)糖尿病诊疗指南,患者均需要口服葡萄糖后多次抽血,给患者带来极大不便^[13,14]。SHBG能特异性地结合和转运性激素,调节性激素的生理效应,并受INT、生长激素、甲状腺激素等内分泌激素的影响。近年来研究表明,INT是SHBG代谢的重要调节激素,SHBG与IR具有密切相关性,SHBG可能是IR特有的生物标记物,可预示非胰岛素依赖性糖尿病的发生^[15,16]。本研究选取45例妊娠期糖尿病患者和45例非糖尿病孕妇为对象,通过血清SHBG水平和IR的比较,探讨血清SHBG水平与GDM孕妇IR的关系,旨在为GDM的诊断和治疗提供参考。

GDM孕妇INS和C肽水平升高,抑制SHBG的生成,循环中SHBG减少,存在IR及高胰岛素血症。本研究发现,观察组孕妇空腹及餐后2h、3h的INT水平高于对照组,观察组孕妇餐后1h和2h的C肽值低于对照组,而餐后3h高于对照组,差异有统计学意义。说明GDM的INT水平增高,可能是与为保证胎儿生长发育充足的能量供应,妊娠妇女的生理性IR状态发生改变,胰岛β细胞功能缺陷,C肽释放曲线分泌峰后移有关^[17]。同时本研究发现,观察组孕妇SHBG、ISI低于对照组,而HOMA-IR、FT、FBG和HbA1c高于对照组,差异有统计学意义。提示GDM孕妇IR及INT水平升高,从而抑制肝脏SHBG的生成,进一步导致血清SHBG减少。SHBG调节血液中性激素水平及其向靶组织的转运,影响血清总睾酮水平,SHBG表达收到葡萄糖或果糖抑制,低水平SHBG导致性激素紊乱,造成糖和脂代谢紊乱,加重IR有关,影响HbA1c水平^[18,19]。进一步研究发现,SHBG与FINS、C肽、HOMA-IR呈负相关,与ISI呈正相关,差异有统计学意义。说明SHBG水平降低可预示GDM的发生,可作为检测其疗效的指标之一。SHBG水平的降低可使游离型睾酮增加,雄激素活性增高,影响INT分泌和葡萄糖内环境稳定,产生IR^[20]。

综上所述,血清SHBG降低可作为检测GDM发病的指标,GDM孕妇胰岛素抵抗性和敏感性下降,血清SHBG水平降低且与INT水平、IR及敏感性相关,检测血清SHBG水平有助

于了解GDM孕妇的IR情况。

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