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糖尿病患者足部溃疡感染的病原菌分布及药敏性分析

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摘要 目的:研究糖尿病患者足部溃疡感染的病原菌分布及药敏性。**方法:**选取 2016 年 2 月至 2017 年 2 月我院收治的糖尿病足患者 102 例作为研究对象,采用全自动细菌鉴定仪和 Kirby-Baure(K-B)法分别检测所有患者足部溃疡分泌物中病原菌分布和药敏性。**结果:**96 例成功分离出菌株的糖尿病患者足部溃疡分泌物中共分离出 107 株菌株,其中革兰阴性菌 61 株(57.01%)、革兰阳性菌 43 株(40.19%)和真菌 3 株(2.80%),占总菌株百分比前三位的病原菌分别为金黄色葡萄球菌 22 株(20.56%)、奇异变形杆菌 14 株(13.08%)和肺炎克雷伯菌 10 株(9.35%);前三位革兰阴性菌(奇异变形杆菌、肺炎克雷伯菌和大肠埃希菌)对亚胺培南、美罗培南、头孢哌酮及阿米卡星的敏感性较高(高于 90.00%);金黄色葡萄球菌和表皮葡萄球菌对万古霉素、利奈唑胺及利福平敏感性较高(高于 95.00%);粪肠球菌对红霉素、氯苄西林、万古霉素及利奈唑胺敏感性较高(高于 90.00%)。**结论:**糖尿病患者足部溃疡感染的病原菌以金黄色葡萄球菌和奇异变形杆菌为主,耐药情况严峻,临床诊疗过程中应根据药敏结果规范使用抗菌药物。

关键词:糖尿病;足部溃疡;病原菌分布;药敏性;感染

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Distribution of Pathogens and Analysis of Drug Susceptibility on Patients with Diabetic Foot Ulcer Infection

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ABSTRACT Objective: To investigate the distribution of pathogens and analysis of drug susceptibility on diabetic foot ulcer infection. **Methods:** 102 patients with diabetic foot who were treated in our hospital from February 2016 to February 2017 were selected as the subjects, fully automatic bacteria identification and Kirby-Baure (K-B) was used to detect the distribution of pathogens and analysis of drug susceptibility of all patients with diabetic foot ulcer infection respectively. **Results:** Separated 107 strains bacteria from the secretions of 96 patients with diabetic foot ulcer infection, including 61 strain (57.01%) of gram-negative bacteria, 43 strains (40.19%) of gram positive bacteria and 3 strains of fungi strains (2.80%). Among the percentage of total isolates, the three pathogens were *staphylococcus aureus* 22 strains (20.56%), *proteus mirabilis* 14 strains (13.08%) and *klebsiella pneumoniae* 10 strains (9.35%). The top three gram-negative bacteria (*proteus mirabilis*, *klebsiella pneumoniae* and *escherichia coli*) were highly sensitive to imipenem, meropenem, cefoperazone and amikacin (higher than 90.00%), *staphylococcus aureus* and *staphylococcus epidermidis* were highly sensitive to vancomycin, linezolid and rifampin (higher than 95.00%), *enterococcus faecalis* was highly sensitive to erythromycin, ampicillin, vancomycin and linezolid (higher than 90.00%). **Conclusion:** The main pathogens of diabetic foot ulcer infection are *staphylococcus aureus* and *singular proteus*, the drug resistance is severe, and antimicrobial agents should be used according to the results of drug sensitivity in clinical diagnosis and treatment.

Key words: Diabetes; Foot ulcer; Distribution of pathogens; Drug susceptibility; Infected

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前言

糖尿病是一种以高血糖为特征的代谢性疾病,其主要是由胰岛素分泌缺陷和 / 或胰岛素作用障碍所致。糖尿病患者常处于持续高血糖与长期代谢紊乱状态,很容易导致心血管及神经系统的损害及其功能障碍,而大血管和微血管病变将引发微循

环障碍,进而使得患者足部发生溃疡和坏疽,久而久之将形成糖尿病足^[1-3]。糖尿病足是糖尿病一种严重的并发症,是糖尿病患者致残,甚至致死的重要原因之一,不但给患者造成生理和心理痛苦,同时也使其增添了巨大的经济负担^[4-6]。糖尿病足大部分是由下肢神经病变引起,少部分是由下肢动脉血管病变引起,另外血糖过高、足趾压力过高、足部畸形、糖尿病病程过长均是糖尿病足的危险因素^[7,8]。糖尿病足患者易发生足部溃疡深部细菌感染,相关研究报道显示^[9],约有 15% 的糖尿病患者患有过糖尿病足部溃疡,而其中需要截肢进行治疗者约占 33%,而

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在需要截肢的患者中约有 85% 的患者是由于足部溃疡感染引起,由此可见,探究糖尿病患者足部溃疡感染具有重要的临床意义。本研究通过分析我院 102 例糖尿病患者足部溃疡感染的病原菌分布及药敏性,望能对临床糖尿病足的治疗提供科学依据,现将研究结果整理如下。

1 资料和方法

1.1 一般资料

选择 2016 年 2 月至 2017 年 2 月我院收治的糖尿病足患者 102 例,纳入标准:(1)所有患者均符合 1999 年世界卫生组织制定的糖尿病标准^[10]和美国 Texas 大学糖尿病足诊断标准^[11];(2)患者自愿参与本研究,对研究知情同意。排除标准:(1)其他疾病引发的足溃疡,如肿瘤长期化疗;(2)使用其他药物引起的足溃疡;(3)全身感染者;(4)精神系统疾病者;(5)对本研究所使用的抗菌药物过敏者。其中男性 60 例,女性 42 例,年龄 46~83 岁,平均年龄(66.30±3.25)岁,糖尿病病程 5~34 年,平均病程(8.68±5.33)年,糖尿病足病程 15~64 天,平均病程(30.61±6.25)天,急性感染 46 例,慢性感染 56 例,Wagner 分级^[11]:2 级 12 例,3 级 40 例,4 级 38 例,5 级 12 例。

1.2 方法

分别采用法国梅里埃公司的全自动细菌鉴定仪对所选取研究对象足部溃疡分泌物的病原菌进行菌种鉴定,采用 Kir-

by-Bauer 法(K-B 纸片扩散法)^[12]测定菌株对常用抗菌药物的敏感性,所有操作均按照《全国临床检验操作规程》^[13]和仪器说明书进行。革兰阳性球菌的质控菌株为金黄色葡萄球菌(ATCC 25923),肠杆菌科德质控菌株为大肠埃希菌(ATCC 25922/35218),非发酵菌的质控菌株为铜绿假单胞菌(ATCC 27853),药敏用的 M-H 培养基、药敏卡和试剂等均由英国 Oxoid 公司提供。药敏结果依据美国临床实验室标准化委员会(CLSI)2007 版标准^[14]进行判断。

1.3 统计学处理

所有数据均用 SPSS20.0 进行统计分析,计数资料以率(%)的形式表示,采用 χ^2 检验,计量资料以($\bar{x} \pm s$)的形式表示,采用 t 检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 糖尿病患者足部溃疡分泌物的病原菌分布情况

102 例糖尿病患者足部溃疡分泌物中,有 96 例成功分离出菌株,6 例未分离出菌株,总阳性率为 94.12%;96 例样本中共分离出 107 株菌株,其中革兰阴性菌 61 株(57.01%)、革兰阳性菌 43 株(40.19%)和真菌 3 株(2.80%),占总菌株百分比前三位的病原菌分别为金黄色葡萄球菌(20.56%)、奇异变形杆菌(13.08%)和肺炎克雷伯菌(9.35%)。结果见表 1、2。

表 1 糖尿病患者足部分泌物前十位病原菌分布(n,%)

Table 1 Distribution of the first ten pathogenic bacteria of foot secretion in diabetic(n,%)

Ranking	Bacteria name	Number of seedling(n=107)	Percentage(%)
1	<i>Staphylococcus aureus</i>	22	20.56
2	<i>Proteus mirabilis</i>	14	13.08
3	<i>Klebsiella pneumoniae</i>	10	9.35
4	<i>Escherichia coli</i>	7	6.54
5	<i>Enterobacter cloacae</i>	5	4.67
6	<i>Staphylococcus epidermidis</i>	5	4.67
7	<i>Pseudomonas aeruginosa</i>	4	3.74
8	<i>Enterococcus faecalis</i>	4	3.74
9	<i>Morganella morganii</i>	4	3.74
10	<i>Bauman/calcium acetate Acinetobacter</i>	3	2.80

表 2 糖尿病患者足部分泌物的病原菌分布(n,%)

Table 2 Distribution of pathogenic bacteria of foot secretion in diabetic(n,%)

Bacteria name	Number of seedling(n=107)	Percentage(%)	Bacteria name	Number of seedling(n=107)	Percentage(%)
Gram negative bacteria	61	57.01	Gram positive bacteria	43	40.19
<i>Proteus mirabilis</i>	14	13.08	<i>Staphylococcus aureus</i>	22	20.56
<i>Klebsiella pneumoniae</i>	10	9.35	<i>Staphylococcus epidermidis</i>	5	4.67
<i>Escherichia coli</i>	7	6.54	<i>Enterococcus faecalis</i>	4	3.74
<i>Enterobacter cloacae</i>	5	4.67	<i>Streptococcus agalactiae</i>	2	1.87
<i>Pseudomonas aeruginosa</i>	4	3.74	<i>Staphylococcus haemolyticus</i>	2	1.87

<i>morganella morganii</i>	4	3.74	<i>Staphylococcus warneri</i>	2	1.87
<i>Bauman / calcium acetate acinetobacter</i>	3	2.80	<i>staphylococcus capitis</i>	2	1.87
<i>Klebsiella oxytoca</i>	2	1.87	<i>Staphylococcus</i>	1	0.93
<i>Serratia marcescens</i>	2	1.87	<i>Enterococcus faecium</i>	1	0.93
Enterobacteriaceae	2	1.87	Other gram positive bacteria	2	1.87
<i>Enterobacter cloacae</i>	2	1.87	Fungus	3	2.80
<i>Citrobacter freundii</i>	1	0.93	<i>Candida krusei</i>	2	1.87
<i>Klebsiella citrate</i>	1	0.93	<i>Candida parapsilosis</i>	1	0.93
Other gram negative bacteria	4	3.74			

2.2 糖尿病足患者足部溃疡病原菌的药敏性分析

2.2.1 足部溃疡常见革兰阴性菌的药敏性分析 前三位革兰阴性菌(奇异变形杆菌、肺炎克雷伯菌和大肠埃希菌)对亚胺培

南、美罗培南、头孢哌酮及阿米卡星的敏感性较高(高于90.0%),对氨苄西林的敏感性较低(低于60.0%),结果见表3。

表3 足部溃疡常见革兰阴性菌的药敏性分析[n(%)]

Table 3 Analysis of drug susceptibility of gram negative bacteria in foot ulcers [n (%)]

Drugs	<i>Proteus mirabilis</i> (n=14)	<i>Klebsiella pneumoniae</i> (n=10)	<i>Escherichia coli</i> (n=7)
Ampicillin	8(57.14)	0(0.00)	3(42.86)
Piperacillin	12(85.71)	8(80.00)	5(71.43)
Sulbactam	11(78.57)	8(80.00)	6(85.71)
Aztreonam	12(85.71)	9(90.00)	5(71.43)
Imipenem	14(100.00)	10(100.00)	7(100.00)
Meropenem	14(100.00)	10(100.00)	7(100.00)
Cefazolin	11(78.57)	8(80.00)	4(57.14)
Ceftazidime	12(85.71)	9(90.00)	5(71.43)
Ceftriaxone	12(85.71)	9(90.00)	5(71.43)
Cefoperazone	14(100.00)	9(90.00)	7(100.00)
Gentamicin	5(35.71)	8(80.00)	5(71.43)
Compound sulfamethoxazole	2(14.29)	9(90.00)	6(85.71)
Ciprofloxacin	5(35.71)	9(90.00)	6(85.71)
Levofloxacin	6(42.86)	9(90.00)	6(85.71)
Amikacin	14(100.00)	10(100.00)	7(100.00)

2.2.2 足部溃疡常见革兰阳性菌的药敏性分析 金黄色葡萄球菌与表皮葡萄球菌对万古霉素、利奈唑胺和利福平敏感性较高(高于95.00%),对青霉素和红霉素的敏感性较低(低于

50.00%);粪肠球菌对红霉素、氨苄西林、万古霉素及利奈唑胺敏感性较高(高于90.00%),对四环素和利福平的敏感性较低(低于50.00%),结果见表4。

表4 足部溃疡常见革兰阳性菌的药敏性分析[n(%)]

Table 4 Analysis of drug susceptibility of gram positive bacteria in foot ulcers [n (%)]

Drugs	<i>Staphylococcus aureus</i> (n=22)	<i>Staphylococcus epidermidis</i> (n=5)	<i>Enterococcus faecalis</i> (n=4)
Penicillin	5(22.73)	0(0.00)	3(75.00)
Erythromycin	10(45.45)		4(100.00)
Ampicillin	-	-	4(100.00)
Rifampicin	21(95.45)	5(100.00)	1(25.00)
Ciprofloxacin	21(95.45)	3(60.00)	-
Levofloxacin	20(90.91)	2(40.00)	3(75.00)

Moxifloxacin	21(95.45)	3(60.00)	3(75.00)
Chloramphenicol	14(63.64)	3(60.00)	3(75.00)
Gentamicin	15(68.18)	2(40.00)	-
Tetracycline	20(90.91)	3(60.00)	0(0.00)
Oxacillin	18(81.82)	1(20.00)	-
Vancomycin	22(100.00)	5(100.00)	4(100.00)
Linezolid	22(100.00)	5(100.00)	4(100.00)

3 讨论

糖尿病足是因下肢远端外周血管病变和/或下肢远端神经异常而导致的足部深层组织破坏、溃疡和/或感染,初期若能及时治疗可得到缓解,若未进行治疗则易导致足部慢性溃疡^[15,16]。糖尿病足的发生是一系列因素相互作用的结果,其危险因素主要有年龄为老年、糖尿病知识缺乏、以往有足溃疡史、继往有神经病变、周围血管病变或肾脏病变等^[17,18]。据国内外报道发现,糖尿病患者中发生足溃疡或坏疽的有5%~20%,大约有1%者被截肢;美国每年的非创伤性截肢患者中糖尿病患者占50%;截至2010年,我国现有糖尿病患者4000万,70%的足病患者合并感染足部溃疡^[19,20]。糖尿病足部溃疡是糖尿病临床诊疗中的一个难题,严重时可导致患者下肢截肢致残,这不仅给患者带来极大痛苦,降低了生存质量,同时也加重了患者家庭和社会的经济负担,因此探究糖尿病足部溃疡的有效治疗方案具有重要的临床意义。临床上抗菌药物的广泛应用和不规范使用,糖尿病足部溃疡感染的抗菌治疗疗效并不佳,耐药情况屡见不鲜,增加了糖尿病足部溃疡抗感染治疗的难度^[21-23]。另外,当足部溃疡发生感染时,由于患者脏器功能不全,机体抵抗力差,伤口感染与平常相比较不易控制,因此,在临床诊疗中应根据病原菌的种类和药敏性正确使用抗菌药物^[24-26]。

本研究针对我院收治的102例糖尿病足患者足部溃疡分泌物的分析发现,102例糖尿病患者足部溃疡分泌物中,有96例成功分离出菌株,6例未分离出菌株,总阳性率为94.12%;96例样本中共分离出107株菌株,其中革兰阴性菌61株(57.01%)、革兰阳性菌43株(40.19%)和真菌3株(2.80%),占总菌株百分比前三位的病原菌分别为金黄色葡萄球菌(20.56%)、奇异变形杆菌(13.08%)和肺炎克雷伯菌(9.35%),说明糖尿病足部溃疡感染率较高,主要病原菌为金黄色葡萄球菌、奇异变形杆菌和肺炎克雷伯菌,因此在今后糖尿病足未确诊前的治疗应把重点放在此三类病原菌上,重点为控制革兰阴性菌的感染。在周莹等人的研究中^[27],108例糖尿病足患者中共检出141株病原菌,其中革兰阳性菌为46.8%(66/141),革兰阴性菌为43.3%(61/141),革兰阳性菌是感染最多的病原菌,与本研究存在一定的差异,我们认为可能是因为本研究中存在较多免疫力低下的患者,增加了感染毒力相对较低的革兰阴性菌的几率,导致革兰阴性菌成为感染最多的病原菌^[28,29]。另外,对病原菌的药敏研究发现,前三位革兰阴性菌(奇异变形杆菌、肺炎克雷伯菌和大肠埃希菌)对亚胺培南、美罗培南、头孢哌酮及阿米卡星的敏感性较高,其中前三位革兰阴性菌对亚胺培南、美罗培南的敏感性均为100.00%,提示这两种药物可作为主要革

兰阴性菌所致的糖尿病足感染的首选治疗方案;前三位革兰阴性菌对氨苄西林的敏感性较低,提示氨苄西林已不适用于治疗主要革兰阴性菌所致的糖尿病足感染;金黄色葡萄球菌与表皮葡萄球菌对万古霉素、利奈唑胺和利福平敏感性较高,对青霉素和红霉素的敏感性较低;粪肠球菌对红霉素、氨苄西林、万古霉素及利奈唑胺敏感性较高,对四环素和利福平的敏感性较低,这说明不同病原菌的药敏性也不尽相同,临床上在对糖尿病足溃疡的诊疗中,应对溃疡分泌物进行细菌鉴定和药敏分析,根据药敏试验的结果来选择合适的抗菌药物,从而开展针对性治疗,达到较好的治疗效果,降低糖尿病足患者的截肢率^[30]。

综上,糖尿病足部溃疡感染以革兰阴性菌和革兰阳性菌为主,其中金黄色葡萄球菌和奇异变形杆菌为主要病原菌,各种病原菌的耐药情况存在一定的差异,临床诊疗过程中应根据药敏结果规范使用抗菌药物。

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