

doi: 10.13241/j.cnki.pmb.2024.12.019

新生儿重症监护室中极低和超低出生体重早产儿院内感染影响因素及病原菌分布变化的分析*

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摘要 目的:分析新生儿重症监护室中极低和超低出生体重早产儿院内感染影响因素及病原菌分布变化情况。**方法:**选择 2018 年 1 月至 2022 年 12 月收治的 493 例极低和超低出生体重早产儿, 根据是否发生院内感染, 分为感染组 (54 例) 与非感染组 (439 例)。比较两组新生儿的临床特征, 使用多因素 Logistic 回归分析院内感染的影响因素, 分析院内感染病原菌的分布及早期临床特点。**结果:**两组胎龄、出生体重、宫内窘迫占比、先天性心脏病占比、肠外营养持续时间 > 14 d 的占比、机械通气时间 > 24 h 的占比、PICC 置管时间 > 14 d 的占比、住院时间比较 ($P < 0.05$); 经多因素 Logistic 回归分析, 肠外营养持续时间 > 14 d、机械通气时间 > 24 h、PICC 置管时间 > 14 d 均是早产儿发生院内感染的独立危险因素 ($P < 0.05$); 在 54 例院内感染患儿中, 共培养出病原菌 41 株, 其中革兰阳性菌 10 株, 以表皮葡萄球菌为主; 革兰阴性菌 24 株, 以肺炎克雷伯杆菌为主; 真菌 7 株, 以白色假丝酵母菌为主; 革兰阳性菌组、革兰阴性菌组与真菌组在胎龄、出生体重、反应低下、发热、消化系统症状、血小板减少、血氧下降或呼吸暂停上差异均无统计学意义 ($P > 0.05$)。**结论:**新生儿重症监护室中极低和超低出生体重早产儿院内感染与肠外营养持续时间、机械通气时间和 PICC 置管时间密切相关, 病原菌以表皮葡萄球菌、肺炎克雷伯杆菌和白色假丝酵母菌为主, 早期临床特点缺乏特异性, 可作为防治院内感染的重要依据。

关键词:新生儿重症监护室; 极低出生体重早产儿; 超低出生体重早产儿; 院内感染; 影响因素; 病原菌

中图分类号: R722 **文献标识码:** A **文章编号:** 1673-6273(2024)12-2302-04

Analysis of Factors Influencing Nosocomial Infection and Pathogenic Bacteria Distribution in Very Low And Ultra-low Birth Weight Premature Infants in Neonatal Intensive Care Unit*

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ABSTRACT Objective: To analyze the influential factors of nosocomial infection and the distribution of pathogenic bacteria in very low and ultra-low birth weight premature infants in neonatal intensive care unit. **Methods:** 493 very low and ultra-low birth weight premature infants from January 2018 to December 2022 were selected. According to whether nosocomial infection occurred, they were divided into infected group (54 cases) and non-infected group (439 cases). The clinical characteristics of the two groups were compared, and the influencing factors of nosocomial infection were analyzed by multi-factor Logistic regression, and the distribution of pathogenic bacteria and early clinical characteristics of nosocomial infection were analyzed. **Results:** There were differences in gestational age, birth weight, intrauterine distress, congenital heart disease, parenteral nutrition duration > 14 d, mechanical ventilation duration > 24 h, PICC catheter duration > 14 d and hospital stay between the two groups ($P < 0.05$). Multivariate Logistic regression analysis showed that the duration of parenteral nutrition > 14 days, the duration of mechanical ventilation > 24 hours, and the duration of PICC catheter > 14 days were all independent risk factors for nosocomial infection in birth weight infants in NICU ($P < 0.05$). In 54 children with nosocomial infection, 41 strains of pathogenic bacteria were cultured, including 10 strains of gram-positive bacteria, mainly *Staphylococcus epidermidis*. There were 24 gram-negative strains, mainly *Klebsiella pneumoniae*. There were 7 strains of fungi, mainly *Candida albicans*. There were no differences in gestational age, birth weight, hyporeactivity, fever, digestive symptoms, thrombocytopenia, hypoxia or apnea between gram-positive bacteria group, gram-negative bacteria group and fungus group ($P > 0.05$). **Conclusion:** Nosocomial infection of very low and ultra-low birth weight premature infants in neonatal intensive care unit is closely related to the duration of parenteral nutrition, mechanical ventilation time and PICC insertion time, *staphylococcus epidermidis*, *klebsiella pneumoniae* and *candida albicans* are the main

* 基金项目: 贵州省科技厅计划项目(黔科合基础-ZK[2023]一般 350)

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(收稿日期: 2023-10-08 接受日期: 2023-10-31)

pathogens, and the early clinical characteristics lack specificity, which can be used as an important basis for prevention and treatment of nosocomial infection.

Key words: Neonatal intensive care unit; Very low birth weight premature infants; Ultra-low birth weight premature infants; Hospital infection; Influencing factors; Pathogenic bacteria

Chinese Library Classification(CLC): R722 **Document code:** A

Article ID: 1673-6273(2024)12-2302-04

前言

近年来,随着早产儿救治水平的不断提高,越来越多的极低和超低出生体重早产儿得到有效治疗,在抢救成功的同时,同时面临着院内感染的风险^[1]。新生儿重症监护室中极低和超低出生体重早产儿是发生院内感染的高危人群,院内感染是导致此类早产儿发生严重并发症,甚至死亡的重要原因^[2,3]。由于极低和超低出生体重早产儿在救治过程中,接受侵入性的诊疗性操作较多,尤其是长时间肠外营养、机械通气、PICC置管等,均可能增大其发生院内感染的可能性。极低和超低出生体重早产儿的院内感染发生率是出生体重>1500 g早产儿的3倍^[4,5],明确新生儿重症监护室中极低和超低出生体重早产儿院内感染的影响因素,提高对其院内感染的防治水平,具有重要的临床意义。另外,抗生素的不合理使用也是导致院内感染的常见原因之一,国内大多数发生院内感染的极低和超低出生体重早产儿接受广谱抗生素治疗,有必要进一步改进^[6]。在临床上,不同的检测群体,其院内感染的病原菌分布亦存在差异,了解早产儿院内感染病原菌分布,有助于指导抗生素的选择^[7,8]。然而现阶段,国内关于新生儿重症监护室中极低和超低出生体重早产儿院内感染的病原菌分布的研究尚未形成统一论。对此,本研究目的在于分析新生儿重症监护室中极低和超低出生体重早产儿院内感染影响因素及病原菌分布变化情况,期望为防治院内感染提供依据。

1 资料与方法

1.1 一般资料

选择2018年1月至2022年12月收治的493例极低和超低出生体重早产儿,根据是否发生院内感染,分为感染组(54例)与非感染组(439例)。经医院伦理委员会批准。

纳入标准:(1)在本院出生;(2)出生体重<1500 g;(3)胎龄<37周;(4)患儿监护人签署知情同意书,配合研究。排除标准:(1)预计住院时间<3 d;(2)合并严重结构畸形者;(3)存在染色体异常者;(4)中途转院者。

1.2 病原菌检测

所有患儿均经动脉无菌抽血进行血培养,注入需氧培养瓶,对患儿行腰椎穿刺术,提取适量脑脊液并培养。使用无菌吸痰管吸取适量呼吸道深部痰液并送检;采集适量大便并送检,进行培养;留取适量尿液行尿培养检查。

1.3 观察指标

比较两组新生儿的临床特征(性别、胎龄、出生体重、分娩方式、宫内窘迫占比、胎膜早破占比、新生儿呼吸窘迫综合征占比、先天性心脏病占比、新生儿低糖血症占比、反复吸痰占比、肠外营养持续时间>14 d的占比、机械通气时间>24 h的占

比、PICC置管时间>14 d的占比、住院时间),使用多因素 Logistic 回归分析院内感染的影响因素,分析院内感染病原菌的分布及早期临床特点(胎龄、出生体重、反应低下、发热、消化系统症状、血小板减少、血氧下降或呼吸暂停)。

1.4 数据处理

采用 SPSS22.0,计量资料以($\bar{x} \pm s$)表示,t检验、方差分析;计数资料以率表示, χ^2 检验;以 $P < 0.05$ 说明差异有统计学意义。

2 结果

2.1 两组新生儿的临床特征比较

两组胎龄、出生体重、宫内窘迫占比、先天性心脏病占比、肠外营养持续时间>14 d的占比、机械通气时间>24 h的占比、PICC置管时间>14 d的占比、住院时间比较($P < 0.05$);数据见表1。

2.2 影响院内感染发生的因素分析

经多因素 Logistic 回归分析,肠外营养持续时间>14 d、机械通气时间>24 h、PICC置管时间>14 d均是新生儿重症监护室中极低和超低出生体重早产儿发生院内感染的独立危险因素($P < 0.05$);数据见表2。

2.3 早产儿院内感染的病原菌分布情况分析

在54例院内感染患儿中,共培养出病原菌41株,其中革兰阳性菌10株,以表皮葡萄球菌为主;革兰阴性菌24株,以肺炎克雷伯杆菌为主;真菌7株,以白色假丝酵母菌为主;数据见表3。

2.4 不同病原菌医院感染早期的临床特点比较

革兰阳性菌组、革兰阴性菌组与真菌组在胎龄、出生体重、反应低下、发热、消化系统症状、血小板减少、血氧下降或呼吸暂停上差异均无统计学意义($P > 0.05$);数据见表4。

3 讨论

近年来,随着新生儿重症监护技术的不断发展和成熟,越来越多的极低和超低出生体重早产儿得以抢救成功。由于极低和超低出生体重早产儿的生长发育较为迟缓,免疫功能尚未成熟,对病原菌高度易感,导致院内感染的风险较大^[9,11]。在临床上,极低和超低出生体重早产儿在院内感染早期,临床表现缺乏特异性,易被忽视,存在确诊率低和预后差的特点。院内感染的早期诊断、及时干预,对改善极低和超低出生体重早产儿的预后及其重要。国内外研究表明,发生院内感染的极低和超低出生体重早产儿的病死率明显升高^[12,13]。因此,明确新生儿重症监护室中极低和超低出生体重早产儿院内感染的影响因素,提高院内感染的防治水平,尤为重要。从本研究表1结果可知,极低和超低出生体重早产儿发生院内感染,可能与胎龄、出生体重、宫内窘迫、先天性心脏病及肠外营养、机械通气和 PICC 置管的时间过长有关,与 Desorcy-Scherer^[14]等的研究结果相符,

这一结果表明, 极低和超低出生体重早产儿发生院内感染, 受 的风险越大。
多因素的影响, 患儿存在的有创操作机会越多, 发生院内感染

表 1 两组新生儿的临床特征比较
Table 1 Comparison of the clinical characteristics of the two neonatal groups

Clinical features	Infection group (54 cases)	Non-infected group (439 cases)	Statistical value	P
Man [n(%)]	28(51.85)	263(59.91)	0.462	0.538
Fetal age (week)	29.77± 5.12	31.56± 1.82	12.425	0.000
Birth weight (g)	1232.778± 118.63	1323.47± 101.27	8.749	0.000
Cesarean section [n (%)]	29(53.70)	272(61.96)	1.246	0.089
Intrauterine distress [n (%)]	30(55.56)	198(45.10)	5.361	0.042
Premature rupture of fetal membranes [n (%)]	8(14.81)	66(15.03)	0.412	0.587
Neonatal respiratory distress syndrome [n (%)]	27(50.00)	246(56.04)	0.124	0.875
Congenital heart disease [n (%)]	33(61.11)	92(20.96)	10.457	0.000
Neonatal hypoglycaemia [n (%)]	5(9.26)	43(9.79)	0.369	0.630
Repeated sputum aspiration [n (%)]	28(51.85)	216(49.20)	0.224	0.765
Duration of parenteral nutrition was> 14 d [n (%)]	43(79.63)	173(39.41)	9.785	0.000
Time of mechanical ventilation was> 24 h [n (%)]	36(66.67)	158(35.99)	13.456	0.000
PICC catheterization time> 14 d [n (%)]	28(51.85)	45(10.25)	12.819	0.000
Length of stay (d)	62.97± 21.47	40.13± 13.56	15.873	0.000

表 2 影响院内感染发生的因素分析
Table 2 Analysis of the factors affecting the occurrence of nosocomial infections

Factor	B	SE	Wald	P	Exp(β)	95.0%CI
Duration of parenteral nutrition was> 14 d [n (%)]	1.612	0.648	7.565	0.036	4.127	1.258-8.532
Time of mechanical ventilation was> 24 h	2.356	0.852	5.260	0.032	1.038	0.034-2.528
PICC catheterization time> 14 d [n (%)]	0.534	1.019	9.081	0.010	4.643	1.359-10.475

表 3 早产儿院内感染的病原菌分布情况分析
Table 3 Analysis of the distribution of nosocomial infections

Nosophyte	Number of strains (strains)	Proportion (%)
<i>Gram-positive strains</i>	10	24.40
<i>Staphylococcus epidermidis</i>	3	7.32
<i>Coagulase negative Staphylococcus</i>	3	7.32
<i>Staphylococcus aureus</i>	2	4.88
<i>Enterococcus faecium</i>	2	4.88
<i>Gram-negative strains</i>	24	58.53
<i>Klebsiella pneumoniae</i>	12	29.27
<i>Serratia viscosus</i>	6	14.63
<i>Escherichia coli</i>	5	12.20
<i>Acinetobacter baumannii</i>	1	2.44
<i>Fungus</i>	7	17.07
<i>Candida albicans</i>	4	9.75
<i>Meyerozyma guilliermondii</i>	2	4.88
<i>Candida glabra</i>	1	2.44

表 4 不同病原菌医院感染早期的临床特点比较

Table 4 Comparison of clinical characteristics in the early stages of nosocomial infection with different pathogens

Clinical features	Gram-positive bacteria group (10 cases)	Gram-negative bacteria group (24 cases)	Fungal group (7 cases)	Statistical value	P
Fetal age (week)	28.75± 4.76	28.43± 5.12	28.66± 5.08	0.463	0.535
Birth weight (g)	1212.42± 120.36	1198.72± 131.47	1223.41± 118.76	0.215	0.784
Low response [n (%)]	2(20.00)	10(41.67)	1(14.29)	0.125	0.872
Fever [n(%)]	3(30.00)	6(5.00)	3(42.86)	0.187	0.811
Digestive system symptoms [n (%)]	1(10.00)	7(29.17)	2(28.57)	0.459	0.540
Thrombocytopenia [n (%)]	3(30.00)	14(58.33)	2(28.57)	0.531	0.468
Drop in blood oxygen or apnea [n (%)]	7(70.00)	19(79.17)	6(60.00)	0.379	0.617

本研究使用多因素 Logistic 回归分析,结果显示:肠外营养持续时间>14 d、机械通气时间>24 h、PICC 置管时间>14 d 均是新生儿重症监护室中极低和超低出生体重早产儿发生院内感染的独立危险因素($P<0.05$);与修文龙^[15]等研究表明肠外营养、新生儿窒息和 PICC 置管是极低和超低出生体重早产儿发生院内感染的主要影响因素的这一观点相契合。对于机械通气时间>24 h 的极低和超低出生体重早产儿,往往存在新生儿窒息,影响黏膜屏障功能及防御能力,加上机械通气时间过长,反复操作增加炎症发生,从而导致感染病原菌的风险增大^[16-18]。PICC 置管有助于极低和超低出生体重早产儿摄取药物及静脉营养,但 PICC 置管属于侵入性操作,在静脉营养期间,存储、配置和注射这些环节的污染率较高^[19]。因此极低和超低出生体重早产儿的 PICC 置管时间及肠外营养持续时间过长,均可增加院内感染的发生风险。基于本研究结果,不难看出,在极低和超低出生体重早产儿诊治期间,需要严格掌握呼吸机撤机及 PICC 拔除的指征,缩短肠外营养时间,尽早移除 PICC 和将呼吸机撤机,有望减少院内感染发生。

既往研究表明,患儿发生感染的病原菌主要为革兰阴性菌,感染病灶为呼吸系统^[20,21]。然而在本研究的 54 例院内感染患儿中,共培养出病原菌 41 株,其中革兰阴性菌 24 株,占 58.53%,以肺炎克雷伯杆菌、大肠埃希菌、粘滞沙雷菌为主,与既往研究报道具有相似性^[22]。本文发现:感染部位为血液系统,主要病原菌为革兰阳性菌,与静脉置管、侵入性操作等因素有关,与既往相关文献报道一致^[23,24]。在本研究中,真菌感染达 17.07%,以近平滑假丝酵母菌感染为主,提示真菌感染成为极低和超低出生体重早产儿发生院内感染的重要原因。李笑^[25]等以极低和超低出生体重早产儿为研究对象,发现真菌感染的发生率高达 20%,以近平滑念珠菌和白色念珠菌感染为主,与本研究结果相似,这很可能与患儿接受静脉置管有关,有必要通过氟康唑预防念珠菌感染。值得注意的是,从本研究表 4 结果可知,在发生院内感染的极低和超低出生体重早产儿中,不同病原菌医院感染早期的临床特点并无特异性,起病均较为隐匿,提示规范诊疗、严格无菌操作原则等。

综上所述,新生儿重症监护室中极低和超低出生体重早产儿院内感染与肠外营养持续时间、机械通气时间和 PICC 置管时间密切相关,病原菌以表皮葡萄球菌、肺炎克雷伯杆菌和白色假丝酵母菌为主,早期临床特点缺乏特异性,可作为防治院

内感染的重要依据。当然,受限于本研究为单中心研究,样本量不多,未分析院内感染影响因素与患儿远期预后的关系,有待日后扩大研究规模,延长随访时间,并进行耐药性分析,为进一步提高院内感染的防治水平提供依据。

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