早发型与晚发型重度子痫前期的临床表现及母婴结局的对比分析*

钱 卫 周 倩 刘憬兰 蔡兰娣 程蔚蔚△

(上海交通大学医学院附属国际和平妇幼保健院产科 上海 200030)

摘要 目的:探讨早发型与晚发型重度子痫前期的不同临床表现及母婴结局,提高对重度子痫前期的临床认识。方法:回顾性分析重度子痫前期患者76例,按照不同的发病孕周,分为早发型(发病孕周<32周)和晚发型(发病孕周≥32周),比较两组孕妇临床情况、孕妇的并发症及围产儿结局。结果:早发型孕妇与晚发型孕妇在上述方面比较,差异均具有统计学意义(P<0.05),早发型孕妇的各项临床表现显著差于晚发型孕妇。结论:对早发型重度子痫前期孕妇,更应加强临床各项监护措施,选择理想的终止妊娠的时机,同时加强预防措施,避免早发型重度子痫前期的发生。

关键词:早发型;晚发型;重度子痫前期;临床表现;母婴结局

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Comparative Analysis of Clinical Manifestations and Maternal and Neonatal Outcomes of Pregnant Women with Early- and Late-Onset Severe Pre-eclampsia*

QIAN Wei, ZHOU Qian, LIU Jing-lan, CAI Lan-di, CHENG Wei-wei △

(Department of Obstetrics, Affiliated International Peace Maternity &Child Health Hospital Medical College of Jiaotong University, Shanghai 200030, China)

ABSTRACT Objective: To observe the the different clinical manifestations and perinatal outcome about early onset and late onset severe pre-eclampsia and research improve the clinical awareness about severe pre-eclampsia.Method:Retrospective analysis 76 patients with severe pre-eclampsia,according to the different incidence of gestational age,they were divided into the early onset group(<32 weeks) and the late onset group(≥32 weeks),then compare the clinical conditions,the complications of pregnant women and the perinatal outcomes.Result:There was a statistical significant (P<0.05) in the above respects,the early onset group's clinical manifestations was statistical bad than late onset group's.Conclusion:For the early onset severe preeclampsia pregnant women,we should strengthen the clinical monitoring measures,select the desired time of termination of pregnancy,while we should strengthen the measures to prevent early onset severe preeclampsia occurs.

Key words: Early onset;Late onset;Severe pre-eclampsia;Clinical manifestations;Maternal and neonatal outcomes

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前言

重度子痫前期是不明病因的特异性、多系统妊娠疾病,严重威胁着母婴健康,导致孕妇和围产儿病死率增高,重度子痫前期是产科并发症,其发生率为14.2%[1-2]。国内外多数学者将重度子痫前期分为早发型(early onset severe pre-eclampsia)和晚发型(late onset severe pre-eclampsia)[3]。到目前为止,终止妊娠是治愈重度子痫前期的唯一方法,对于已接近预产期的晚发型者,由于胎儿已接近或达到成熟,立即终止妊娠对孕妇和胎儿皆有益无害[4]。但早发型重度子痫前期患者,其临床以发病早、进展迅速、靶器官损害出现早且症状重为特点,若治疗时间短,终止妊娠必将因胎儿不成熟导致围产儿死亡率增加;若长期期待治疗则有增加孕妇发生各种严重并发症的危险。因此,对早发型重度子痫前期患者进行临床分析,显得十分必要[5]。作者探讨了早发型与晚发型重度子痫前期的不同临床表现及母婴结局,旨在提高对重度子痫前期的临床认识,现报告如下。

作者简介:钱卫(1969-),女,主治医师,研究方向:病理产科

△通讯作者:程蔚蔚,电话:021-64070434-26608,研究方向:产科,高危产科;e-mail:littleone.1998@yahoo.com.cn

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1 资料与方法

1.1 一般资料

回顾性分析2009年6月~2011年2月期间,在我院住院治疗的重度子痫前期患者76例,诊断标准符合《Williams Obstetrics》关于重度子痫前期的诊断标准[6],上述孕妇均为单胎初产妇,且均无高血压、糖尿病、肾炎、甲状腺功能亢进等内科疾病病史,按照发病孕周的不同,分为早发型和晚发型。早发型孕妇32例,发病孕周<32周,晚发型孕妇44例,发病孕周≥32周。两组孕妇就诊时,将其临床情况进行统计并比较,见表1。

1.2 治疗方法

上述两组孕妇入院时,即完善各项相关检查,包括血尿常规、肝肾功能常规检查、24h尿蛋白定量、心电图、B超检查、电解质及凝血功能检查等,治疗原则以休息、镇静、解痉为主,根据患者具体病情,根据产妇具体血压情况,给予降压治疗,必要

时给予利尿剂。解痉治疗选择硫酸镁，首次剂量为 5g 负荷量静脉滴注，30～60min 滴完，然后以 1～2g/h 静脉滴注维持。上述孕妇均采取密切的临床护理及观察，定时进行血压监测、肝肾功能检查及尿蛋白检测 ;加强对胎儿的动态观察，包括检查胎儿每日的胎动和胎心率、超声多普勒脐带血流变化及胎儿的生长情况。对于早发型孕妇采取期待疗法，即在密切监护母胎情况下尽量延长孕周，促进胎儿的生长。若治疗效果不明显或病情恶化时，应积极终止妊娠，在终止妊娠前给予地塞米松 10mg 肌肉注射，1 次 /d，连续使用 2d，以促进胎儿肺成熟。

1.3 观察内容及临床评价标准

两组孕妇入院时，进行相关临床检查，并记录两组孕妇年龄、发病孕周、分娩孕周、治疗时间、收缩压、舒张压和 24h 尿蛋白定量，统计后进行比较；记录两组孕妇并发症情况，包括：HELLP 综合征、肝肾功能损害、低蛋白血症、心功能不全、尿蛋白≥(++)、胎盘早剥和凝血功能异常，HELLP 综合征诊断标准为[7]：(1)溶血：外周血涂片见变形红细胞 ;乳酸脱氢酶(LDH)＞600U/L ;总胆红素(TBIL)＞17μmol/L ;(2)天冬氨酸转氨酶(AST)或丙氨酸转氨酶(ALT)＞70U/L ;(3)血小板＜100×10⁹/L ;记录两组孕妇围产儿结局，包括：胎儿生长受限、新生儿体重、低出生体重儿、新生儿窒息、Apgar 评分≤7 分和围生儿死亡，出生时体重＜2500g 计为低出生体重儿，Apgar 评分方法为新生儿产后 1min 按照临床相关评判标准进行评价[8]。

1.4 统计学方法 两组孕妇以上临床观察内容记录所得的计数数据采用百分率表示，计量数据采用 $\bar{X}\pm S$ 表示，使用 spss16.0 软件行 x^2 检验和 t 检验，以 $P<0.05$ 计为差异具有统计学意义。

2 结果及分析

2.1 两组孕妇入院时及一般临床情况比较

两组孕妇年龄比较，$P>0.05$，差异无统计学意义 ;发病孕周、分娩孕周、治疗时间、收缩压、舒张压和 24h 尿蛋白定量比较，均 $P<0.05$，差异具有统计学意义。见表 1。

表 1 两组孕妇入院时及一般临床情况比较($\bar{X}\pm S$)

Table 1 Comparison of the general clinical condition in two groups

Groups	Cases	Age(years)	Incidence of gestational age (weeks)	Childbirth of gestational age (weeks)	Treatment time (days)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	24h urine protein(mg)
early onset group	32	27.6± 2.6	28.1± 2.7	31.4± 3.1	13.5± 3.3	174.2± 25.6	112.8± 13.6	7531.7± 2013.4
late onset group	44	26.8± 2.2	35.4± 3.2	37.6± 4.0	7.5± 1.8	161.3± 20.7	102.5± 10.3	4177.8± 1562.8
t value		0.411	1.703	1.715	1.955	1.695	1.682	2.033
P		P＞0.05	P＞0.05	P＞0.05	P＞0.05	P＞0.05	P＞0.05	P＞0.05

2.2 两组孕妇并发症情况比较

两组孕妇发生 HELLP 综合征、肝肾功能损害、低蛋白血症、心功能不全、尿蛋白≥(++)、胎盘早剥和凝血功能异常并发症例数比较，均 $P<0.05$，差异具有统计学意义，晚发型孕妇上述并发症的发生率，显著少于早发型孕妇的发生率。见表 2。

表 1 两组孕妇入院时及一般临床情况比较($\bar{X}\pm S$)

Table 1 Comparison of the general clinical condition in two groups

Groups	Cases	HELLP syndrome	Liver and kidney dysfunction	Hypoproteine-mia	Heart failure	Urine protein≥(++)	Placental abruption	Coagulopathy
Early onset group	32	7(21.9%)	9(28.1%)	15(46.9%)	8(25.0%)	19(59.4%)	6(18.8%)	5(15.6%)
Late onset group	44	2(4.5%)	4(9.1%)	10(22.7%)	3(6.8%)	16(36.4%)	2(4.5%)	1(2.3%)
x^2value		5.329	4.734	4.894	4.947	3.949	3.969	4.542
P				P＞0.05				

2.3 两组孕妇的新生儿结局情况比较

两组孕妇的新生儿胎儿生长受限、新生儿体重、低出生体重儿、新生儿窒息、Apgar 评分≤7 分和围生儿死亡比较，均 $P<0.05$，差异具有统计学意义，晚发型孕妇新生儿结局显著好于早发型孕妇新生儿结局。见表 3。

表 3 两组孕妇的新生儿结局情况比较 [($\bar{X}$± S),(n,%)]

Table 3 Comparison of the neonatal outcomes in two groups

Groups	Cases	Fetal growth restriction	Birth weight	Low birth weight children	Asphyxia	Apgar score ≤7 分	Death of perinatal children
Early onset group	32	17(53.1%)	1983.6± 387.5	20(62.5%)	11(34.4%)	13(40.6%)	9(28.1%)
Late onset group	44	13(29.5%)	2335.4± 413.7	16(36.4%)	6(13.6%)	8(18.2%)	4(9.1%)
x^2 value and t value		4.311	2.016	5.076	4.589	4.667	4.734
P				P＞0.05			

3 讨论

子痫前期 - 子痫是妊娠期特有的严重并发症，常常累及心、脑、肾和胎盘等重要器官，引起这些终末耙器官损害。尤其是发生较早的早发型重度子痫前期，存在着最为尖锐的母胎之间的利益冲突，严重影响着母婴的生命安全[9]。目前国内外尚无早发型重度子痫前期的统一分类标准。多数学者认为妊娠 32 周前发病与妊娠 32 周以后发病的重度子痫前期临床特征有所不同，因此将 32 周之前发病者称为早发型重度子痫前期，32 周以后发病者称为晚发型重度子痫前期[10-11]。

早发型重度子痫前期对患者的危害很大，轻者可以对孕妇的肝、肾、脑、凝血系统等多器官系统造成损害并对生命造成危险，重者还会造成胎盘血栓形成，组织缺血坏死从而危害胎儿。它的临床特点有：⑴ 重度妊娠早中期即发生蛋白尿、高血压；且随着妊娠进展，血压越来越高且增高的幅度较大，尿蛋白出现的早而且量也比较高；⑵ 并发症比较多，常常合并胎儿生长受限(FGR)等；⑶ 围生期结果一般很差；⑷ 孕妇一般都能自觉感觉到；⑸ 容易对靶器官造成损害；⑹ 容易复发，临床风险较高[12]。目前认为子痫前期的发病机制可用一元化理论阐明，即遗传背景下母胎免疫耐受异常 - 滋养细胞侵袭能力降低、胎盘浅着床 - 胎盘缺血缺氧 - 脂质过氧化 - 毒性物质释放 - 血管内皮细胞损伤或激活 - 临床症状。目前尚不能确定早发型子痫前期和晚发型存在不同的发病机制，但是随着研究的深入已发现早发型子痫前期的发病机制在许多环节上与晚发型呈现不同的特点[13]：⑴ Heikila 等[14]研究发现多肿瘤抑制物基因和生长调节基因在早发型子痫前期表达明显上调，其中最明显的有磷脂蛋白合成酶 2、phospholipid scramblase-1、转录延长因子和黑素瘤粘附分子；⑵ Kadyrov 等[15]发现早发型子痫前期患者的胎盘组织凋亡明显增加，滋养细胞侵入受限，胎盘着床较浅，螺旋型小动脉管腔狭窄，因此倾向于早发型重度子痫前期是一种胎盘疾病，而晚发型则可能与母亲因素有关；⑶ Zhong 等[16]研究发现早发型子痫前期血液中胎儿促肾上腺皮质激素释放激素 mRNA 明显增加，而晚发型患者增加不明显；⑷ Gupta 等研究发现[17]，血管内皮细胞功能受损的标志性产物在早发型子痫前期增加非常明显，其血浆弹性蛋白酶水平较晚发型明显增高。Itoh 等研究发现[18]，早发型患者抑制素水平明显高于晚发型患者。

作者通过对早发型与晚发型重度子痫前期的不同临床表现及母婴结局进行临床对比发现，早发型重度子痫前期孕妇的临床表现与母婴结局明显差于晚发型重度子痫前期孕妇，两者入院时及治疗后在发病孕周、分娩孕周、治疗时间、收缩压、舒张压和 24h 尿蛋白定量比较，差异均具有统计学意义 (P＜0.05)；两组孕妇发生 HELLP 综合征、肝肾功能损害、低蛋白血症、心功能不全、尿蛋白≥(++)、胎盘早剥和凝血功能异常并发症例数比较，差异均具有统计学意义(P＜0.05)；两组孕妇的新生儿胎儿生长受限、新生儿体重、低出生体重儿、新生儿窒息、Apgar 评分≤7 分和围生儿死亡比较，差异均具有统计学意义(P＜0.05)。因此，对于早发型重度子痫前期孕妇，更应加强临床各项监护措施，选择理想的终止妊娠的时机，在孕妇发生并发症的潜在危险性与新生儿生存能力间找到平衡点，妥善处理好早发型重度子痫前期患者，同时加强预防措施，避免早发型重度子痫前期的发生。

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