

妊娠晚期血脂水平与不同类型子痫前期相关性分析

苏秀梅, 李林娜

(潮州市人民医院妇产一科 广东 潮州 521000)

摘要:【目的】通过比较子痫前期不同发病类型患者妊娠晚期血脂指标的变化,探讨血脂代谢异常与不同发病类型子痫前期的发生发展的相关性。【方法】收集子痫前期患者 198 例:轻度子痫前期 108 例,晚发型重度子痫前期 54 例,早发型重度子痫前期 36 例。选择同期无妊娠并发症的健康孕妇 200 例为对照组。检测血清总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白(HDL)、低密度脂蛋白(LDL)、载脂蛋白 A(ApoA)、载脂蛋白 B(ApoB)、计算 AI、LDL/HDL、ApoB/ApoA 进行比较。【结果】子痫前期组与正常妊娠组相比,TG、Chol、LDL、ApoB、AI、LDL/HDL、ApoB/ApoA 均明显升高 ($P < 0.05$);早发型重度子痫前期组血脂指标异常尤为明显 ($P < 0.05$);用于早发型重度子痫前期预测分析 ROC 曲线下面积 > 0.7 且差异有显著意义 ($P < 0.05$) 的指标有 ApoB、AI、LDL/HDL、ApoB/ApoA。【结论】血脂代谢异常不仅参与子痫前期的发生及发展,且与病情轻重、子痫前期不同发病类型密切相关。血脂指标对早发型重度子痫前期有较好诊断价值,但各指标仍未取得较理想的截断值以预测该疾病。

关键词:子痫前期,早发型,晚发型,血脂

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Analysis of Association between Blood Lipid Level in Third Trimester of Pregnancy and Different Types of Preeclampsia

SU Xiu-mei, LI Lin-na

(First Department of Obstetrics and Gynecology, People's Hospital of Chaozhou, Chaozhou 521000, China)

Corresponding to: SU Xiu-mei, E-mail: 645979639@qq.com

Abstract: 【Objective】 To probe into the relationship between dyslipidemia and the onset and development of preeclampsia in different classifications through a comparison of the changes in blood lipid indices in the patients with different classifications of preeclampsia during the third trimester of pregnancy. 【Methods】 Data were collected from 198 cases with preeclampsia, of which 108 were diagnosed as mild preeclampsia, 54 as late onset severe preeclampsia and 36 as early onset severe preeclampsia. Controls were 200 healthy pregnant women in the same stage of pregnancy who suffered no pregnancy complications. A comparison was made based on the test of serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), ApoA and ApoB, and the calculation of AI, LDL/HDL and ApoB/ApoA ratios. 【Results】 The levels of TG, Chol, LDL, ApoB, AI, LDL/HDL and ApoB/ApoA were significantly higher in the preeclampsia group than in controls ($P < 0.05$). The blood lipid indices in particular were significantly abnormal in the severe early onset preeclampsia group ($P < 0.05$). Area under the ROC curves for predicting severe early onset preeclampsia in the indices of ApoB, AI, LDL/HDL and ApoB/ApoA were larger than 0.7 and significant differences were noted in them ($P < 0.05$). 【Conclusion】 Dyslipidemia plays a significant part in the onset and development of preeclampsia and is closely related to the severity and classification of preeclampsia. The blood lipid indices are of value to the diagnosis of severe early onset preeclampsia. However, this study didn't generate the optimal cutoff value of the above indices for the prediction of the disease.

Key words: pre-eclampsia; early onset; late onset; blood lipids

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作者简介:苏秀梅,通信作者,硕士研究生,主治医师,E-mail:645979639@qq.com

子痫前期(PE)是妊娠期特有的疾病,可伴有心、脑、肝、肾等多脏器损害,是孕产妇及围产儿死亡的主要原因之一。子痫前期发病越早、病情越重,母儿的预后相对越差。其组织学特征是胎盘血管床及蜕膜血管床及蜕膜螺旋动脉的脂质沉积、急性动脉粥样硬化^[1]。Risto等^[2]指出,血脂代谢异常不仅是子痫前期的临床表现,亦是子痫前期的发病机制之一。Williams Obstetrics中提出检测包括游离脂肪酸、甘油三酯和脂蛋白等的血脂水平对先兆子痫有预测价值。本研究采用病例-对照研究分析子痫前期不同发病类型患者血脂指标的变化,探讨血脂代谢异常与不同发病类型子痫前期的发生发展的关系及其临床意义。

1 材料与方法

1.1 研究对象

选取潮州市人民医院2011年01月至2012年12月底妊娠晚期住院分娩的孕产妇为研究对象,收集子痫前期病例198例为研究组,年龄17~41岁,平均 (28.2 ± 4.2) 岁;孕周28~39周,平均 (35.1 ± 2.5) 周;其中轻度子痫前期(Mild preeclampsia, M-PE)108例,重度子痫前期(Severe preeclampsia, S-PE)90例,其中早发型重度子痫前期(Early onset severe preeclampsia, ES-PE)36例,晚发型重度子痫前期(Late onset severe preeclampsia, LS-PE)54例。另随机选择同期在我院住院的正常孕妇200例为正常妊娠组,年龄17~39岁,平均 (26.9 ± 2.8) 岁;孕周28~39周,平均 (36.2 ± 2.6) 周。两组孕妇年龄、孕周、基础血压、体质量指数经统计学分析,差异无统计学意义($P > 0.05$),具有可比性。

1.2 纳入标准

入组患者诊断均依照谢幸主编的《妇产科学》第8版^[3]及相关参考文献的分类标准确定:子痫前期:血压正常的女性,妊娠20周后首次出现收缩压 ≥ 140 mmHg或舒张压 ≥ 90 mmHg,尿蛋白 ≥ 0.3 g/24 h;重度子痫前期:出现下述任一不良情况可诊断:①血压持续升高:收缩压 ≥ 160 mmHg和(或)舒张压 ≥ 110 mmHg;②蛋白尿 ≥ 5.0 g/24 h;③持续性头痛或视觉障碍或其它脑神经症状;④持续性上腹部疼痛,肝包膜下血肿或肝破裂症状;⑤肝脏功能异常:肝酶ALT或AST水平升

高;⑥肾脏功能异常:少尿(24 h尿量 < 400 mL或每小时尿量 < 17 mL)或血肌酐 $> 10^6$ $\mu\text{mol/L}$;⑦低蛋白血症伴胸水或腹水;⑧血液系统异常:血小板呈持续性下降并低于 $100 \times 10^9/L$;血管内溶血、贫血、黄疸或血LDH升高;⑨心力衰竭、肺水肿;⑩胎儿生长受限或羊水过少;⑪早发型即妊娠34周以前发病。入组病例为单胎产妇,无原发性高血压、肝肾疾病及其他影响血脂代谢的疾病无其他妊娠合并症和并发症。

1.3 方法

受检者于入院第2天取空腹清晨肘静脉血3 mL,置于含抗凝剂的试管内,静置30 min后分离血浆,采用美国贝克曼DxC800全自动生化分析仪测定TG、TC、LDL、HDL、ApoA、ApoB;计算动脉粥样硬化指数(AI)=[$(TC-HDL)/HDL$]、LDL/HDL、ApoB/ApoA,同时收集患者身高、体质量,计算BMI。

1.4 统计方法

采用SPSS16.0软件进行统计学处理,定量数据结果以均数 \pm 标准差($\bar{x} \pm s$)表示,统计采用单因素方差分析,通过LSD-test进行均数的两两比较;ROC曲线分析指标诊断价值及其敏感性、特异性。 $P < 0.05$ 为差异有统计学意义。

2 结果

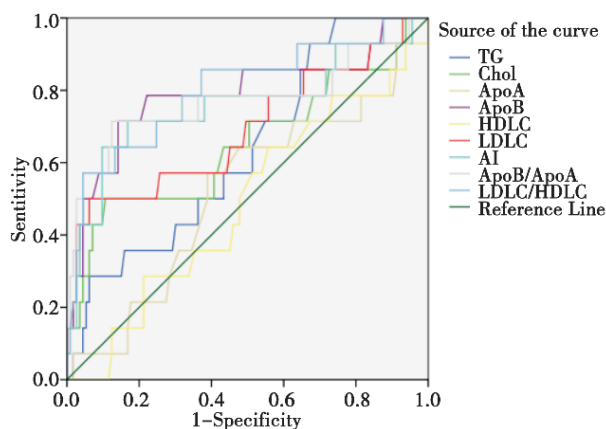
2.1 子痫前期组与正常妊娠组各血脂水平比较

各子痫前期组TC、TG、LDL、ApoB、AI、LDL/HDL、ApoB/ApoA均高于正常妊娠组,其中早发型重度子痫前期组各指标早发现差异有统计学意义($P < 0.05$);轻度子痫前期及晚发型重度子痫前期组TC、HDL、ApoA、LDL指标差异无统计学意义($P > 0.05$),AI、ApoB/ApoA、LDL/HDL指标差异有统计学意义($P < 0.05$)。各子痫前期组ApoA、HDL低于正常妊娠组,差异无统计学意义($P > 0.05$)。轻度子痫前期、晚发型重度子痫前期、早发型重度子痫前期TC、ApoB、LDL、AI、L/HDL、ApoB/A水平呈逐步上升趋势(表1)。

2.2 各子痫前期分型组间血脂水平比较

早发型重度子痫前期组与晚发型重度子痫前期、轻度子痫前期组间比较,ApoB、LDL、AI、LDL/HDL、ApoB/ApoA水平明显升高,差异均有统计学意义($P < 0.05$);TG、ApoA、HDL组间

差异无统计学意义($P > 0.05$)。晚发型重度子痫前期与轻度子痫前期组比较, TG、TC、ApoB、LDLC、AI、L/HDL、ApoB/A 水平升高, 差异无统计学意义($P < 0.05$; 表 1)。



Area under the ROC curves for predicting severe early onset preeclampsia in the indices of ApoB, LDLC, AI, LDLC/HDL, ApoB/ApoA were 0.79, 0.69, 0.76, 0.77, and 0.80 ($P < 0.05$).

图 1 各血脂指标预测早发型重度子痫前期 ROC 曲线分析
Fig.1 ROC curve analysis of each lipid indexes predictive value in ES-PE

2.3 ApoB、LDLC、AI、LDLC/HDL、ApoB/ApoA 指标

用于预测早发型重度子痫前期 ROC 曲线下面积分别为 0.79、0.69、0.76、0.77、0.80 ($P < 0.05$, 图 1)。

3 讨论

3.1 妊娠期血脂代谢变化情况

正常孕妇在妊娠期常伴有血脂的代谢变化, 胎儿的发育、胎脂储备、产程体能消耗、产后哺育等都必须大量脂肪储存, 因此 TC、TG、HDL、LDLC、ApoA、ApoB 水平均会升高, 表现为生理性高血脂状态, 至产褥期恢复正常^[4-5]。其意义在于帮助母体减少糖原消耗, 储备足够的能量保证胎儿的正常生长发育。但正常孕妇并不会因此而发生血管病变, 原因在于正常孕妇体内存在着对抗血管病变的保护性机制。目前认为 ApoB/ApoA、LDLC/HDL 比值为动脉粥样硬化危险因子, 反映血管病变的危险性, 正常妊娠时虽 HDLC、LDLC、ApoA、ApoB 水平均会升高, 但 ApoB/ApoA、LDLC/HDL 比值并无明显变化, 从而保持一定的均衡关系, 避免血管内皮损伤, 故不易发生血管动脉粥样硬化病变^[6-7]。

3.2 血脂水平与子痫前期

子痫前期的主要发病机理是内皮细胞激活和损伤, 脂质过氧化物和炎症细胞因子是导致内皮损伤的主要原因。子痫前期患者血清中 TG 和 LDLC 明显升高, 增强脂质过氧化作用, 导致脂质过氧化物增多, 脂质过氧化物及其产生的自由基直接引起血管内皮细胞损伤, 使血管内皮收缩因子血栓素 A2 释放增加, 出现血管痉挛收缩等病理改变导致血压升高。HDL 是血液中胆固醇以及磷脂的运输形式, 有助于乳糜微粒和极低密度脂蛋白胆固醇的合成, 阻止自由胆固醇积累在动脉壁和其他组织中, 有从血管壁清除脂质的作用, 子痫前期患者 HDLC 低于正常孕妇, 其减低血管的胆固醇转运减少, 对血管的保护作用减低, 促使血

表 1 各组间血脂水平单因素方差分析结果

Table 1 Single factor analysis of variance of serum lipid levels among groups

| Index/group | Control | M-PE | LS-PE | ES-PE | F | P |
|-------------|-------------|---------------------------|---------------------------|-------------------------------|-------|------|
| TG | 2.99 ± 0.13 | 3.52 ± 0.16 | 4.0 ± 0.30 ²⁾ | 3.41 ± 0.35 | 5.02 | 0.00 |
| TC | 6.67 ± 0.29 | 6.10 ± 0.17 | 6.39 ± 0.30 | 7.18 ± 0.71 ³⁾⁵⁾ | 2.74 | 0.04 |
| ApoA | 1.74 ± 0.03 | 1.74 ± 0.04 | 1.68 ± 0.05 | 1.71 ± 0.14 | 0.32 | 0.81 |
| ApoB | 1.23 ± 0.06 | 1.26 ± 0.04 ¹⁾ | 1.32 ± 0.35 ²⁾ | 1.53 ± 0.15 ³⁾⁵⁾⁶⁾ | 12.8 | 0.00 |
| HDL | 1.71 ± 0.04 | 1.54 ± 0.04 ¹⁾ | 1.56 ± 0.08 | 1.58 ± 0.13 | 2.3 | 0.08 |
| LDLC | 3.63 ± 0.09 | 3.84 ± 0.15 | 4.0 ± 0.24 | 4.9 ± 0.59 ³⁾⁵⁾⁶⁾ | 4.61 | 0.00 |
| AI | 2.59 ± 0.07 | 3.12 ± 0.16 ¹⁾ | 3.27 ± 0.18 ²⁾ | 4.11 ± 0.84 ³⁾⁵⁾⁶⁾ | 8.84 | 0.00 |
| L/HDL | 2.17 ± 0.05 | 2.62 ± 0.14 ¹⁾ | 2.6 ± 0.14 ²⁾ | 3.56 ± 0.73 ³⁾⁵⁾⁶⁾ | 9.70 | 0.00 |
| ApoB/A | 0.63 ± 0.01 | 0.77 ± 0.04 ¹⁾ | 0.81 ± 0.04 ²⁾ | 1.04 ± 0.21 ³⁾⁵⁾⁶⁾ | 10.52 | 0.00 |

1) $P < 0.05$; Control group vs M-PE group; 2) $P < 0.05$; Control group vs LS-PE group; 3) $P < 0.05$; Control group vs ES-PE group; 4) $P < 0.05$; M-PE group vs LS-PE group; 5) $P < 0.05$; M-PE group vs ES-PE group; 6) $P < 0.05$; ES-PE group vs LS-PE group.

管发生急性粥样硬化病变^[8-9]。ApoA、ApoB 分别是高密度脂蛋白 HDLC 和低密度脂蛋白 LDLC 的主要载体蛋白。ApoA 和 HDLC 是抵御血管粥样硬化的保护因素,而 ApoB 和 LDLC 是致血管粥样硬化的危险因素^[10-12]。Singh 等^[13]对比了 50 例子痫前期患者及正常妊娠妇女血脂水平,发现子痫前期组动脉粥样硬化指数(AI)明显高于正常妊娠组。本研究发现,在妊娠期晚期,相对于正常妊娠组,各类型子痫前期组 LDLC、ApoB、TC 水平均升高,而 HDLC、ApoA 水平降低。在轻度子痫前期及晚发型重度子痫前期中,TC、HDLC、ApoA、LDLC 水平与正常妊娠组比较虽差异无统计学意义,但 AI、ApoB/ApoA、LDLC/HDLC 指标差异有显著统计学意义,提示脂质成分代谢紊乱,脉粥样硬化保护因子与危险因子的比值失衡在子痫前期疾病发生中起更为重要的作用。在各子痫前期分型比较中,早发型重度子痫前期组与轻度子痫前期、晚发型重度子痫前期组比较,LDLC、ApoB、TC、AI、ApoB/ApoA、LDLC/HDLC 水平进一步升高,组间差异有显著统计学意义;而晚发型重度子痫前期与轻度子痫前期组比较各血脂指标差异则无统计学意义,提示着早发型重度子痫前期中存在着更为显著的脂代谢紊乱。Shenhav^[14]认为,早发型子痫前期与晚发型子痫前期存在不同发病机制,早发型存在绒毛浸润的障碍,导致胎盘的浅着床、胎盘血栓形成、功能障碍,由此导致的全身血流动力学改变,造成孕妇全身各主要脏器功能损害,与脂肪氧化代谢缺陷密切相关;而晚发型者,胎盘功能改变较小,为机体系统性疾病,其发生过程更象是机体与疾病之间一个长期耐受最终失衡的温和过程。本研究结果亦支持上述理论,血脂代谢异常在早发型重度子痫前期疾病发生发展中有更大贡献。

3.3 血脂指标在子痫前期疾病诊断中的预测价值

本研究资料显示,在轻度子痫前期及迟发型重度子痫前期中,TC、HDLC、ApoA、LDLC 水平与正常妊娠组比较虽差异无统计学意义,但 AI、ApoB/ApoA、LDLC/HDLC 指标差异有显著统计学意义。血脂成分比值 AI、ApoB/ApoA、LDLC/HDLC 子痫前期发生风险评估中优于单个血脂指标。血脂代谢异常在早发型重度子痫前期中更为显著,ApoB、AI、LDLC/HDLC、ApoB/ApoA 指标用于预测早发型重度子痫前期 ROC 曲线下面积分别为 0.79、0.76、0.77、0.80, $P < 0.05$,对该疾病有较好

诊断价值,但各指标仍未能取得较理想的截断值以预测疾病的发生、发展。

综上所述,血脂代谢异常参与了子痫前期疾病的发生发展,且与疾病严重程度相关,尤其在早发型重度子痫前期发生中有重大意义。对于妊娠中期即出现脂质代谢异常的孕妇,应及早进行干预,通过正确的饮食生活指导,积极随访监测其血脂变化,尽量减低子痫前期的发生。对于存在严重高脂血症孕妇应高度警惕罹患早发型子痫前期的可能,应予密切监测并积极干预。子痫前期的发病机制无法用一元化理论阐明,它受多种因素影响。各血脂指标对早发型重度子痫前期有一定诊断意义,但目前仍未能取得理想截断值,尚有待进一步大样本临床研究。

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