

妊娠期糖尿病产后血糖转归与瘦素水平相关性研究

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[摘要] **目的** 分析妊娠期糖尿病 (GDM) 孕妇产后 42 d 75 g 葡萄糖耐量实验 (OGTT) 结果, 探讨其与瘦素水平间关系. **方法** 收集 2011 年 4~11 月重庆医科大学第二附属医院产科 36 例 GDM 孕妇的临床资料, 根据产后 42 d 行 75 g 葡萄糖耐量实验 (75 g OGTT) 的结果分 2 组 (血糖浓度正常组 (I 组) 和异常组 (II 组)), 检测空腹胰岛素、瘦素, 进行统计分析. **结果** I 组产后空腹血糖明显低于 II 组 ($P < 0.05$), 瘦素水平明显高于 II 组 ($P < 0.05$). 2 组间年龄、BMI、空腹胰岛素、HOMA-IR 无明显差异 ($P > 0.05$). 多元线性回归分析结果表明: 瘦素与空腹血糖存在明显负相关性 ($R = -0.51, P = 0.02$), 与 HOMA-IR 存在明显正相关性 ($R = 0.7, P = 0.003$). BMI、年龄等与空腹血糖、HOMA-IR 均没有显著相关性. 一元线性回归结果表明: 空腹血糖与 HOMA-IR 存在明显负相关性 ($R = -0.56, P = 0.01$). 瘦素与空腹胰岛素间存在显著正相关性 ($R = 0.73, P = 0.001$). **结论** I 组产后空腹血糖明显低于 II 组, 瘦素水平明显高于 II 组. 瘦素水平与空腹血糖存在明显负相关性, 与 HOMA-IR 存在明显正相关性. BMI 年龄与空腹血糖、HOMA-IR 无显著相关性.

[关键词] 妊娠期糖尿病; 产后; 糖代谢; 瘦素

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Relationship Between Leptin and 6 Postpartum Glucose Metabolism in Gestational Diabetes

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[Abstract] **Objective** To analyze the results of the 75g oral glucose tolerance test (OGTT) in gestational diabetes mellitus (GDM) at six weeks after delivering to investigate the relationship between the leptin and 6 weeks postpartum glucose metabolism in gestational diabetes. **Methods** A retrospective study was conducted on the clinical data of 36 women with GDM, who delivered and underwent a 2 hours 75g OGTT at 42 days postpartum from April to November in 2011 in our hospital. On the basis of the results of OGTT, they were reclassified into two groups (normal group (I group) and abnormal group (II group) to test leptin and fasting insulin levels. **Results** In the I group, the mean fasting blood-glucose level was much lower than that of the II group ($P < 0.05$), and the mean leptin concentration was significantly higher than that of the II group ($P < 0.05$). There was not significant differences in age, BMI, fasting blood-insulin and HOMA-IR between two groups. The multiple logistic regression model showed that the leptin concentration was significantly negatively correlated with fasting blood-glucose ($R = -0.51, P = 0.02$), and was significantly positively correlated with HOMA-IR ($R = 0.7, P = 0.003$). There was no significant correlation between BMI and age with fasting blood-glucose, so did BMI and age with HOMA-IR. The linear regression model showed that the fasting blood-glucose was significantly negatively correlated ($R = -0.56, P = 0.01$) with HOMA-IR, the leptin concentration was significantly positively correlated with fasting blood-in-

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sulin concentration ($R = 0.73$, $P = 0.001$). **Conclusion** In the I group, the mean fasting blood-glucose is much lower than that of the II group, the mean leptin concentration is significantly higher than that of the II group. The leptin concentration is significantly negatively correlated with fasting blood-glucose, and is significantly positively correlated with HOMA-IR. There is no significant correlation between BMI and age with fasting blood-glucose, so do BMI and age with HOMA-IR.

[**Key words**] Gestational Diabetes; Postpartum; Glucose metabolism; Leptin

妊娠期糖尿病 (gestational diabetes mellitus, GDM) 是指在妊娠期首次发生或发现不同程度的糖耐量异常, 是妊娠期常见严重危害母婴健康的并发症之一. 随着脂肪因子的相继发现, 研究认为引起 GDM 的胰岛素抵抗 (Insulin Resistance, IR) 发生的主要原因可能是脂肪因子的异常分泌^[1-4].

瘦素是第一个被确定的脂肪因子, 最初被界定为一种抗肥胖激素, 其在能量过剩条件下通过下丘脑机制调节食物摄入. 文献报道, GDM 病人孕期瘦素水平与正常孕妇相比升高^[4,5]. 高瘦素水平可能通过影响胰岛素受体和受体后信号转导、抑制胰岛素对葡萄糖的摄取作用或降低胰岛素的敏感性, 使胰岛素不能发挥正常的生理作用, 因而胰岛素代偿性分泌增加; 反之, 高胰岛素血症又能刺激机体分泌瘦素增加, 互相促进, 形成恶性循环, 进一步加重 IR^[6]. 本研究旨在探讨 GDM 患者产后瘦素浓度与糖代谢间的相关性.

1 资料与方法

1.1 研究对象

选取 2011 年 4~11 月确诊为妊娠期糖尿病并于产后 6 周复查 75 g 葡萄糖耐量实验 (OGTT) 的单胎孕妇. 根据产后 OGTT 结果分为血糖恢复正常组 (I 组), 24 例, 平均年龄 (30.9 ± 2.5) 岁; 血糖仍未恢复正常组即异常组 (II 组), 12 例, 平均年龄 (30.8 ± 3.2) 岁.

1.2 诊断标准及排除标准

1.2.1 妊娠期糖尿病的诊断 (1) 2 次或 2 次以上空腹血糖 ≥ 5.8 mmol/L; (2) 妊娠 24~28 周进行 50 g 葡萄糖筛查 (GCT) ≥ 7.8 mmol/L, 再行 75 g 葡萄糖耐量试验 (OGTT), 其中有 2 项或 2 项以上达到或超过正常值 (空腹 5.6 mmol/L, 1 h 10.3 mmol/L, 2 h 8.6 mmol/L, 3 h 6.7 mmol/L); (3) GCT ≥ 11.2 mmol/L, 空腹 ≥ 5.8 mmol/L^[7].

1.2.2 排除标准 排除以下情况, 多胎妊娠、妊娠期高血压疾病, 甲状腺功能异常 (甲亢及甲减). 妊娠 20 周前确诊糖尿病, 肾脏、肝脏疾病, 其他内分泌性疾病及慢性病.

产后 6 周按 WHO 对糖尿病 (Diabetes mellitus, DM) 的诊断标准^[8]: 空腹血糖 ≥ 7.0 mmol/L 和 (或) 口服葡萄糖后 2 h 血糖 ≥ 11.1 mmol/L 或有糖尿病症状、非空腹 (随意) 血糖 11.1 mmol/L, 诊断为 DM; 空腹血糖正常, 2 h 血糖在 7.8~11.1 mmol/L 之间为糖耐量减低 (Impaired Glucose Tolerance, IGT); 空腹血糖正常, 2 h 血糖 < 7.8 mmol/L 为正常.

1.3 材料收集及标本测定

36 名妊娠期糖尿病患者产后 6~8 周复诊, 禁食 12 h, 行 75 g OGTT 试验及血常规检查.

$$\text{BMI} = \frac{\text{体质量}}{\text{身高}^2} \quad (\text{kg/m}^2)$$

HOMA-IR = FINS X FBG/22.5. 测定血糖采用葡萄糖氧化酶法. 测定瘦素、胰岛素采用酶联免疫吸附测定法 (enzyme-linked immunosorbent assay, ELISA).

1.4 统计学处理

所有计量资料结果用均数 \pm 标准差 ($\bar{x} \pm s$) 表示, 统计分析均使用 SPSS 统计软件进行. 组间数据采用两个独立样本的 t 检验分析. 参数相关性采用 spearman 相关分析, $P < 0.05$ 为差异有统计学意义.

2 结果

2.1 随访结果

产后糖耐量恢复正常者 (normal glucose tolerance, NGT) 24 名 (I 组), 占 67%, 存在糖代谢异常者 12 名 (II 组), 占 33%, 其中 IGT 6 例, DM 6 例, 各占 16.65%.

2.2 对比分析 I 组和 II 组资料

I、II 组间行 t 检验证实: 2 组间年龄、BMI 无明显差异 ($P > 0.05$); 2 组间年龄、空腹胰岛素、HOMA-IR 亦无明显差异 ($P > 0.05$), 见表 1. 空腹血糖 I 组明显低于 II 组 ($P < 0.05$), 见图 1. 瘦素水平 I 组明显高于 II 组 ($P < 0.05$), 见图 2.

表 1 各组受试者临床检查指标比较 ($\bar{x} \pm s$)Tab. 1 The comparison of clinical indicators between two groups ($\bar{x} \pm s$)

组别	年龄(岁)	BMI	胰岛素($\mu\text{g/L}$)	HOMA-IR	瘦素(ng/mL)	空腹血糖(mmol/L)	脂联素($\mu\text{g/mL}$)
正常组	30.9 \pm 2.5	23.9 \pm 2.6	16.75 \pm 10.67	3.58 \pm 2.09	15.22 \pm 11.45	5.01 \pm 0.56	6.28 \pm 5.86
非正常组	30.8 \pm 3.2	24.1 \pm 2.7	11.34 \pm 9.74	2.74 \pm 2.33	5.18 \pm 5.42*	5.78 \pm 0.60*	10.40 \pm 6.19

与正常组比较, * $P < 0.05$.

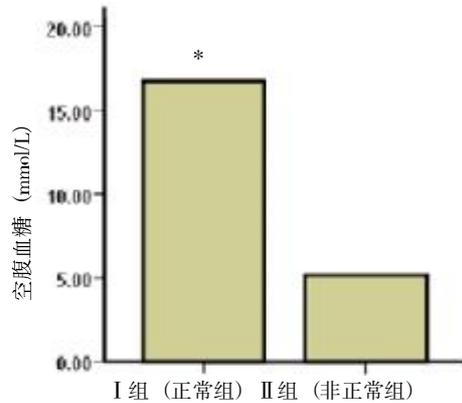


图 1 各组平均空腹血糖水平

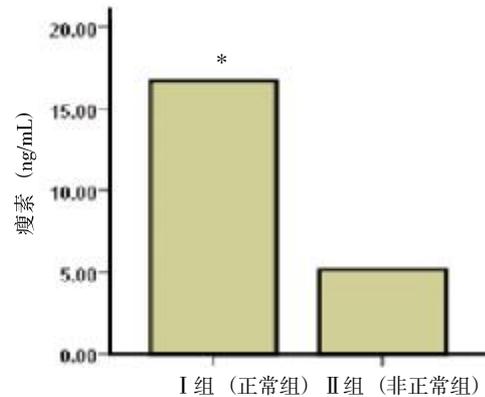
Fig. 1 The average fasting blood sugar level with II group comparison, * $P < 0.05$.

图 2 各组平均空腹瘦素水平

Fig. 2 The average fasting leptin level with II group comparison, * $P < 0.05$.

以空腹血糖为因变量, 瘦素、BMI、年龄为自变量的多元线性回归分析(见表 2)结果表明: 瘦素与空腹血糖间存在显著负相关($R = -0.51$, $P =$

0.02), 见图 3, BMI、年龄与空腹血糖没有显著相关性。

表 2 瘦素、BMI、年龄与空腹血糖之间相关性

Tab. 2 The relationships of leptin, BMI and age with fasting blood glucose

变量	回归系数 (b)	标准误 (Sb)	标准回归系数 (β)	t 值	P 值
常数项	5.643	0.232	0	24.366	0.000
瘦素	-0.033	0.015	-0.503	-2.179	0.047

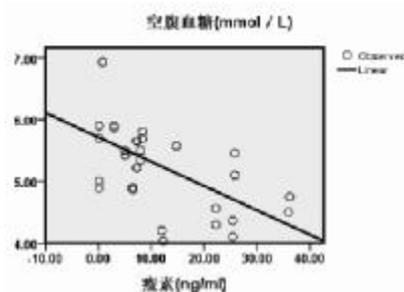


图 3 瘦素与空腹血糖相关曲线

Fig. 3 Leptin and fasting blood glucose related curve

以 HOMA-IR 为因变量, 瘦素、BMI、年龄为自变量的多元线性回归分析(见表 3)结果表明: 瘦素与 HOMA-IR 之间存在显著正相关性($R = 0.73$, $P = 0.001$), 见图 4, 而 BMI、年龄与 HOMA-IR 没有显著相关性。

一元线性回归结果表明: 空腹血糖与 HOMA-IR 存在显著负相关性($R = -0.56$, $P = 0.01$), 见图 5. 瘦素与空腹胰岛素间存在显著正相关性($R = 0.73$, $P = 0.001$), 见图 6.

3 讨论

3.1 GDM 患者产后随访情况分析

GDM 已成为危害母婴健康的常见产科并发症之一, 本研究中 36 例曾患 GDM 产妇产后 6 周的 OGTT 结果, 有 12 例 OGTT 异常, 占 33.3%, 高于国外同类研究^[9], 可能与样本量及人种有关. 其中 IGT 和 DM 各占 16.65%, IGT 属于血糖调节异常, 是正常血糖代谢与糖尿病之间的中间状态, 是发生糖尿病的危险因素. 如果在产后及时发现并积

表 3 瘦素、年龄、BMI 与 HOMA-IR 之间相关性
Tab. 3 The relationship of leptin, BMI and age with HOMA-IR

变 量	回归系数 b	标准误 Sb	标准回归系数 β	t 值	P 值
常数项	0.309	0.097	0	3.171	0.007
瘦素	0.023	0.006	0.700	3.664	0.003

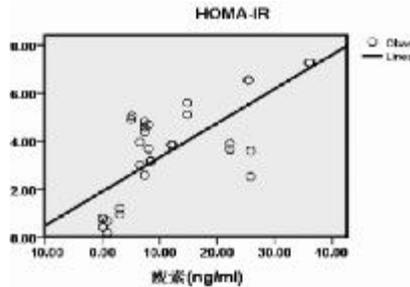


图 4 瘦素与 HOMA-IR 相关曲线
Fig. 4 Leptin and HOMA-IR related curve

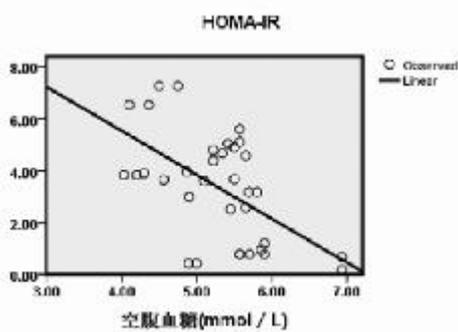


图 5 空腹血糖与 HOMA-IR 相关曲线
Fig. 5 Fasting blood glucose and HOMA-IR related curve

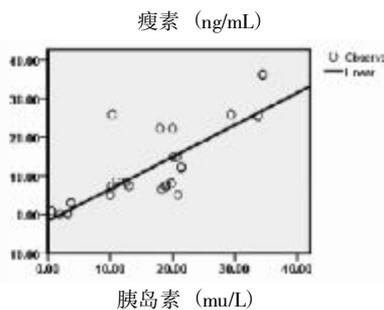


图 6 瘦素与胰岛素相关曲线
Fig. 6 Leptin and insulin related curve

极干预, 可有效避免或减少 GDM 向糖尿病的转化。本次研究中 DM 发生率亦较高, 考虑可能与孕前已有不同程度的糖代谢异常, 较年轻、无自觉症状、孕前未检测血糖有关。

本研究结果提示: 应将检测血糖作为孕前体检的一个常规项目, 以早期发现 GDM 患者, 及时治疗。GDM 孕妇产后仍需监测血糖变化, 将其作为

GDM 孕妇产后访视的常规项目。

3.2 瘦素与 GDM 产后恢复的关系

本研究结果显示母体血清中瘦素浓度与 HOMA-IR 明显正相关, 这与国外研究结果一致^[10-11]。可能是血糖恢复正常组相对较高的胰岛素水平导致了高瘦素水平^[12]。从实验角度讲, 胰岛素水平增高可能刺激脂肪细胞, 分泌瘦素增加, 同时, 瘦素水平的升高可能会加重胰岛素抵抗^[13]。I 组的瘦素水平高于 II 组, 高瘦素水平是低空腹血糖水平的原因还是结果尚不能明确。

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病机制.

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