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先天性心脏病患儿术后并发医院感染的危险因素及其病原菌分布和药敏实验分析*

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摘要 目的:统计先天性心脏病(CHD)患儿术后医院感染的病原菌分布及细菌耐药性情况,分析影响CHD患儿术后医院感染的危险因素。**方法:**回顾性选取2010年3月-2017年10月我院行CHD手术治疗的患儿3800例,收集临床标本进行致病菌培养并进行药敏试验,统计CHD术后医院感染患儿病原菌种类及主要致病菌的耐药情况,分析影响CHD患儿术后医院感染的危险因素。**结果:**3800例CHD患儿术后医院感染率为3.13%(119/3800),共分离出菌株172株,G⁻菌、G⁺菌、真菌分别占55.81%(96/172)、26.74%(46/172)、17.44%(30/172)。肺炎克雷伯菌、大肠杆菌对头孢类抗生素高度耐药,鲍曼不动杆菌检出率逐年增高,且仅对多黏菌素B保持敏感;肺炎链球菌、凝固酶阴性葡萄球菌、金黄色葡萄球菌对大环内酯类抗生素、克林霉素、青霉素高度耐药,对万古霉素和替加环素保持敏感。术后医院感染与年龄、体重、病程、手术时间、体外循环时间、机械通气时间、ICU停留时间、住院时间、合并肺动脉高压、吸痰次数、静脉营养、应用丙种球蛋白或白蛋白有关($P<0.05$),且合并肺动脉高压、体外循环时间 ≥ 100 min、机械通气时间 ≥ 120 h、吸痰次数 ≥ 5 次/d是CHD患儿术后医院感染的危险因素($P<0.05$)。**结论:**G⁻菌、G⁺菌是CHD患儿术后医院感染的主要致病菌,且对常用抗生素高度耐药,此外鲍曼不动杆菌的检出率和耐药性上升极为明显,合并肺动脉高压、体外循环时间及机械通气时间过长、吸痰次数多的CHD患儿医院感染风险升高。

关键词:先天性心脏病;医院感染;危险因素;病原菌;药敏试验

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Risk Factors of Postoperative Nosocomial Infection in Children with Congenital Heart Disease and Their Pathogenic Bacteria Distribution and Drug Sensitivity Analysis*

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ABSTRACT Objective: To investigate the distribution of pathogens and bacterial resistance of postoperative nosocomial infection in children with congenital heart disease (CHD), and analyze the risk factors of postoperative nosocomial infection in children with CHD. **Methods:** 3800 cases of CHD children after surgical treatment in our hospital from March 2010 to October 2017 were selected retrospectively. Clinical specimens were collected for pathogen culture and drug sensitivity test, the types of pathogens and the drug resistance of main pathogens were analyzed, the risk factors of postoperative nosocomial infection in children with CHD were analyzed. **Results:** The hospital infection rate of 3800 children with CHD was 3.13% (119/3800), A total of 172 strains were isolated, G⁻ strain, G⁺ strain and fungi accounted for 55.81% (96/172), 26.74% (46/172) and 17.44% (30/172) respectively. *Klebsiella pneumoniae* and *Escherichia coli* have high resistance rate to cephalosporins, the detection rate of *Acinetobacter baumannii* is increasing year by year, and it was sensitive to polymyxin B only; *Streptococcus pneumoniae*, coagulase negative *Staphylococcus* and *Staphylococcus aureus* are highly resistant to lipid antibiotics, clindamycin and penicillin, and sensitive to vancomycin and tegacyclin. The postoperative hospital infection were related to age, weight, course of disease, time of operation, time of cardiopulmonary bypass, mechanical ventilation time, ICU stay time, length of stay, whether pulmonary hypertension, phlegm times, intravenous nutrition, use of gamma globulin or white protein ($P<0.05$), and pulmonary hypertension, cardiopulmonary bypass time greater than or equal to 100 min, mechanical ventilation time greater than or equal to 120 h, sputum number greater than or equal to 5 times/d were risk factors for postoperative hospital infection in children with CHD ($P<0.05$).

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Conclusion: G⁻ strain, G⁺ strain are the main pathogenic bacteria of postoperative hospital infection in children with CHD, and highly resistant to common antibiotics, in addition, the detection rate and drug resistance of *Acinetobacter baumannii* increased significantly, the risk of infection in children with pulmonary hypertension, cardiopulmonary bypass and mechanical ventilation time too long, too many sputum number is increased.

Key words: Congenital heart disease; Nosocomial infection; Risk factors; Distribution of pathogens; Drug sensitivity analysis

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前言

先天性心脏病(Congenital heart disease, CHD)患儿由于年龄偏小,机体抵抗力较弱,各器官、组织功能发育迟缓,术后易出现感染,感染率高达 5%-21%^[1,2]。CHD 患儿经历术中体外循环、术后机械通气和频繁侵入性操作,加之营养状态较差等多种因素影响,医院感染率有升高趋势,易感病原菌常累及呼吸系统、血液系统,严重感染可导致脓毒血症和多器官功能衰竭,延长患儿住院时间,且长时间的抗生素滥用导致病菌易出现耐药性,均可导致患儿死亡^[3-5]。由于病原菌分布及耐药特征因时间、地区的差异性,相关报道关于医院感染的病原菌分布和耐药情况不尽相同^[6,7],为了解我院 CHD 患儿术后医院感染的常见病原菌特征、耐药性以及导致感染的因素,为临床防治感染以及合理使用抗生素提供参考,本研究拟对我院 3800 例 CHD 患儿进行回顾性分析,现报道如下。

1 资料与方法

1.1 一般资料

回顾性选取 2010 年 3 月至 2017 年 10 月我院行 CHD 手术治疗的 3800 例患儿,收集其临床资料。纳入标准:(1)经临床确诊为 CHD^[8]患儿;(2)符合 CHD 手术指征;(3)均成功完成了 CHD 手术。排除标准:(1)川崎病、风湿等后天因素所致心脏病患儿;(2)术前即发现病菌感染的患儿。依据术后医院感染的诊断标准将患儿分为感染组和未感染组,感染判定:有感染的症状体征或影像学阳性以及微生物学证据的感染,血或其他送检标本培养阳性,并伴有相应的临床感染证据^[9]。

1.2 病原菌培养和药敏实验方法

采集血液、痰液、分泌物、尿液、灌洗液或咽拭子等标本进行细菌培养和药敏试验。培养方法:对收集的标本进行涂片观察后选取合格标本(鳞状上皮细胞<10 个 HP)培养 24 h,采用法国生物-梅里埃 ATB 系列微生物检验仪和配套细菌鉴定试条进行致病菌鉴定,操作流程严格遵守美国临床实验室标准化研究所(CLSI)颁布的标准^[9]。药敏试验主要采取 MIC 法或 K-B 法,取纯菌落标本,应用法国梅里埃 ATB 系列自动药敏鉴定分析仪进行药敏试验。

1.3 统计学分析

采用 SPSS22.0 软件进行数据分析,计量资料以($\bar{x} \pm s$)表示,实施 t 检验,计数资料以%表示,采用 χ^2 检验,单因素和多因素 Logistic 回归分析 CHD 患儿术后医院感染的危险因素,设置检验水准 $\alpha=0.05$ 。

2 结果

2.1 CHD 患儿医院感染情况和致病菌谱

3800 例患儿术后医院感染 119 例,无感染 3681 例;共分离出菌株 172 株,其中 G⁺ 菌株 46 株,占 26.74%(46/172),G⁻ 菌株 96 株,占 55.81%(96/172),真菌菌株 30 株,占 17.44%(30/172)。G⁻ 菌以肺炎克雷伯菌(28.13%)检出率最高,G⁺ 菌以凝固酶阴性葡萄球菌(26.09%)检出率最高,真菌以白假丝酵母菌(36.67%)检出率最高。见表 1。

表 1 CHD 患儿术后医院感染病原菌分布

Table 1 Distribution of pathogenic bacteria in children with CHD after surgery

Pathogenic bacteria	Number of bacteria[n(%)]
G ⁻	
<i>Klebsiella pneumoniae</i>	27(28.13)
<i>Escherichia coli</i>	21(21.88)
<i>Acinetobacter baumannii</i>	19(19.79)
<i>Pseudomonas aeruginosa</i>	16(16.67)
<i>Stenotrophomonas maltophilia</i>	7(7.29)
<i>Klebsiella oxytoca</i>	4(4.17)
<i>Acinetobacter lwoffii</i>	2(2.08)
G ⁺	
<i>Coagulase negative Staphylococcus</i>	12(26.09)
<i>Staphylococcus aureus</i>	10(21.74)
<i>Streptococcus pneumoniae</i>	9(19.57)
<i>Pyogenic cocci</i>	7(15.22)
<i>Enterococcus faecalis</i>	5(10.87)
<i>Staphylococcus haemolyticus</i>	3(6.52)
Fungus	
<i>Candida albicans</i>	11(36.67)
<i>Aspergillus</i>	9(30.00)
<i>Aspergillus niger</i>	6(20.00)
<i>Candida near smooth</i>	4(13.33)

2.2 主要致病菌的药敏鉴定结果

2010 年 3 月-2013 年 3 月(T1)、2013 年 4 月-2016 年 3 月(T2)、2016 年 4 月-2017 年 10 月(T3)期间检出主要细菌菌株数(G⁻ 菌和 G⁺ 菌)分别为 36 株、49 株、57 株,鲍曼不动杆菌在细菌菌株的检出率分别为 8.33%、10.20%、19.30%,呈明显增

长趋势。肺炎克雷伯菌、大肠杆菌对头孢类抗生素有较高的耐药率,且耐药率逐渐上升,对亚胺培南、哌拉西林/他唑巴坦保持较低的耐药率;鲍曼不动杆菌对头孢类和亚胺培南、碳青霉烯类抗生素均有较高的耐药率,但对多黏菌素 B 保持敏感;铜

绿假单胞菌对亚胺培南、左旋氧氟沙星的耐药率较高,且耐药率有上升趋势。肺炎链球菌、凝固酶阴性葡萄球菌、金黄色葡萄球菌对大环内脂类抗生素、克林霉素、青霉素均高度耐药,对万古霉素和替加环素完全不耐药,见表 2、3。

表 2 G⁻ 菌株药物耐药情况 [例(%)]
Table 2 Drug resistance of G⁻ strains [n(%)]

Antibiotics	<i>Klebsiella pneumoniae</i>			<i>Escherichia coli</i>			<i>Acinetobacter baumannii</i>		
	T1(n=9)	T2(n=8)	T3(n=10)	T1(n=5)	T2(n=7)	T3(n=9)	T1(n=3)	T2(n=5)	T3(n=11)
Imipenem	2(22.22)	1(12.50)	3(30.00)	0(0.00)	1(14.29)	0(0.00)	2(66.67)	3(60.00)	10(90.91)
Piperacillin / tazobactam	1(11.11)	2(25.00)	0(0.00)	0(0.00)	1(14.29)	0(0.00)	2(66.67)	4(80.00)	10(90.91)
Cefepime	1(11.11)	4(50.00)	6(60.00)	3(60.00)	5(71.43)	7(77.78)	1(33.33)	3(60.00)	9(81.82)
Amikacin	1(11.11)	2(25.00)	1(10.00)	2(40.00)	3(42.86)	5(55.56)	/	/	/
Levofloxacin	/	/	/	/	/	/	1(33.33)	3(60.00)	8(72.73)
Ceftazidime	4(44.44)	4(50.00)	6(60.00)	2(40.00)	3(42.86)	5(55.56)	1(33.33)	2(40.00)	6(54.55)
Amoxicillin	3(33.33)	2(25.00)	4(40.00)	0(0.00)	2(28.57)	4(44.44)	/	/	/
Cefoperazone / sulbactam	3(33.33)	4(50.00)	3(30.00)	1(20.00)	2(28.57)	2(22.22)	/	/	/
Compound Xinnuoming	3(33.33)	5(62.50)	7(70.00)	2(40.00)	3(42.86)	5(55.56)	1(33.33)	3(60.00)	7(63.64)
Cefotaxime	5(55.56)	6(75.00)	8(80.00)	3(60.00)	5(71.43)	7(77.78)	2(66.67)	4(80.00)	10(90.91)
Ceftriaxone	4(44.44)	5(62.50)	9(90.00)	4(80.00)	6(85.71)	8(88.89)	1(33.33)	5(100.00)	11(100.00)
polymyxin B	0(0.00)	0(0.00)	0(0.00)	/	/	/	0(0.00)	0(0.00)	0(0.00)

Notes: "/" shows undetected items.

表 3 G⁺ 菌株药物耐药率[例(%)]
Table 3 Drug resistance of G⁺ strains [n(%)]

Antibiotics	<i>Streptococcus pneumoniae</i>			<i>Coagulase negative Staphylococcus</i>			<i>Staphylococcus aureus</i>		
	T1(n=2)	T2(n=5)	T3(n=2)	T1(n=2)	T2(n=3)	T3(n=7)	T1(n=5)	T2(n=3)	T3(n=2)
Clindamycin	1(50.00)	4(80.00)	2(100.00)	1(50.00)	1(33.33)	2(28.57)	5(100.00)	2(66.67)	2(100.00)
Gentamicin	/	/	/	0(0.00)	1(33.33)	1(14.29)	1(20.00)	0(0.00)	0(0.00)
Erythromycin	1(50.00)	4(80.00)	2(100.00)	2(100.00)	2(66.67)	7(100.00)	4(80.00)	3(100.00)	2(100.00)
Penicillin	2(100.00)	5(100.00)	2(100.00)	2(100.00)	3(100.00)	7(100.00)	/	/	/
Levofloxacin	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(33.33)	0(0.00)
Compound Xinnuoming	1(50.00)	2(40.00)	1(50.00)	1(50.00)	0(0.00)	3(42.86)	2(40.00)	1(33.33)	1(50.00)
Tetracycline	1(50.00)	3(60.00)	1(50.00)	2(100.00)	3(100.00)	7(100.00)	/	/	/
Vancomycin	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	/	/	/
Tegafycline	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Ciprofloxacin	0(0.00)	1(20.00)	1(50.00)	/	/	/	0(0.00)	0(0.00)	1(50.00)
Meropenem	/	/	/	1(50.00)	1(33.33)	1(14.29)	/	/	/

Notes: "/" shows undetected items.

2.3 CHD 术后感染的单因素分析

与未感染组相比,感染组患儿年龄偏小、体重偏轻($P<0.05$),病程、手术时间、体外循环时间、机械通气时间、ICU 停

留时间、住院时间均长于未感染组患儿($P<0.05$),合并肺动脉高压、吸痰次数 ≥ 5 次/d、静脉营养、应用两种球蛋白或白蛋白的患儿比例明显高于未感染组($P<0.05$),见表 4。

表 4 感染患儿和未感染患儿临床基线资料对比

Table 4 Clinical baseline data comparison with infected and uninfected children

Factors	Infection group(n=119)	Uninfected group(n=3681)	t/ χ^2	P
Gender[n(%)]				
Male	62(52.10)	1871(50.83)	0.075	0.785
Female	57(47.90)	1810(49.17)		
Age(years)	1.81± 0.93	3.52± 2.09	8.896	0.000
Weights(kg)	8.05± 3.21	12.54± 5.33	9.135	0.000
Course of disease(years)	1.22± 0.39	0.84± 0.13	28.087	0.000
Pulmonary hypertension[n(%)]				
Yes	49(41.18)	801(21.76)	25.025	0.000
No	70(58.82)	2880(78.24)		
Operative time(min)	329.51± 171.05	183.66± 82.41	18.095	0.000
cardiopulmonary bypass time(min)	106.41± 53.70	50.32± 18.66	29.144	0.000
mechanical ventilation time(h)	163.05± 92.17	21.62± 9.11	81.828	0.000
ICU stay time(h)	368.25± 105.44	51.32± 26.42	106.45	0.000
Length of stay(d)	25.03± 10.95	17.05± 3.19	23.245	0.000
Use of intravenous nutrition support [n(%)]	26(21.85)	357(9.70)	18.777	0.000
sputum number greater than or equal to 5 times/d [n(%)]	37(31.09)	499 (13.56)	29.259	0.000
use of gamma globulin or white protein[n(%)]	42(35.29)	231(6.28)	35.065	0.000

2.4 先天性心脏病患儿术后医院感染的 Logistic 非条件回归分析

以 CHD 患儿术后是否发生医院感染为因变量, 以表 4 中有统计学意义的项目为自变量, 建立 Logistic 回归分析模型,

结果显示合并肺动脉高压、体外循环时间 ≥ 100 min、机械通气时间 ≥ 120 h、吸痰次数 ≥ 5 次/d 是 CHD 患儿术后感染的危险因素($P<0.05$), 见表 5。

表 5 CHD 患儿术后医院感染的多因素分析结果

Table 5 Multi-factor analysis results of postoperative infection of children with CHD

Factors	β	SE	Wald χ^2	P	OR	95%CI
Pulmonary hypertension	0.526	0.026	6.035	0.002	2.311	1.981-2.564
cardiopulmonary bypass time greater than or equal to 100 min	0.356	0.048	21.562	0.000	5.621	4.264-6.619
mechanical ventilation time greater than or equal to 120 h	0.369	0.037	10.255	0.001	4.862	3.336-5.769
sputum number greater than or equal to 5 times/d	0.723	0.041	29.034	0.000	5.261	4.264-5.961

3 讨论

本研究显示 G⁻ 菌、G⁺ 菌是我院 CHD 患儿术后医院感染的主要致病菌, 这与既往研究中发现术后医院感染的致病菌分布情况相一致^[10-12]。G⁻ 菌以肺炎克雷伯菌检出率最高, 其次为大肠埃希菌、鲍曼不动杆菌、铜绿假单胞菌, 且自 2010 年至 2017 年肺炎克雷伯菌、大肠埃希菌、铜绿假单胞菌一直稳定保持着较高的检出率, 说明非发酵菌已经成为我院院内感染的主要病

原菌, 这是因为非发酵菌为条件致病菌, 可通过多种传播途径引起呼吸道感染、泌尿道感染、皮肤感染, 而在医院中环境相对封闭, 且各类病人较多, 因此肺炎克雷伯菌、大肠埃希菌是医院感染的主要致病菌^[13-15]。徐红亮^[16]等人分析了 112 株来自下呼吸道的 CHD 患儿痰液标本, 发现 G⁻ 菌以肺炎克雷伯菌、鲍曼不动杆菌、铜绿假单胞菌居多, 与本研究结果基本一致, 不同的是大肠埃希菌构成比较低仅 6.2%, 与本研究存在一定的差异, 可能与病原菌地区差异性有关。

药敏试验显示肺炎克雷伯菌、大肠杆菌对头孢类抗生素有较高的耐药率,且耐药程度逐年上升,且存在多重耐药,可能与临床广泛使用头孢类抗生素有关^[17,18]。位居第三位的鲍曼不动杆菌检出率逐年提高,由 8.83% 增加到 19.30%,且对头孢类、亚胺培南、碳青霉烯类等抗生素产生高度耐药,且耐药率逐渐提高。鲍曼不动杆菌是一种广泛存在于自然界和医院环境中的条件致病菌,除多黏菌素 B 外几乎对常规抗菌药物全部耐药,引起医药和微生物学界的关注,被称为“超级细菌”^[19-21],虽然多黏菌素 B 不良反应大,不宜作为小儿抗感染首选药物,但当 CHD 术后感染鲍曼不动杆菌时,宜考虑使用多黏菌素 B 进行抗感染治疗,同时本研究结果显示 G⁺ 菌对大环内脂类抗生素、克林霉素、青霉素均有高度耐药性,而对万古霉素和替加环素的耐药性普遍较低,提示万古霉素和替加环素可作为抗 G⁺ 菌感染的有效手段。

本研究还分析了 CHD 患儿术后医院感染的危险因素因素,结果显示肺动脉高压、体外循环时间 ≥ 100 min、机械通气时间 ≥ 120 h、吸痰次数 ≥ 5 次/d 是 CHD 患儿术后感染的危险因素,这是因为肺动脉高压是 CHD 常见的合并症,也是 CHD 患儿围术期死亡的主要原因,由于肺动脉高压患儿心肌受累严重,对手术耐受性差,术后发生感染的危险性高^[22,23]。体外循环可能始动全身炎症反应综合征,引发炎症介质释放,术后易发生的呼吸机相关性肺炎、脓毒症,甚至多器官功能衰竭等^[24,25]。张建国^[26]研究结果显示,CHD 患儿术后合并呼吸道感染与体外循环时间显著相关。机械通气患者免疫力低下,为条件致病菌侵袭提供了条件,丁艳苓^[27]等人研究显示持续机械通气时间不仅增加呼吸机相关肺炎的感染机率,同时对下呼吸道病原菌分布产生影响,这可能与机械通气患者下呼吸道病原菌特点及上机前和维持机械通气期间的经验治疗等有关。机械通气时间越长,下呼吸道开放时间越长,直接接触病原菌的机会越多,预防性使用抗生素量越大,耐药性越重,感染越重,同时机械通气时间的延长促使气管内壁形成细菌生物膜,减弱抗菌药物对细菌杀伤作用导致耐药形成^[28-30]。

综上,合并肺动脉高压、术中体外循环时间过长、机械通气时间过长、频繁吸痰的 CHD 患儿术后感染风险较高,且主要致病菌 G⁻ 菌、G⁺ 菌均存在明显的耐药现象,其中鲍曼不动杆菌的耐药性极为突出,临床需合理选择抗生素,提高患儿机体免疫力,严格无菌操作,减少不必要的侵入性操作以降低 CHD 患儿术后医院感染的几率。

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