· 临床研究 ·

先兆流产患者抗菌药物治疗介入时机对妊娠结局的影响

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摘要：目的　探讨有宫内感染高危因素的先兆流产患者应用抗菌药物的效果及介入时机对妊娠结局的影响。**方法**　回顾性调查郑州市妇幼保健院 2018 年 1 月至 2022 年 12 月有宫内感染高危因素的先兆流产患者 1 527 例，按是否应用抗菌药物分为用抗菌药物组（n=471）和未用抗菌药物组（n=1 056），分别观察其妊娠结局；并观察两组存在 1、2、≥3 个宫内感染高危因素时对妊娠结局的影响。**结果**　两组孕产妇的年龄、孕次、体质量指数（BMI）、孕周延长值、产褥感染率及新生儿的胎龄、出生体重差异无统计学意义（P>0.05）。用抗菌药物组新生儿存活率低于未用抗菌药物组（61.36% *vs* 82.39%，χ^2=78.735，P<0.01），存活新生儿中并发症发生率高于未用抗菌药物组（26.64% *vs* 10.57%，χ^2=44.973，P<0.01）。分层分析显示，有 1、2、≥3 个宫内感染高危因素时，两组新生儿存活率和并发症发生率比较差异无统计学意义（P>0.05）。**结论**　用与不用抗菌药物对新生儿结局总体有影响，但在合并不同数量宫内感染高危因素分层中无差异。

关键词：先兆流产；宫内感染；抗菌药物；妊娠结局
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Effect of timing of antimicrobial therapy intervention on pregnancy outcome in patients with threatened abortion

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Abstract: Objective　To investigate the effect of applying antimicrobial drugs and the timing of intervention on pregnancy outcome in patients with risk factors for threatened abortion combined with intrauterine infection. **Methods**　A retrospective survey of 1 527 patients with risk factors for threatened abortion combined with intrauterine infection from January 2018 to December 2022 in Zhengzhou Women & Infants Hospital was conducted, divided into the group with antimicrobial drugs (n=471) and the group without antimicrobial drugs (n=1 056) according to whether antimicrobial drugs were applied, and their pregnancy outcomes were observed separately. The impact of the presence of 1, 2, ≥3 intrauterine infection high-risk factors on pregnancy outcomes in both groups was also observed. **Results**　There was no statistically significant difference in the age, parity, body mass index (BMI), gestational age prolongation, postpartum infection rate of pregnant women, fetal gestational age, and birth weight between the two groups (P>0.05). The neonatal survival rate in the antimicrobial agent group was lower than that in the non-antimicrobial agent group (61.36% *vs* 82.39%, χ^2=78.735, P<0.01), and the rate of complications in surviving newborns was higher in the antimicrobial agent group compared to the non-antimicrobial agent group (26.64% *vs* 10.57%, χ^2=44.973, P<0.01). Stratified analysis showed no statistically significant differences in neonatal survival rates and complication rates when there were 1, 2, ≥3 intrauterine infection high-risk factors in both groups (P>0.05). **Conclusion**　There is an overall effect of

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using or not using antimicrobial drugs on neonatal outcome, but there is no difference in the stratification of different numbers of risk factors.

Keywords: Threatened abortion; Intrauterine infection; Antimicrobial drugs; Pregnancy outcome

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先兆流产患者合并宫内感染,特别是宫内感染无明显临床表现时,易被忽视,一旦出现明显的临床表现时已难以挽回,对母体、胎儿及新生儿造成较大危害,若不加区别的对所有先兆流产患者进行抗感染治疗,则会增加细菌耐药的风险,并造成医疗资源的浪费[1-2]。目前对有宫内感染高危因素的先兆流产患者是否给予抗菌药物治疗,临床持不同意见[3-4]。这对抗菌药物的合理应用和规范管理,造成一定的困扰。因此,本研究探讨合并几种宫内感染高危因素时,给予抗菌药物治疗对先兆流产患者妊娠结局的影响,为规范此类患者的抗菌药物治疗时机提供参考。

1　资料与方法

1.1　*一般资料*　本研究已由郑州市妇幼保健院伦理委员会批准(编号:ZZFY-LL-2020021)。选取郑州市妇幼保健院 2018 年 1 月至 2022 年 12 月有宫内感染高危因素的先兆流产患者进行回顾性调查。纳入标准:存在宫内感染高危因素的先兆流产孕妇,宫内感染高危因素包括异位妊娠史、生殖道微生物菌群异常、B 族溶血性链球菌携带、产前侵入性诊断操作、受孕前后感染疾病史(细菌性阴道病、滴虫阴道炎、盆腔炎、尿路感染、肠道感染)、宫内感染或产褥感染史、减胎术、孕前半年内盆腹腔手术史等[5-7]。排除标准:有生殖器结构异常(除外宫颈机能不全已手术者)、免疫功能异常、内分泌异常、全身性疾病、双胎及多胎妊娠、有明确临床感染指征者、近期有外伤史、近期使用糖皮质激素、强烈应激与不良习惯、精神刺激、环境因素等造成的先兆流产者。最终纳入 1 527 例。

1.2　*抗菌药物品种选择*　抗菌药物品种:阿莫西林胶囊+红霉素胶囊、氨苄西林针+红霉素针/阿奇霉素针、头孢西丁针、头孢唑林针/头孢呋辛针+甲硝唑针[4,8-9]。

1.3　*方法*　1 527 例病例按是否应用抗菌药物分为用抗菌药物组(n = 471)和未用抗菌药物组(n = 1 056),分别观察两组的妊娠结局(延长孕周、产褥感染率、围产儿死亡率、存活新生儿),并发症(新生儿呼吸窘迫症、脑室内出血、坏死性小肠结肠炎、新生儿败血症)发生率。按宫内感染高危因素个数分为存在 1 个(n = 693)、2 个(n = 531)、≥3 个(n = 303,3 个危险因素 287 例和 4 个危险因素 16 例),分别观察各组内应用抗菌药物对妊娠结局的影响。

1.4　*统计学方法*　应用 SPSS 20.0 软件分析数据。计量资料以 $\bar{x}\pm s$ 表示,应用独立样本 t 检验;计数资料以例(%)表示,采用 χ^2 检验或校正 χ^2 检验。P<0.05为差异有统计学意义。

2　结　果

2.1　*孕产妇和新生儿一般情况*　两组孕产妇的年龄、孕次、身体质量指数(BMI)差异无统计学意义(P>0.05);两组存活新生儿的胎龄及出生体重比较差异无统计学意义(P>0.05)。见表 1、表 2。

2.2　*两组孕产妇妊娠结局及新生儿并发症情况*　两组孕产妇孕周延长值、产褥感染率相比差异无统计学意义(P>0.05)。用抗菌药物组围产儿存活率低于未用抗菌药物组,存活新生儿中并发症发生率高于未用抗菌药物组[26.64%(77/289) *vs* 10.57%(92/870), χ^2 = 44.973, P<0.01]。见表 3。

表 1　两组孕产妇一般资料比较　($\bar{x}\pm s$)

Tab. 1　Comparison of general data between two groups　($\bar{x}\pm s$)

组别	例数	年龄(岁)	孕次(次)	BMI(kg/m^2)
用抗菌药物组	471	31.87±3.36	2.82±1.45	23.61±5.75
未用抗菌药物组	1 056	30.41±4.31	2.41±1.44	22.57±4.22
t 值		0.755	1.842	0.466
P 值		0.451	0.065	0.642

表 2　两组新生儿胎龄、体重比较　($\bar{x}\pm s$)

Tab. 2　Comparison of gestational age and weight between two groups　($\bar{x}\pm s$)

组别	例数	胎龄(周)	出生体重(kg)
用抗菌药物组	289	35.50±3.90	2.74±0.84
未用抗菌药物组	870	37.08±3.10	3.01±0.70
t 值		0.181	0.116
P 值		0.856	0.908

表 3　两组孕产妇妊娠结局比较

Tab. 3　Comparison of pregnancy outcomes between two groups

组别	例数	孕周延长(周,$\bar{x}\pm s$)	产褥感染[例(%)]	围产儿存活[例(%)]
用抗菌药物组	471	16.38±10.45	13(2.76)	289(61.36)
未用抗菌药物组	1 056	16.70±10.66	20(1.89)	870(82.39)
t/χ^2 值		0.092	1.156	78.735
P 值		0.770	0.282	<0.001

2.3　两组孕产妇有不同数量宫内感染高危因素时新生儿存活率和并发症比较　有 1、2、≥3 个宫内感染高危因素时，两组新生儿存活率和并发症发生率比较差异无统计学意义（P>0.05）。见表 4、表 5。

表 4　两组孕产妇有不同数量宫内感染高危因素时新生儿存活率比较　［例(%)］

Tab. 4　Comparison of neonatal survival rates in two groups of pregnant women with different numbers of high-risk factors for intrauterine infection　［case(%)］

组别	例数	1 个高危因素		2 个高危因素		≥3 个高危因素	
		例数	新生儿存活	例数	新生儿存活	例数	新生儿存活
用抗菌药物组	471	103	89(86.41)	97	74(76.29)	271	126(46.49)
未用抗菌药物组	1 056	590	525(88.98)	434	335(77.19)	32	10(31.25)
χ^2 值			0.576		0.036		2.689
P 值			0.448		0.849		0.101

表 5　两组孕产妇有不同数量宫内感染高危因素时新生儿并发症发生率比较　［例(%)］

Tab. 5　Comparison of neonatal complication rates in two groups of pregnant women with different numbers of high-risk factors for intrauterine infection　［case(%)］

组别	例数	1 个高危因素		2 个高危因素		≥3 个高危因素	
		例数	新生儿并发症	例数	新生儿并发症	例数	新生儿并发症
用抗菌药物组	289	89	12(13.48)	74	15(20.27)	126	50(39.68)
未用抗菌药物组	870	525	43(8.19)	335	42(12.54)	10	7(70.00)
χ^2 值			2.614		3.022		2.363
P 值			0.106		0.082		0.124

3　讨　论

早产儿的死亡与胎龄大小相关，约半数的新生儿死亡归因于早产，胎龄越小，存活率越低[10-11]。先兆流产患者进行抗菌药物等治疗的目的是尽量避免早产，特别是出生胎龄<28 周的超早产儿。但本研究结果显示，有宫内感染高危因素的先兆流产产妇使用抗菌药物与否在产妇年龄、孕次、BMI 和存活新生儿的胎龄、出生体重方面差异无统计学意义，在孕周延长、产褥感染率方面差异亦无统计学意义。故是否使用抗菌药物对有宫内感染高危因素的先兆流产孕妇及胎儿上述情况的影响，有待进一步探讨。

近年来随着新生儿重症监护救治水平的提高，早产儿的存活率大幅度提升，但因为其出生时发育不成熟及其母亲围产期的不良因素，导致早产儿存在多种问题影响其生存质量。本研究在妊娠结局方面显示，用抗菌药物组围产儿存活率低于未用抗菌药物组，存活新生儿中并发症发生率高于未用抗菌药物组。有不同数量（1、2、≥3 个）宫内感染高危因素时，应用抗菌药物组围生儿存活率未见明显提升，存活新生儿并发症发生率未见明显降低。与本课题组前期研究先兆流产患者亚临床宫内感染应用抗菌药物未能使妊娠结局改善的结果相近[12]。表明虽然感染是先兆流产的原因之一，但不是只要合并宫内感染高危因素，先兆流产患者都需要使用抗菌药物[13]。虽然分层分析未能提示抗菌药物时机如何优选，但未用抗菌药物组仅合并 1 个宫内感染高危因素者占多数，且≥3 个宫内感染高危因素时用抗菌药物组存活新生儿合并症发生率有降低趋势，故当宫内感染高危因素多时，是否使用抗菌药物应根据先兆流产患者的阴道出血和腹痛等临床情况严重程度综合考虑[14]。

综上所述，有宫内感染高危因素的先兆流产产妇一般不需要应用抗菌药物；在有 3、4 个宫内感染高危因素时，应根据产妇的阴道出血和腹痛等临床情况严重程度综合判断。由于本研究的局限性：合并≥4 个宫内感染高危因素的病例偏少，缺乏多中心对照研究，尚未能对抗菌药物治疗时机做出明确结论。且未对孕产妇产后及新生儿进行远期随访。因此，尚需大样本量、多中心随机对照研究进一步探讨。

利益冲突　无

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