·论　　著·

妊娠糖尿病患者血清MFG-E8与胰岛素抵抗的关系研究

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[摘要] **目的**　探讨妊娠糖尿病(GDM)患者血清乳脂肪球表皮生长因子Ⅷ(MFG-E8)水平与胰岛素抵抗(IR)的关系。**方法**　选取GDM患者47例(GDM组)、OGTT正常孕妇44例(NGT组)、健康的非妊娠妇女40例(NC组),采用酶联免疫吸附法检测血清MFG-E8的水平、糖脂代谢指标和HOMA-IR,并作相关分析。**结果**　GDM组血清MFG-E8水平均明显高于NGT组和NC组,差异均有统计学意义(t分别=3.21、2.86,P均<0.05)。GDM组患者血清MFG-E8均与HbA1c和HOMA-IR呈正相关(r分别=0.31、0.52,P均<0.05),多因素*logistic*回归分析显示,GDM患者HOMA-IR是MFG-E8水平的独立相关因素(OR=2.17,P<0.05)。**结论**　GDM患者存在血清MFG-E8水平异常升高,与HOMA-IR密切相关。

[关键词]　乳脂肪球表皮生长因子Ⅷ;　妊娠糖尿病;　胰岛素抵抗

Relationship between serum MFG-E8 and insulin resistance in patients with gestational diabetes mellitus

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[Abstract] Objective　To evaluate the relationship between serum MFG-E8 and insulin resistance in patients with gestational diabetes mellitus. **Methods**　Totally 47 cases of GDM patients were enrolled as GDM group, 44 cases of pregnant women whose oral glucose tolerance test (OGTT) were normal as NGT group, and 40 cases of healthy un-pregnancy people as NC group. The MFG-E8, the index of glycometabolism, and HOMA-IR were measured with ELISA and their relationships were analyzed by using spearman correlation and logistic regression analysis. **Results**　The serum MFG-E8 of GDM group was significantly higher than NGT group and NC group (t=3.21, 2.86, P<0.05). And the MFG-E8 level was positively correlated with HbA1c and HOMA-IR (r=0.31, 0.52, P<0.05). Logistic analysis showed that the HOMA-IR was independent factor of serum MFG-E8 level in GDM patients (OR=2.17, P<0.05). **Conclusion**　The level of serum MFG-E8 is abnormally high in GDM patients and closely relate to HOMA-IR.

[Key words]　milk fat globule-epidermal growth factor 8;　gestational diabetes mellitus;　insulin resistance

妊娠期糖尿病(gestational diabetes mellitus, GDM)是指孕妇妊娠期间首次出现的糖耐量异常[1],该病的临床经过复杂,母子都有风险,并会对其产生极大损害,但目前病因和发病机制尚未完全阐明,有推测可能与炎症应激和胰岛素抵抗(insulin resistance, IR)有关[2]。乳脂肪球表皮生长因子Ⅷ(milk fat globule-epidermal growth factor 8, MFG-E8),广泛表达在机体组织与细胞中,并参与机体多种病理生理过程[3]。有研究发现T2DM患者血清MFG-E8水平增加[4,5]。但目前对GDM患者血清MFG-E8水平变化及相关因素的研究尚较少。本次研究旨在观察GDM患者血清MFG-E8水平变化情况,探讨其与IR的关系。现报道如下。

1　资料与方法

1.1　一般资料　选择2014年5月至2016年6月龙游县人民医院收治的妊娠24~34周,75 g葡萄糖筛查异常的孕妇,按美国国家糖尿病资料组推荐诊断标准,经OGTT诊断为GDM的患者47例作GDM组。并选择本院之年龄、孕周、体重相匹配的

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OGTT正常孕妇44例作NGT组，同时选择健康非孕妇女40例作对照(NC组)。所有入选个体均排除严重心脏、肝肾疾病及高血压。三组患者的年龄、采血孕周、孕前体重指数(body mass index,BMI)等一般资料比较见表1。三组比较,差异均无统计学意义(P均>0.05)。

表1 一般资料比较

组别	年龄	孕周	孕前BMI/kg/m²
GDM组	27.13±4.37	28.04±5.17	23.22±3.16
NGT组	26.82±4.68	28.51±5.32	23.12±3.43
NC组	26.14±5.12	–	23.16±4.10

1.2 方法 清晨空腹采肘静脉血5 ml,3 000 r/min离心10 min,取血清-70℃保存。采用酶联免疫吸附法检测血清MFG-E8水平,采用全自动血生化分析仪测定总胆固醇(total cholesterol,TC)、三酰甘油(triacylglycerol,TG)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol,HDL-C)、低密度脂蛋白胆固醇(low density lipoprotein cholesterol,LDL-C)、空腹血糖(fasting blood glucose,FBG)浓度,采用化学发光免疫分析法测定空腹血清胰岛素(fasting serum insuli,FINS),采用全自动糖化血红蛋白分析仪测定糖化血红蛋白(glycosylated hemoglobin,HbA1c)。所有检测步骤按说明书操作。胰岛素抵抗指数按HOMA-IR公式计算。

1.3 统计学方法 采用SPSS 17.0进行统计学分析。计量资料以均数±标准差($\bar{x}\pm s$)表示,组间比较采用单因素方差分析;MFG-E8水平与临床指标相关性分析及影响因素采用*Spearman*分析和*logistic*回归分析。设P<0.05为差异有统计学意义。

2 结果

2.1 三组临床指标比较见表2

由表2可见，三组间TG、LDL-C、FBG、FINS、HOMA-IR、HbA1c和MFG-E8等指标比较,差异均有统计学意义(F分别=2.35、1.94、2.06、2.18、4.25、3.41、2.66,P均<0.05)。GDM组和NGT组TG、LDL-C和MFG-E8均明显高于NC组，差异均有统计学意义(t分别=1.87、2.54、2.86、3.62、2.90、4.12,P均<0.05);GDM组TG、LDL-C、FBG、FINS、HOMA-IR、HbA1c和MFG-E8均明显高于NGT组(t分别=3.86、2.49、2.07、2.91、1.83、2.55、3.21,P均<0.05),GDM组HbA1c和HOMA-IR明显高于NC组(t分别=3.51、2.74,P均<0.05)。

表2 三组临床指标比较

指标	GDM组	NGT组	NC组
TC/mmol/L	4.64±0.95	4.52±1.13	4.39±0.74
TG/mmol/L	1.85±0.71*#	1.49±0.59*	1.22±0.32
HDL-C/mmol/L	1.15±0.28	1.25±0.40	1.27±0.36
LDL-C/mmol/L	3.32±0.55*#	2.81±0.47*	2.41±0.39
FBG/mmol/L	8.27±1.12*#	4.91±0.91	4.69±1.02
FINS/mU/L	14.51±3.77*#	9.72±2.08	9.48±1.65
HOMA-IR	3.56±0.48*#	1.80±0.32	1.51±0.27
HbA1c/%	6.91±1.36*#	5.52±1.14	5.11±0.88
MFG-E8/μg/L	0.48±0.11*#	0.25±0.06*	0.22±0.05

注:*:与NC组比较,P<0.05;#:与NGT组比较,P<0.05。

2.2 三组血清MFG-E8水平与各临床指标的相关性分析 *Spearman*相关分析显示,GDM组MFG-E8水平与HbA1c和HOMA-IR呈正相关(r分别=0.31、0.52,P均<0.05)。

2.3 影响MFG-E8水平相关因素分析 以MFG-E8水平为应变量,经单因素分析后纳入年龄、孕周、FINS和HOMA-IR等指标作为自变量，多因素*logistic*回归分析显示,GDM患者HOMA-IR是MFG-E8水平的独立相关因素(OR=2.17,P<0.05)。

3 讨论

GDM是一种高危妊娠,会对产妇及胎儿较大危害,但其病因与发病机制尚未被完全阐明。目前认为GDM发病机制与2型糖尿病相似,与胰岛β细胞功能受损及IR密切相关[2],但具体原因尚不明确。

MFG-E8在近期的研究中发现可调节机体许多病理生理过程,包括炎症反应、免疫反应、细胞凋亡、细胞增殖及肿瘤的发生发展等[6~8]。研究表明MFG-E8可以拮抗炎症反应,提示了MFG-E8与炎症应激间的关联，但MFG-E8与妊娠糖尿病及IR是否存在关联,目前相关研究较少,因此进行该方面的探索很有必要。

本次研究结果显示GDM组血清MFG-E8水平均明显高于NGT组和NC组(P均<0.05),与Li等[9]关于GDM患者血清MFG-E8水平升高的研究结果一致，均提示MFG-E8可能参与了GDM的发生发展有关。本次研究相关性分析提示GDM组患者血清MFG-E8与HOMA-IR、HbA1c呈正相关(P均<0.05),这与Li等[9]研究不完全一致,表明GDM患者血清MFG-E8水平与HbA1c及GDM发病有着紧

密联系,部分差别可能与研究对象孕期不同和检测方法有所差异有关,具体还有待进一步研究。本次研究的 *logistic* 回归分析还发现显示,GDM 患者 HOMA-IR 是 MFG-E8 水平的独立相关因素(P均<0.05),提示 MFG-E8 与 IR 间存在密切关联。

综上所述,GDM 患者存在血清 MFG-E8 水平异常升高,与 HOMA-IR 密切相关,提示 MFG-E8 可能参与了 GDM 和 IR 发生与发展,值得进一步深入研究。

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