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某三甲医院儿童和成年女性尿培养病原菌分布和耐药性分析*

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摘要 目的:了解尿路感染儿童和成年女性尿培养病原菌种类和耐药性的差异,为临床合理选用抗菌药物提供依据。**方法:**分别收集 2018 年 1 月~2019 年 12 月期间在我院住院的尿路感染儿童的尿培养标本 1618 份和尿路感染成年女性的尿培养标本 1044 份,分析其病原菌的分布和耐药性。**结果:**1618 份儿童尿培养标本中分离出 267 株病原菌,居首位的病原菌是屎肠球菌,占 43.82%(117/267);1044 份成年女性尿培养标本中分离出 139 株病原菌,居首位的病原菌是粪肠球菌,占 28.78%(40/139)。在两种人群尿培养病原菌中大肠埃希菌和肺炎克雷伯菌构成比均分别为第二位和第三位。儿童尿培养屎肠球菌对青霉素 G、氨苄西林、环丙沙星等喹诺酮类药物的耐药率高于成年女性尿培养粪肠球菌,对克林霉素、奎奴普丁/达福普汀、四环素的耐药率低于成年女性尿培养粪肠球菌($P<0.05$);未发现对高浓度庆大霉素、高浓度链霉素、利奈唑胺、万古霉素、替加环素耐药的肠球菌。儿童尿培养大肠埃希菌对氨苄西林/舒巴坦、头孢吡肟的耐药率均高于成年女性尿培养大肠埃希菌($P<0.05$)。儿童尿培养肺炎克雷伯菌对头孢唑啉/舒巴坦、氨苄西林/舒巴坦、哌拉西林/他唑巴坦、氨基曲南、厄他培南、亚胺培南、美洛培南、呋喃妥因、头孢唑啉等头孢菌素类药物的耐药率高于成年女性尿培养肺炎克雷伯菌($P<0.05$)。**结论:**尿路感染儿童和成年女性尿培养病原菌均以肠球菌为主,大肠埃希菌和肺炎克雷伯菌构成比分别为第二位和第三位,两种人群尿培养主要病原菌耐药性均有不同程度的差异,临床医生应根据尿培养和药敏结果合理用药。

关键词:尿培养;成年女性;儿童;病原菌;耐药性

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Distribution and Drug Resistance of Pathogenic Bacteria Isolated from Urine Culture of Children and Adult Women in a Tertiary Hospital*

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ABSTRACT Objective: To understand the differences in the types and drug resistance of pathogenic bacteria in urine culture between children and adult women with urinary tract infection, so as to provide basis for rational selection of antimicrobial agents in clinical practice. **Methods:** A total of 1618 urine culture specimens of children with urinary tract infection and 1044 urine culture specimens of adult women with urinary tract infection were collected from January 2018 to December 2019 in our hospital respectively, to analyze the distribution and drug resistance of their pathogenic bacteria. **Results:** Among the 1618 urine culture specimens of children, 267 strains of pathogenic bacteria were isolated and *enterococcus faecalis* was the first pathogenic bacteria, accounting for 43.82%(117/267). 139 strains of pathogenic bacteria were isolated from 1044 adult female urine culture specimens and *enterococcus faecalis* was the leading pathogenic bacteria, accounting for 28.78%(40/139). The composition ratios of *Escherichia coli* and *Klebsiella pneumoniae* were the second and the third respectively in the two kinds of human pathogenic bacteria cultured in urine. The drug resistance rate of *enterococcus faecalis* in urine culture of children to quinolones such as penicillin G, ampicillin and ciprofloxacin was higher than that in urine culture of adult women, the drug resistance rate of clindamycin, quinupristin/dafopristin and tetracycline was lower than that of *enterococcus faecium* in adult female urine culture($P<0.05$). Enterococci with high concentrations of gentamicin, streptomycin, linezolid, vancomycin and tegacycline were not found. The drug resistance rate of *escherichia coli* in urine culture of children to ampicillin/sulbactam and cefepime was higher than that in urine culture of adult women($P<0.05$). The drug resistance rate of *klebsiella pneumoniae* in urine culture of children to cephalosporin drugs such as cefoperazone/sulbactam, ampicillin/sulbactam, piperacillin/tazobactam, amikacin, imipenem, meropenem, furantoin and cefazolin were higher than that of adult female *klebsiella pneumoniae* ($P<0.05$). **Conclusion:** Enterococci is the main pathogenic bacteria in urine culture of children and adult female with urinary tract infection, the composition ratios of *escherichia coli* and *klebsiella pneumoniae* are second and third respectively, the drug resistance of the two main pathogenic bacteria in human urine

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culture is different in different degrees, the clinician should rationally use the drug according to the results of urine culture and drug sensitivity.

Key words: Urine culture; Adult women; Children; Pathogen; Drug resistance

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前言

尿路感染是仅次于呼吸系统感染的临床常见感染性疾病之一,尿培养作为尿路感染病原学诊断的"金标准"存在培养周期长等缺点,可能会延误患者的最佳治疗时机,因此经验性用药对尿路感染的及时治疗有着重要意义^[1-3],但由于抗菌药物的不合理使用,耐药菌株的不断出现给临床尿路感染的治疗带来巨大挑战。儿童作为特殊人群,其生理特点的特殊性及对抗菌药物的使用局限性使得儿童泌尿系统感染的病原菌分布及耐药性成为医学界的研究热点之一;另外,女性由于其特殊的生理结构,尿道口与生殖道、肛门均较为接近,且尿道短而宽,同时女性体质偏弱,抵抗力较差等因素使得女性的尿道易受到条件致病菌的侵袭,进而导致尿路感染的发生率相对较高,并且尿路感染的致病菌相对复杂,致病菌种类繁多对于治疗药物的选择造成一定的难度^[4-6]。因此研究不同人群尿路感染病原菌分布和耐药性的差异有利于临床医生根据不同人群的特点选用适宜的抗菌药物,从而可以有效地降低抗生素不合理使用频率,减少耐药菌株的产生。本研究回顾性分析了在成都市妇女儿童中心医院住院的尿路感染儿童和成年女性尿培养病原菌的种类及主要病原菌耐药性的差异,以期为临床经验性合理使用抗菌药物提供依据。

1 材料与方法

1.1 菌株来源

收集 2018 年 1 月~2019 年 12 月期间在我院住院的尿路感染儿童的尿培养标本共计 1618 份,尿路感染成年女性的尿培养标本共计 1044 份。剔除同一患者重复分离菌株,1618 份儿童尿培养标本中分离出 267 株病原菌,1044 份成年女性尿培养标本中分离出 139 株病原菌。

1.2 仪器与试剂

法国梅里埃 VITEK 2 Compact System 全自动微生物鉴定及药敏分析系统,药敏纸片购自温州市康泰生物科技有限公司,培养基购自广州市迪景生物科技有限公司。

1.3 方法

按照《全国临床检验操作规程》第 4 版的要求进行标本采集和分离培养^[7],采用清洁中段尿采集法,清洗患者外阴、尿道口之后留取清洁中段尿置于无菌容器中;留置导尿管患者可用 75%酒精消毒导管口后,夹住导管口 10-20 min,用无菌注射器从导管口抽取 5-10 mL 尿液,置于无菌容器中;不可采集尿袋内的尿液;婴儿、中段尿检测结果无法确定和怀疑厌氧菌感染时可行膀胱穿刺采集尿液,将采集的样本立即送检进行细菌学培养实验,采用 VITEK 2 Compact System 全自动微生物鉴定及药敏分析系统进行病原菌的鉴定和药敏分析,依据美国临床和实验室标准化协会 CLSI(2019 年)的药敏折点标准进行药敏

结果的判断^[8]。

1.4 统计学分析

使用 WHONET 5.6 软件对病原菌的药敏结果进行统计分析。计数资料以例或率表示,采用 SPSS 23.0 软件进行分析,比较采用 χ^2 检验,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 儿童和成年女性尿培养病原菌分布

1618 份儿童尿培养标本中检出菌株 267 株,检出率为 16.50%(267/1618),构成比前三位的病原菌分别为尿肠球菌 43.82%(117/267)、大肠埃希菌 27.72%(74/267)、肺炎克雷伯菌 13.11%(35/267),见表 1;1044 份成年女性尿培养标本中检出菌株 139 株,检出率为 13.31%(139/1044),构成比前三位的病原菌分别为粪肠球菌 28.78%(40/139)、大肠埃希菌 26.62%(37/139)、肺炎克雷伯菌 15.83%(22/139)。见表 2。

2.2 主要肠球菌的耐药性分析

儿童尿培养尿肠球菌对呋喃妥因的耐药率与成年女性尿培养粪肠球菌对呋喃妥因的耐药率对比无统计学差异($P > 0.05$)。儿童尿培养尿肠球菌对青霉素 G、氨苄西林、环丙沙星等喹诺酮类药物的耐药率高于成年女性尿培养粪肠球菌,对克林霉素、奎奴普丁/达福普汀、四环素的耐药率低于成年女性尿培养粪肠球菌($P < 0.05$);未发现对高浓度庆大霉素、高浓度链霉素、利奈唑胺、万古霉素、替加环素耐药的肠球菌。见表 3。

2.3 大肠埃希菌的耐药性分析

儿童尿培养大肠埃希菌与成年女性尿培养大肠埃希菌对氨苄西林、头孢哌酮/舒巴坦、哌拉西林/他唑巴坦、头孢唑啉、头孢呋辛、头孢他啶、头孢曲松、头孢替坦、氨曲南、厄他培南、亚胺培南、美洛培南、阿米卡星、庆大霉素、妥布霉素、环丙沙星、左旋氧氟沙星、复方新诺明、呋喃妥因的耐药率对比无统计学差异($P > 0.05$)。儿童尿培养大肠埃希菌对氨苄西林/舒巴坦、头孢吡肟的耐药率均高于成年女性尿培养大肠埃希菌($P < 0.05$)。见表 4。

2.4 肺炎克雷伯菌的耐药性分析

儿童尿培养肺炎克雷伯菌和成年女性尿培养肺炎克雷伯菌对氨苄西林、阿米卡星、庆大霉素、妥布霉素、环丙沙星、左旋氧氟沙星、复方新诺明的耐药率对比无统计学差异($P > 0.05$)。儿童尿培养肺炎克雷伯菌对头孢哌酮/舒巴坦、氨苄西林/舒巴坦、哌拉西林/他唑巴坦、氨曲南、厄他培南、亚胺培南、美洛培南、呋喃妥因、头孢唑啉等头孢菌素类药物的耐药率高于成年女性尿培养肺炎克雷伯菌($P < 0.05$)。见表 5。

3 讨论

因儿童生理具有特殊性,故其对外界病原体抵抗能力弱于成人,进而容易导致感染性疾病的发生,且儿童生活自理能力

表 1 儿童尿培养病原菌种类及构成比

Table 1 Types and composition ratio of pathogenic bacteria in urine culture of children

Pathogenic bacteria	n	Composition ratio(%)
<i>Enterococcus faecium</i>	117	43.82
<i>Escherichia coli</i>	74	27.72
<i>Klebsiella pneumoniae</i>	35	13.11
<i>Enterococcus faecalis</i>	11	4.12
<i>Pseudomonas aeruginosa</i>	6	2.25
<i>Proteus mirabilis</i>	5	1.87
<i>Enterobacter cloacae</i>	2	0.75
<i>Enterobacter aerogenes</i>	2	0.75
<i>Klebsiella oxytoca</i>	2	0.75
<i>Morganella morganii</i> subsp	2	0.75
Fungus	3	1.12
Other	8	3.00
Total	267	100.0

表 2 成年女性尿培养病原菌种类及构成比

Table 2 Types and composition ratio of pathogenic bacteria in adult female urine culture

Pathogenic bacteria	n	Composition ratio(%)
<i>Enterococcus faecalis</i>	40	28.78
<i>Escherichia coli</i>	37	26.62
<i>Klebsiella pneumoniae</i>	22	15.83
<i>Enterobacter cloacae</i>	9	6.47
<i>Staphylococcus epidermidis</i>	7	5.04
<i>Enterobacter aerogenes</i>	4	2.88
<i>Pseudomonas aeruginosa</i>	3	2.16
<i>Streptococcus agalactiae</i>	3	2.16
<i>Citrobacter freundii</i>	2	1.44
<i>Enterococcus faecium</i>	2	1.44
<i>Proteus mirabilis</i>	2	1.44
Other	8	5.76
Total	139	100.0

较差,对尿道的卫生护理不当容易引发尿路感染,特别是住院患儿,因其常常施行导尿或者留置导尿管致使尿路感染的发生率更高^[9-11]。女性由于尿道短、宽、直,尿道口与肛门、阴道接近等生理特点相较于男性更容易罹患尿路感染^[12,13]。由于地域、人群分布的不同,尿路感染病原菌的分布及耐药性均有可能存在差异,因此了解本地区不同人群尿路感染病原菌的分布及耐药性对临床合理选用抗菌药物具有重要意义。

本研究显示尿路感染儿童和成年女性尿培养病原菌以肠球菌为主,与一些地区报道尿培养病原菌以大肠埃希菌为主不同,也有报道指出儿童尿培养病原菌以肠球菌为主,占 35.15%^[14],与本研究相似。屎肠球菌(占比 43.8%)为儿童尿培养标本中分离最多的菌株,而成年女性尿培养标本中则以粪肠球菌(占比 28.8%)为主,两种病原菌耐药性差异较大。儿童尿培养

样本中检出的屎肠球菌对青霉素 G、氨苄西林、环丙沙星等喹诺酮类药物均表现出较高的耐药性,与四川省儿童患者细菌耐药监测数据^[15]相似,而成年女性尿培养标本中检出的粪肠球菌对青霉素 G、氨苄西林、高浓度庆大霉素、高浓度链霉素、呋喃妥因、利奈唑胺、万古霉素、替加环素的耐药率均低于全国耐药监测数据^[16,17]。由于氨基糖苷类和喹诺酮类药物对儿童有肾毒性和耳毒性,因此临床在选择抗菌药物时要结合多方面因素综合考虑^[18,19]。对于成年女性来说,由肠球菌所致的尿路感染则可经验性使用呋喃妥因、青霉素类、喹诺酮类药物进行治疗。两种人群均未检出对高浓度庆大霉素、高浓度链霉素、万古霉素、利奈唑胺、替加环素耐药的肠球菌。然而国外多项研究显示屎肠球菌对万古霉素耐药率已接近 40%^[20-22],因此还是要引起足够重视,规范抗生素使用准则,防止该类耐药菌株出现。

表 3 尿培养主要肠球菌的耐药性分析[n(%)]

Table 3 Drug resistance analysis of major enterococci in urine culture[n(%)]

Medicine	<i>Enterococcus faecium</i> cultured in urine of children (n=117)		Urine culture of <i>enterococcus faecalis</i> in adult women (n=40)	
	Drug resistance	Sensitive	Drug resistance	Sensitive
Penicillin G	117(100.00)	0(0.00)	0(0.00)*	40(100.00)
Ampicillin	117(100.00)	0(0.00)	0(0.00)*	40(100.00)
High concentration gentamicin	0(0.00)	117(100.00)	0(0.00)	40(100.00)
High concentration streptomycin	0(0.00)	117(100.00)	0(0.00)	40(100.00)
Ciprofloxacin	70(59.83)	47(40.17)	2(5.00)*	38(95.00)
Levofloxacin	63(53.85)	54(46.15)	2(5.00)*	38(95.00)
Moxifloxacin	106(90.60)	11(9.40)	2(5.00)*	38(95.00)
Clindamycin	78(66.67)	39(33.33)	40(100.00)*	0(0.00)
Nitrofurantoin	5(4.27)	112(95.73)	0(0.00)	40(100.00)
Linezolid	0(0.00)	117(100.00)	0(0.00)	40(100.00)
Vancomycin	0(0.00)	117(100.00)	0(0.00)	40(100.00)
Quinupristin / daptomycin	0(0.00)	117(100.00)	40(100.00)*	0(0.00)
Tetracycline	51(43.59)	66(56.41)	33(82.50)*	7(17.50)
Tigecycline	0(0.00)	117(100.00)	0(0.00)	40(100.00)

Note: compared with drug resistance rate of *enterococcus faecium* in urine culture of children, * $P<0.05$.

表 4 尿培养大肠埃希菌的耐药性分析[n(%)]

Table 4 Analysis of the drug resistance of *escherichia coli* in urine culture[n(%)]

Medicine	<i>Escherichia coli</i> in urine culture of children (n=74)		Adult female urine culture <i>escherichia coli</i> (n=37)	
	Drug resistance	Sensitive	Drug resistance	Sensitive
Ampicillin	55(74.32)	19(25.68)	28(75.68)	9(24.32)
Cefoperazone / sulbactam	14(18.92)	60(81.08)	3(8.11)	34(91.89)
Ampicillin / sulbactam	41(55.41)	33(44.59)	12(32.43)*	25(67.57)
Piperacillin / tazobactam	5(6.76)	69(93.24)	1(2.70)	36(97.30)
Cefazolin	55(74.32)	19(25.68)	28(75.68)	9(24.32)
Cefuroxime	53(71.62)	21(28.38)	27(72.97)	10(27.03)
Ceftazidime	25(33.78)	49(66.22)	7(18.92)	30(81.08)
Ceftriaxone	53(71.62)	21(28.38)	27(72.97)	10(27.03)
Cefepime	23(31.08)	51(68.92)	4(10.81)*	33(89.19)
Cefotetan	3(4.05)	71(95.95)	1(2.70)	36(97.30)
Aztreonam	34(45.95)	40(54.05)	16(43.24)	21(56.76)
Ertapenem	3(4.05)	71(95.95)	1(2.70)	36(97.30)
Imipenem	3(4.05)	71(95.95)	1(2.70)	36(97.30)
Meropenem	3(4.05)	71(95.95)	1(2.70)	36(97.30)
Amikacin	1(1.35)	73(98.65)	2(5.40)	35(94.60)
Gentamicin	29(39.19)	45(60.81)	11(29.73)	26(70.27)
Tobramycin	10(13.51)	64(86.49)	2(5.41)	35(94.59)
Ciprofloxacin	44(59.46)	30(40.54)	23(62.16)	14(37.84)
Levofloxacin	39(52.70)	35(47.30)	21(56.76)	16(43.24)
Compound sulfamethoxazole	37(50.00)	37(50.00)	23(62.16)	14(37.84)
Nitrofurantoin	2(2.70)	72(97.30)	0(0.00)	37(100.00)

Note: compared with drug resistance rate of *escherichia coli* isolated in urine of children, * $P<0.05$.

表 5 尿培养肺炎克雷伯菌的耐药性分析 [n(%)]
Table 5 Drug resistance analysis of klebsiella pneumoniae in urine culture [n(%)]

Medicine	<i>Klebsiella pneumoniae</i> cultured in urine of children (n=35)		Urinary culture of <i>klebsiella pneumoniae</i> in adult women (n=22)	
	Drug resistance	Sensitive	Drug resistance	Sensitive
Ampicillin	35(100.00)	0(0.00)	22(100.00)	0(0.00)
Cefoperazone / sulbactam	20(57.14)	5(42.86)	2(9.09)*	20(90.91)
Ampicillin / sulbactam	31(88.57)	4(11.43)	4(18.18)*	18(81.82)
Piperacillin / tazobactam	19(54.29)	16(45.71)	0(0.00)*	22(100.00)
Cefazolin	33(94.29)	2(5.71)	6(27.27)*	16(72.73)
Cefuroxime	32(91.43)	3(8.57)	4(18.18)*	18(81.82)
Ceftazidime	27(77.14)	8(22.86)	4(18.18)*	18(81.82)
Ceftriaxone	32(91.43)	3(8.57)	4(18.18)*	18(81.82)
Cefepime	24(68.57)	11(31.43)	0(0.00)*	22(100.00)
Cefotetan	15(42.86)	20(57.14)	2(9.09)*	20(90.91)
Aztreonam	28(80.00)	7(20.00)	2(9.09)*	20(90.91)
Ertapenem	16(45.71)	19(54.29)	2(9.09)*	20(90.91)
Imipenem	16(45.71)	19(54.29)	2(9.09)*	20(90.91)
Meropenem	16(45.71)	19(54.29)	0(0.00)*	22(100.00)
Amikacin	2(5.71)	33(94.29)	4(18.18)	18(81.81)
Gentamicin	7(20.00)	28(80.00)	4(18.18)	18(81.81)
Tobramycin	5(14.29)	30(85.71)	8(36.36)	14(63.64)
Ciprofloxacin	12(34.29)	21(65.71)	8(36.36)	14(63.64)
Levofloxacin	6(17.14)	29(82.86)	2(9.09)	20(90.91)
Compound sulfamethoxazole	8(22.86)	27(77.14)	2(9.09)	20(90.91)
Nitrofurantoin	16(45.71)	19(54.29)	3(13.64)*	19(86.36)

Note: compared with drug resistance of klebsiella pneumoniae isolated in urine of children, * $P < 0.05$.

本研究显示大肠埃希菌和肺炎克雷伯菌在两种人群尿培养病原菌中构成比均分别占第二位和第三位。尿培养大肠埃希菌对氨苄西林 / 舒巴坦、头孢吡肟的耐药率在儿童和成年女性之间的差异有统计学意义。两种人群尿培养标本中大肠埃希菌对于头孢哌酮 / 舒巴坦、哌拉西林 / 他唑巴坦、头霉素类、碳青霉烯类、呋喃妥因、阿米卡星和妥布霉素均表现出低耐药率,因此临床在治疗儿童或成年女性由大肠埃希菌引起的尿路感染时可优先选择以上药物,避免药物地不合理使用。本研究中儿童尿培养大肠埃希菌对在儿科中极少使用的喹诺酮类抗菌药物耐药率均大于 50%,与成年女性尿培养大肠埃希菌喹诺酮类抗菌药物耐药率结果接近,其原因可能与周围环境和摄入食品中的天然抗生素引起耐药有关^[23,24]。在两种人群尿培养病原菌中构成比均占第三位的肺炎克雷伯菌耐药性差异较大。有报道显示,儿童患者对于碳青霉烯类抗菌药物产生耐药的主要机制是机体的致病菌产生金属酶(主要为 NDM-1),而对于碳青霉烯类耐药菌株的治疗最有效的抗菌药物是多黏菌素 B、磷霉素等^[25-27]。成年女性尿培养标本中检出的肺炎克雷伯菌除了氨苄西林外,对于其他几类抗生素敏感性均较好,提示临床可优先

选择呋喃妥因、喹诺酮类等尿液中浓度较高的抗菌药物^[28-30]。

综上所述,尿路感染儿童和成年女性尿培养病原菌均以肠球菌为主,大肠埃希菌和肺炎克雷伯菌在两种人群尿培养病原菌中构成比均分别占第二位和第三位,两种人群尿培养主要病原菌耐药性均有不同程度的差异,临床在治疗过程中应结合两种人群生理病理特点及药敏结果及时合理地调整抗生素的种类和用量,以达到良好的治疗效果。

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