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低分子肝素对早发型重度子痫前期治疗对母婴结局的影响分析 *

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摘要 目的:探讨低分子肝素对早发型重度子痫前期治疗情况,并分析治疗对母婴结局的影响。**方法:**选择我院 2012 年 1 月～12 月收治的早发型重度子痫前期患者 120 例,随机分为观察组和对照组,每组 60 例。对照组给予常规治疗,观察组在对照组治疗基础上加用低分子肝素。比较两组血压、24 h 尿量、尿蛋白定量、尿酸、血常规、凝血功能及孕周延长时间、围产儿结局和产妇并发症。**结果:**两组患者临床指标无差异(P＞0.05),治疗后两组血压、24 h 尿量、尿蛋白定量均显著改善,观察组红细胞压积、纤维蛋白原降低明显高于对照组,而观察组患者的产妇并发症和围产儿不良结局发生率均低于对照组,且产妇孕周延长时间明显多于对照组,差异有统计学意义(P＜0.05)。两组患者的血小板、凝血酶原时间等治疗前后均无明显变化(P＞0.05)。**结论:**低分子肝素对早发型重度子痫前期的治疗能有效抑制高凝状态,改善肾功能,延长孕周时间,可有效减少患者并发症的发生,改善母婴预后,值得临床推广应用。

关键词:低分子肝素;早发型重度子痫前期;母婴结局;影响分析

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Low Molecular Heparin for the Treatment of Early Hairstyle Severe Preeclampsia Impact Analysis of Maternal and Infant Outcomes*

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ABSTRACT Objective: To discuss low molecular heparin for the treatment of early hairstyle severe preeclampsia, and analyze the treatment effects on maternal and infant outcomes. **Methods:** 120 patients with early hairstyle severe preeclampsia in our hospital from January 2012 to December were selected and randomly divided into observation group and control group, 60 cases in each group. Patients in control group were given conventional treatment, patients i in the control group were given low molecular heparin besides treatment in the observation group. 24 h blood pressure, urine output, quantitative, uric acid, blood routine, urine protein, blood coagulation function and gestational age to extend the time, maternal complications and perinatal outcome in two groups were compared. **Results:** Clinical indicators of patients were similar between the two groups (P＞0.05), blood pressure after treatment, 24 h urinary volume, urinary protein in two groups were significantly improved, of red blood cells deposited, fibrinogen decrease in observation group were significantly higher than those in the control group, patients with obstetric complications and the incidence of poor perinatal outcomes in the observation groupwere lower than those in the control group, and maternal gestational week was longer obviously than that in the control group, the difference was statistically significant (P＜0.05). Platelet, prothrombin time and others before and after treatment of patients in two groups had no significant change (P＞0.05).**Conclusion:** Low molecular heparin treatment for early hairstyle severe preeclampsia can effectively restrain high coagulation state, improve renal function, prolong gestational age, and also can effectively reduce the complications of patients, improve maternal and infant prognosis, thus is worthy of clinical popularization and application.

Keywords: Low molecular heparin; Early hairstyle severe preeclampsia; Maternal and neonatal outcomes; The impact analysis

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前言

子痫是孕产妇特有的疾病，是指怀孕前血压正常的孕妇在妊娠 20 周以后出现高血压、蛋白尿。是妊娠期高血压疾病的五种状况之一，为妊娠期特发疾病，可影响机体各器官系统。而早发型重度子痫前期发病孕周早，病情重，围生儿结局差，并发症和后遗症严重，所以临床上为保证母亲安全，采用终止妊娠来解除病因，造成人为的医源性早产，且孕产妇的用药严重受限，临床往往只能针对病理生理过程进行对症处理，治疗效果不佳[1]。因此探讨一种行之有效的治疗方法，在保证母亲安全的前提下尽量延长分娩孕龄，提高胎儿的生存能力迫在眉睫。我院妇产科在传统期待疗法的基础上联合应用低分子肝素治疗早发型重度子痫前期，效果满意，现报道如下。

1 材料与方法

1.1 一般资料

所有入选患者来自于我院 2012 年 1 月 -2012 年 12 月收治的早发型重度子痫前期患者，共 132 例，全部符合《妇产科学》第 7 版早发型重度子痫前期的诊断标准，且均为单胎妊娠，24h 内不会分娩，排除心血管、肝脏、肾脏、出血性等疾病，既往无肝素过敏史或过敏体质。随机分为观察组和对照组，观察组 60 例，年龄 20-38 岁，平均(28.1± 3.3)岁；孕周 30-33+4 周，平均(31.2± 1.4)周，其中初产妇 42 例，经产妇 18 例。对照组 60 例，年龄 21-39 岁，平均 (27.8± 3.6) 岁；孕周 30-34+3 周，平均(31.3± 1.5)周，其中初产妇 40 例，经产妇 20 例。两组患者的年龄、孕周、孕产次比较差异无统计学意义(P＞0.05)，具有可比性。

1.2 方法

对照组采用常规治疗方法，主要包括解痉、降压、扩容、镇静等保守治疗。采用硫酸镁解痉，给药方法：首次给药为硫酸镁 5 g 配合 5%葡萄糖溶液 100 mL 静脉滴注，之后改用硫酸镁 15g 配合 5%葡萄糖 500 mL 静脉滴注，在解痉基础上，予以低分子右旋糖酐氨基酸 500 mL，地西泮片 5 mg 口服，每日 1 次以镇静，疏通微循环，保证休息，当血压≥ 160/110 mmHg 时用氨氯地平 10 mg 口服，出现急性心力衰竭、水肿患者时用地塞米松 6 mg 每日 2 次，连用 2 d，促胎儿肺成熟[2]。观察组在对照组治疗的基础上加用低分子肝素 0.5 mL，皮下注射，2 次 /d，至少持续 5 d。用药前告知患者并签署知情同意书。必要时终止妊娠。

1.3 监测指标

入院时和入院治疗后的血压、24 h 尿量、尿蛋白定量、血常规及凝血功能，包括红细胞压积(HCT)、血小板计数(PLT)，凝血酶原时间(PT)，纤维蛋白原(Fib)等。并记录孕周延长时间、围生儿结局及产妇并发症后遗症[3]。

1.4 统计学分析

在本次研究过程中所得到的所有相关数据，均采用 SPSS 17.0 统计学数据处理软件进行处理分析，正态分布、方差齐性的计量资料用 $\bar{x}\pm s$，计量资料的比较用 t 检验，计数资料的比较用 x^2，P＜ 0.05 为差异有统计学意义。

2 结果

2.1 两组患者治疗前血压、24 h 尿量、尿蛋白定量比较

两组患者治疗前血压、24 h 尿量、尿蛋白定量比较差异均无统计学意义(P＞ 0.05)，治疗后两组的血压和尿蛋白定量均显著低于治疗前，且观察组治疗后血压和尿蛋白定量的改善效果优于对照组，比较差异有统计学意义(P＜ 0.05) 详见表 1。

表 1 治疗前血压、24 h 尿量、尿蛋白定量比较

Table 1 24 h blood pressure, urine output, the comparison of urine protein before treatment in two groups

Group	The number of cases	Blood pressure		P	Urine output		P	Urine protein quantitative		P
		Before the treatment	After the treatment		Before the treatment	After the treatment		Before the treatment	After the treatment	
Control	60	134.5± 7.9	118.3± 8.1	<0.05	1022.3± 111.3	2098.9± 159.5	<0.05	10.1± 4.1	7.9± 2.5	<0.05
Observation	60	135.2± 8.5	101.7± 8.4	<0.05	1024.1± 113.7	2762.2± 174.3	<0.05	9.1± 5.2	5.7± 3.1	<0.05
P		>0.05	<0.05		>0.05	<0.05		>0.05	<0.05	

2.2 两组患者治疗前后血常规及凝血功能指标比较

两组的血常规及凝血功能指标比较，治疗前后凝血酶原时间、活化部分凝血酶时间、血小板无显著变化(P＞ 0.05)，而观察组治疗后红细胞压积、D- 二聚体、纤维蛋白原与对照组比较明显下降，且观察组患者红细胞压积下降比对照组更为明显，两

表 2 两组患者治疗前后血常规及凝血功能指标比较

Table 2 Blood routine and blood coagulation function comparison before and after treatment in two groups

Group	The number of cases	PLT		P	HCT		P	PT		P
		Before the treatment	After the treatment		Before the treatment	After the treatment		Before the treatment	After the treatment	
Control	60	162.5± 9.3	168.4± 8.8	>0.05	56.7± 1.8	43.9± 2.5	<0.05	11.7± 1.3	11.9± 1.5	>0.05
Observation	60	165.4± 8.5	171.7± 9.4	>0.05	56.4± 3.1	35.2± 2.3	<0.05	12.1± 1.6	11.7± 1.1	>0.05
P		>0.05	>0.05		>0.05	<0.05		>0.05	>0.05	

Group	The number of cases	Fib(g/L)		P	D-Di(mg/L)		P
		Before the treatment	After the treatment		Before the treatment	After the treatment	
Control	60	6.5± 0.9	5.3± 0.8	＞0.05	3.5± 0.3	3.3± 0.5	＞0.05
Observation	60	5.9± 0.5	3.6± 0.8	＜0.05	3.6± 0.7	2.1± 0.3	＜0.05
P		＞0.05	＜0.05		＞0.05	＜0.05	

组比较差异有统计学意义(P＜0.05),具体见表2。

2.3 两组患者母婴结局比较

两组孕产妇孕周延长时间、围生儿结局及产妇并发症后遗症比较,观察组孕周延长时间明显多于对照组,围生儿结局优于对照组,并发症和后遗症明显少于对照组(P＜0.05)。详见表3。

表3 两组患者母婴结局比较

Table 3 Maternal gestational outcome in extension of the time, perinatals and maternal complications between two groups

Group	Gestational extend the number of days	Wai begat situation		Maternal conditions		
		Birth weight	Mortality rate	Postpartum blood loss	Deterioration of kidney function	Heart failure
Control	4± 1.5	1649.6± 112.7	3.3	147.4± 51.3	2	2
Observation	8± 1	1632.1± 118.4	0	136.3± 47.7	0	0
P	＜0.05	＞0.05	＜0.05	＞0.05	＜0.05	＜0.05

3 讨论

早发型重度子痫前期的患者,促凝因子和抗凝因子平衡失调使血液处于高凝状态,血管内皮细胞受损使血管内微血栓形成,导致各组织器官的灌流量降低和功能减退。早发型子痫前期患者器官受累出现时间早,并主要表现在胎盘组织等部位[4-7]。因此可以把抗凝治疗作为治疗早发型重度子痫前期新方法。本研究发现,在传统治疗的基础上联合运用低分子肝素,在改善患者症状、延长孕周时间、减少产妇并发症后遗症等方面优于传统治疗方法。

肝素是一种抗凝剂,是由两种多糖交替连接而成的多聚体,具有抗凝、抗炎、抗免疫反应、保护血管内皮等作用,而低分子肝素是普通肝素通过酶或化学解聚成的一类分子量较低的肝素总称[8-10]。相比普通肝素,具有与抗凝血酶Ⅲ结合抗活化凝血因子Ⅹa的作用,减少了对凝血因子Ⅱa的抑制作用,在达到有效抗血栓作用的同时,减少了出血等不良反应的发生;还能补充内源性肝素的不足,保护血管内皮的完整性;并且不通过胎盘,亦不分泌于乳汁中,在妊娠期及分娩期应用对胎儿安全[11,12]。另据文献报道,低分子肝素皮下注射,其生物利用度提高了75%-80%,半衰期也增加了2-4倍[13-15]。本文通过对比分析两组孕产妇的血压、24 h尿量、尿蛋白定量、尿酸、血常规、凝血功能及孕周延长时间、围产儿结局和产妇并发症,证明低分子肝素在治疗早发型重度子痫前期母婴的有效性和安全性。近年来国内外对早发型重度子痫前期的治疗普遍关注,保守治疗方法获得较大认可,治疗目的都是在保证母亲安全的前提下,尽可能延长孕周时间,提高胎儿成熟度,从而获得理想的母胎结局[16-19]。本统计分析显示,观察组血压、24h尿量、尿蛋白定量的改善情况明显优于对照组 (P＜0.05);HCT、Fib、D-Di水平有助于早发型重度子痫前期的辅助诊断和病情监测,结果显示观察组明显低于对照组(P＜0.05);孕周延长时间显著长于对照组(P＜0.05),表明对早发型重度子痫前期确实有药物作用;产后出血差异无统计学意义(P＞0.05),表明低分子肝素用药的安全性;产妇的并发症和围产儿不良结局显著减少(P＜0.05)。因此,笔者认为低分子肝素治疗早发型重度子痫前期能有效抑制高凝状态,改善肾功能,延长孕周时间,改善母婴结局。表明早发型重度子痫前期孕妇应用低分子肝素对改善其母婴结局有明显的作用[20]。

综上所述,低分子肝素对早发型重度子痫前期治疗是有效、安全的,其母婴结局好,未观察到新生儿畸形,产妇并发症及后遗症出现。但该实验规模、数量较小,还需要大规模、大数量、多中心的临床实验来验证。

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(下转第3093页)

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