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妊娠期糖尿病视网膜病变的危险因素

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[摘要] 目的: 分析妊娠糖尿病(gestational diabetes mellitus, GDM)视网膜病变的危险因素, 为临床防治提供依据。方法: 选取郑州大学第一附属医院产前检查的10 172例孕妇, 其中103例孕妇(A组)GDM伴糖尿病视网膜病变(diabetic retinopathy, DR), 108例(B组)孕妇GDM不伴DR, 101例(C组)正常孕妇。分别在妊娠6个月、9个月和产后6个月检查3组孕妇眼底、糖化血红蛋白(HbA1c)、24 h尿微量白蛋白(24-hour urine microalbumin, 24hALB)。结果: 单因素方差分析结果显示HbA1c和24hALB水平在妊娠6个月、9个月和产后6个月均为A组>B组>C组($P<0.05$)。拟合非条件logistic回归模型的多因素分析结果显示病程 ≥ 9 个月的患者发生DR的风险是病程 <9 个月者的5.47倍; HbA1c(界值为6.22%)和24hALB(界值为7.15 mg/L)水平较高的GDM患者, 其合并DR的风险较高, OR值分别为5.12和3.43。结论: 妊娠会促进DR进展, 病程进展、HbA1c及24hALB增高是视网膜病变加重的警示灯。密切监测及控制血糖、HbA1c及24hALB能有效减少或减轻糖尿病孕妇视网膜病变。

[关键词] 视网膜病变; 糖化血红蛋白; 24 h尿微量白蛋白

Risk factors of retinopathy in gestational diabetes mellitus

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Abstract **Objective:** To evaluate the risk factors for retinopathy in gestational diabetes mellitus (GDM). **Methods:** A total of 10 172 pregnant women were screened for GDM at the First Affiliated Hospital of Zhengzhou University, in which 103 women diagnosed with GDM and diabetic retinopathy (DR) were classified into group A, 108 women diagnosed with GDM without DR were classified into group B, and 101 healthy pregnant women were classified into group C. Fundus photography, glycosylated hemoglobin (HbA1c) and 24-hour urine microalbumin (24hALB) examinations at gestational 6 months, 9 months, and postpartum 6 months, were performed on all study participants. **Results:** One-way ANOVA indicated that HbA1c and 24hALB levels were highest in group A, followed by groups B and C, respectively, at all three time points ($P<0.05$). The multivariate analysis with unconditional logistic regression model showed that the risk of DR occurrence was 5.47 times higher in patients

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with GDM ≥ 9 months as compared to those with GDM < 9 months. Patients with higher levels of HbA1c and 24hALB had relatively higher risk of DR, with OR values of 5.12 and 3.43, respectively. **Conclusion:** Pregnancy could exaggerate the progress of DR. Long-term GDM, and higher levels of HbA1c and 24hALB are indicators for exaggeration of DR. Close surveillance and strict control of blood glucose would help to effectively reduce or alleviate DR in patients with GDM.

Keywords gestational diabetes mellitus; diabetic retinopathy; glycosylated hemoglobin; 24-hour urine microalbumin

妊娠糖尿病(gestational diabetes mellitus, GDM)是指妊娠后才发生或首次发现的糖尿病^[1]。GDM对母子危害极大,而糖尿病视网膜病变(diabetic retinopathy, DR)是糖尿病常见且严重的微血管并发症之一,主要有视物模糊和视力下降,部分患者有颜色识别能力障碍及眼内压增高引起疼痛等临床表现,严重者可导致后天性失明^[2]。随着近年来生活水平的提高,GDM的患病率也逐步上升,其DR的患病率和致盲率也呈逐年增高趋势^[3-4]。妊娠期糖尿病合并DR的病理生理关系纷繁错杂,如不及时警惕,可能致盲。为提高孕妇生活质量及预防DR的发生发展,本研究对GDM患者进行眼科随访及监测HbA1c, 24 h尿微量白蛋白(24-hour urine microalbumin, 24hALB),以探讨GDM患者视网膜病变的发生、进展及预后。

1 对象与方法

1.1 对象

选取郑州大学第一附属医院妇产科2014年6月至2016年10月产前检查的10 172例孕妇,经常规体检及糖尿病筛查后,884例确诊为GDM。GDM患者进行眼科眼底检查发现:129例合并DR,755例GDM不伴DR。将129例GDM合并DR者设为A组,分别从同期GDM不伴DR者和健康孕妇中,按照年龄 ± 2 岁进行1:1配对,分别为B组和C组。所有研究对象签署知情同意书,研究获得郑州大学第一附属医院医学伦理委员会批准。随访过程中,排除流产、早产、失访、资料不完整病例及并发其他疾患者,最终A组余103例,年龄(28.31 ± 6.05)岁;B组余108例,年龄(27.29 ± 3.21)岁;C组余101例,年龄(27.81 ± 5.41)岁。3组年龄、孕次、产次差异无统计学意义($P > 0.05$)。

1.2 方法

所有纳入对象除接受定期产检外,在孕6个月、9个月和产后6个月均接受直接检眼镜检查、眼底照相,并进行HbA1c, 24hALB检查。视网膜病变分级依照DR分级标准^[5],GDM确诊依据文献^[6-7]的诊断标准。

1.3 统计学处理

采用SPSS 19.0统计学软件进行数据分析。组间比较用单因素方差分析,均数两两比较采用重复测量方差分析;以发生DR为应变量,其他变量为自变量,拟合非条件logistic回归模型,计算比值比(odds ratio, OR)及其95%可信区间(95% confidence interval, 95%CI),进行多因素分析。显著性水平采用双侧检验($\alpha = 0.05$)。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 A组妊娠6个月、9个月和产后6个月眼底的改变

在103例中,妊娠6~9个月时27例(26.20%)发生DR进展和加重,包括21例DR1进展到DR2,4例DR2进展到DR3,2例DR3进展到DR4,1例DR3进展到DR5;孕妊娠9个月至到产后6个月44例(42.72%)DR减轻,包括17例DR1完全消失,18例DR2缓解为DR1,6例DR3缓解为DR2,2例DR4和1例DR5在接受视网膜激光治疗术后正常。B组15例(13.89%)在妊娠9个月时从无DR进展至DR1,产后6个月时消失。C组中无DR发生(表1)。

2.2 妊娠6个月、9个月和产后6个月的HbA1c改变

HbA1c水平在妊娠6个月、9个月和产后6个月时,均为A组>B组>C组,差异有统计学意义($P < 0.05$,表2)。

2.3 妊娠6个月、9个月和产后6个月的24hALB改变

24hALB在妊娠6个月、9个月和产后6个月时的表达水平均为A组>B组>C组, 差异有统计学意义($P<0.05$, 表3)。

2.4 GDM合并DR的危险因素

以年龄、病程、妊娠9个月时HbA1c, 24hALB

等因素拟合logistic回归模型, 结果示: 病程 ≥ 9 个月的患者发生DR的风险是病程 <9 个月者的5.47倍; HbA1c和24hALB水平较高的GDM患者, 其合并DR的风险较高, OR值分别为5.12和3.43。提示病程、HbA1c和24hALB可能是糖尿病患者发生视网膜病变的独立危险因素(表4)。

表1 A组于妊娠6个月、9个月和产后6个月的眼底病变程度分布

Table 1 Distribution of fundus lesions in group A among 6 months in pregnancy, 9 months in pregnancy and 6 months after postpartum

时间	患者数				
	DR1	DR2	DR3	DR4	DR5
孕6个月	73	17	13	—	—
孕9个月	52	34	14	2	1
产后6个月	53	22	8	—	—

表2 妊娠6个月、9个月和产后6个月的HbA1c水平比较

Table 2 Comparison of HbA1c levels among 6 months in pregnancy, 9 months in pregnancy and 6 months after postpartum

组别	HbA1c水平/%		
	妊娠6个月	妊娠9个月	产后6个月
A组	8.52 ± 2.71	9.35 ± 3.00	6.22 ± 1.87
B组	6.33 ± 2.02	7.54 ± 1.99	5.63 ± 1.42
C组	5.17 ± 1.33	5.12 ± 1.48	4.14 ± 1.33
F	67.152	90.888	15.54
P	0.02	<0.01	0.02

表3 妊娠6个月、9个月和产后6个月的24hALB水平比较

Table 3 Comparison of ALB levels of 24 hours among 6 months in pregnancy, 9 months in pregnancy and 6 months after postpartum

组别	24hALB/(mg·L ⁻¹)		
	妊娠6个月	妊娠9个月	产后6个月
A组	8.38 ± 1.79	9.00 ± 2.54	6.99 ± 1.87
B组	6.31 ± 1.29	7.14 ± 2.01	6.20 ± 1.35
C组	5.44 ± 1.58	5.44 ± 1.66	5.41 ± 1.54
F	5.21	8.74	13.02
P	<0.01	0.01	0.01

表4 GDM患者发生DR的危险因素多因素分析结果

Table 4 Multivariate analysis of risk factors for DR in GDM patients

研究因素	发生DR(n=103)	未发生DR(n=108)	OR*	95%CI
病程/月				
<9	36	81	1.00	—
≥9	67	27	5.47	2.13~11.11
HbA1c/%				
<6.22	42	84	1.00	—
≥6.22	61	24	5.12	2.14~10.22
24hALB/(mg·L ⁻¹)				
<7.15	49	82	1.00	—
≥7.15	54	26	3.43	1.43~6.32

*P<0.05.

3 讨论

GDM发生率为1%~14%^[8],对母婴的健康可能造成严重危害。DR是糖尿病常见的微血管病变之一,是成人后天性致盲的主要原因,其确切的发病机制目前尚未明确。现已知慢性血糖升高引起机体多种生理、生化改变,对于眼底微血管相继造成微血管瘤、小出血点,硬性渗出,棉絮状软性渗出,新生血管形成、玻璃体积血,显微血管增殖、玻璃体机化,最终因纤维组织牵拉引起视网膜脱离、失明的恶性后果^[9]。本次通过病例对照研究发现妊娠时程、HbA1c及24hALB水平升高是GDM视网膜病变发生的危险因素。

妊娠时程是DR进展的重要危险因素。妊娠期5%~10%的1型糖尿病孕妇由无视网膜病变或背景性视网膜病变(background diabetic retinopathy, BGDR)进展为增殖性糖尿病视网膜病变(proliferative diabetic retinopathy, PDR)^[10-12]。本研究结果显示GDM病程越长,DR的患病率越高,发生视网膜病变的危险更大。因此,DR的发生、发展与GDM的妊娠时程呈正相关。HbA1c可反映机体2~3个月的平均血糖,是衡量GDM治疗方案及GDM病情的最佳指标^[13]。在长期高血糖状况下,机体血红蛋白中的HbA1c比例不断增高,血红蛋白与2,3-二磷酸甘油酸的结合受到阻碍,导致红细胞的携氧量降低。同时由于HbA1c对于氧的亲合力要大于正常的血红蛋白,导致氧在视网膜等外周组织的释放障碍,长期低氧引起血液中其他组分的改变及视网膜微循环结构的损害,因此HbA1c水平增高可加重视网膜缺血缺氧,加

重视视网膜组织病变^[14-17]。有研究^[18-21]报道妊娠妇女的HbA1c可能受妊娠因素其值的变化波动更大,加速上述生理过程的发生,甚至建议将其参考值上调有可能更好地控制血糖及预防低血糖的发生。

本研究结果也证实:GDM合并DR的发生发展与HbA1c高水平呈正相关。因此应严格控制血糖,使糖基化血红蛋白维持在理想水平,可有效地防止DR的发生发展。尿中微量白蛋白是衡量GDM肾血管病变的指标,同样反映GDM微血管病变程度,其异常变化可能出现在视网膜病变之前,以帮助衡量以及预示GDM视网膜病变^[22-23]。本研究结果提示24hALB增多出现于视网膜病变之前,可以用来提示眼底的病变。因此,GDM患者应每月筛查眼底病变,及早发现GDM视网膜病变,对于眼底病变较轻者,每2个月筛查尿中的微量白蛋白、每3个月筛查HbA1c,可以及早发现病变。对于眼底病变严重的及时进行视网膜激光治疗,以控制病变发展。

本实验研究尚存在一些不足,即样本筛选并未排除其他代谢性疾病及心脑血管疾病,因此对于妊娠前患有高血脂或原发性高血压或其他心脑血管疾病的GDM患者,其血压、血脂是否对视网膜病变程度及发展有影响,高血压、高血脂是否与高血糖有协同作用,还有待进一步探究。

综上所述,有众多因素影响GDM患者视网膜病变,其中以病程长、HbA1c水平升高、24hALB的增多为主要危险因素。因此我们可对GDM患者定期进行眼底、24hALB及HbA1c检查,及时做好防治,以减少或延缓GDM视网膜病变的发生进展。

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