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晚期肺癌化疗患者发生医院感染的病原菌分布及危险因素分析

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摘要 目的:研究晚期肺癌化疗患者发生医院感染的病原菌分布及危险因素,为临床预防及降低医院感染提供参考。**方法:**选择从2012年9月-2015年9月在我院接受化疗治疗的晚期肺癌患者235例进行研究。调查并统计所有患者的病历资料,对感染者的鼻拭子、痰标本及腹水等标本进行细菌鉴定及药敏试验,分析晚期肺癌化疗患者发生医院感染的危险因素。**结果:**235例晚期肺癌化疗患者中,发生医院感染65例,感染率为27.66%,共检出病原菌75株,其中革兰阴性菌41株,占54.67%,革兰阳性菌26株,占34.67%,真菌8株,占10.67%。肺炎克雷伯菌对氨苄西林的耐药率最高,为80.00%,对万古霉素的敏感率最高,为100.00%;金黄色葡萄球菌对青霉素的耐药率最高,为94.74%,对利奈唑胺的敏感率最高,为100.00%。根据Logistic回归分析法评价可知,晚期肺癌化疗患者发生医院感染的危险因素主要有:年龄 ≥ 60 岁、临床分期为IV期、接受放疗、存在贫血、使用抗生素以及住院时间 ≥ 15 d。**结论:**导致晚期肺癌化疗患者发生医院感染的主要病原菌为肺炎克雷伯菌以及金黄色葡萄球菌,且年龄 ≥ 60 岁、临床分期为IV期、接受放疗、存在贫血、使用抗生素以及住院时间 ≥ 15 d均为影响晚期肺癌化疗患者发生医院感染的危险因素,值得临床重视。

关键词:晚期肺癌;化疗;医院感染;病原菌;分布;危险因素

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Pathogenic Bacteria Distribution and Risk Factors of Nosocomial Infections in Advanced Lung Cancer Patients Underwent Chemotherapy

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ABSTRACT Objective: To study the pathogenic bacteria distribution and risk factors of nosocomial infections in advanced lung cancer patients underwent chemotherapy, so as to provide the reference for clinical prevention and reduction of nosocomial infections. **Methods:** A total of 235 patients with advanced lung cancer who were underwent chemotherapy in our hospital from September 2012 to September 2015 were selected for the research, the clinical data were investigated and analyzed, and the bacteria identification and drug sensitivity test were carried out on nasal swab, sputum specimen and ascites, etc. The risk factors of nosocomial infection in patients with advanced lung cancer underwent chemotherapy were analyzed. **Results:** In those 235 patients, 65 patients occurred nosocomial infection, the infection rate was 27.66%, 75 strains of pathogenic bacteria were detected, including 41 strains of gram negative bacteria, accounting for 54.67%, 26 strains of gram positive bacteria, accounting for 34.67%, and 8 strains of fungi, accounting for 10.67%. Drug resistance rate of *Klebsiella pneumoniae* to ampicillin was highest to 80.00%, and the sensitive rate to vancomycin was highest to 100.00%; Drug resistance rate of *Staphylococcus aureus* to penicillin was highest to 94.74%, and the sensitive rate to linezolid was highest to 100.00%. Logistic regression analysis showed that, the mainly risk factors of nosocomial infection in patients with advanced lung cancer underwent chemotherapy were: age ≥ 60 years old and clinical stage IV, radiotherapy, anemia, using antibiotics and hospitalization time ≥ 15 days. **Conclusion:** The main pathogenic bacterias causing nosocomial infection in patients with advanced lung cancer underwent chemotherapy were *Klebsiella pneumoniae* and *Staphylococcus aureus*, and age ≥ 60 years old and clinical stage IV, radiotherapy, anemia, using antibiotics and hospitalization time ≥ 15 days were its risk factors, which should pay attention in clinical practice.

Key words: Advanced lung cancer; Chemotherapy; Nosocomial infection; Pathogenic bacteria; Distribution; Risk factors

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前言

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晚期肺癌化疗患者由于肿瘤长时间负荷以及消耗作用,导致其机体免疫功能低下,并且持续性接受化学药物治疗,容易出现骨髓抑制和致病菌侵入等,进而发生医院感染。医院感染不仅直接影响患者治疗结果,延长住院时间,而且极易导致死亡,对患者生活以及生命安全均可造成严重威胁^[1,2]。据临床统

计^[3,4],肺癌住院患者中,由于医院感染导致死亡的高达 10%左右,且直接死亡原因均为因肺部感染引发的呼吸衰竭。因此,深入研究导致肺癌患者发生医院感染的病原菌和危险因素,对预防和控制患者医院感染,提高生存率以及延长生存时间均十分关键。鉴于此,本文通过观察分析晚期肺癌化疗患者发生医院感染的病原菌分布及危险因素,旨在更加全面地掌握化疗患者医院感染的实际情况,现报道如下。

1 资料与方法

1.1 临床资料

选择从 2012 年 9 月 -2015 年 9 月间在我院接受化疗治疗的晚期肺癌患者 235 例进行研究。男 142 例,女 93 例;年龄 32~72 岁,平均(63.2±1.6)岁。纳入标准:(1)符合 WHO 关于肺癌的相关诊断标准^[5,6];(2)经过病理组织学或者细胞学等检查方式确诊;(3)TNM 分期为Ⅲ~Ⅳ期。排除标准:(1)其他类型的恶性肿瘤;(2)接受手术治疗者;(3)研究期间即已死亡者。根据我国卫计委制定的 2001 年版《医院感染诊断标准》对患者的医院感染进行诊断。

1.2 研究方法

调查并统计所有患者的病历资料数据,主要调查内容包含如下方面:(1)性别;(2)年龄;(3)病理类型;(4)临床分期;(5)是否放疗;(6)是否贫血;(7)是否使用抗生素;(8)住院时间。分析以上因素与晚期肺癌化疗患者发生医院感染相关性。

1.3 菌株培养与药敏试验

对感染者的鼻拭子、痰标本及腹水等标本进行病原菌培养及鉴定,分析感染者的病原菌分布情况,而后依据纸片扩散法的标准步骤对病原菌进行药敏试验。

1.4 统计学方法

通过 SPSS13.0 统计软件进行分析,计数数据比较采用 χ^2 检验,危险因素使用 Logistic 回归分析法进行评价, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 病原菌分布

235 例晚期肺癌化疗患者中,发生医院感染 65 例,感染率为 27.66%,共检出病原菌 75 株,其中革兰阴性菌 41 株,占 54.67%,包括肺炎克雷伯菌 15 株(20.00%)、铜绿假单胞菌 11 株(14.67%)、大肠埃希菌 8 例(10.67%)、其他 7 例(9.33%);革兰阳性菌 26 株,占 34.67%,包括金黄色葡萄球菌 19 株(25.33%)、表皮葡萄球菌 5 株(6.67%)、其他 2 例(2.67%);真菌 8 株,占 10.67%,包括白色假丝酵母菌 6 株(8.00%)、热带假丝酵母菌 2 株(2.67%)。

2.2 主要革兰阳、阴性菌病原菌耐药性

肺炎克雷伯菌对氨苄西林的耐药率最高,为 80.00%,对万古霉素的敏感率最高,为 100.00%;金黄色葡萄球菌对青霉素的耐药率最高,为 94.74%,对利奈唑胺的敏感率最高,为 100.00%。见下表 1。

表 1 肺炎克雷伯菌及金黄色葡萄球菌的耐药率(%)
Table 1 Resistance rate of *Klebsiella pneumoniae* and *Staphylococcus aureus*(%)

Antibacterial drugs	<i>Klebsiella pneumoniae</i> (n=15)		<i>Staphylococcus aureus</i> (n=19)	
	Strain	Resistant rate	Strain	Resistant rate
Ampicillin	12	80.00	16	84.21
Vancomycin	0	0.00	1	5.26
Linezolid	5	33.33	0	0.00
Penicillin	11	73.33	18	94.74
Erythromycin	9	60.00	16	84.21
Gentamicin	10	66.67	13	68.42
Cefotaxime	6	40.00	8	42.11
Amikacin	5	33.33	6	31.58
Imipenem	6	40.00	5	26.32

2.3 晚期肺癌化疗患者发生医院感染的单因素分析

单因素分析显示,晚期肺癌化疗患者发生医院感染与年龄、临床分期、放疗、贫血、使用抗生素以及住院时间有关($P<0.05$)。见下表 2。

2.4 晚期肺癌化疗患者发生医院感染的多因素分析

根据 Logistic 回归分析法评价可知,影响晚期肺癌化疗患者发生医院感染的危险因素主要有:年龄 ≥ 60 岁、临床分期为Ⅳ期、接受放疗、存在贫血、使用抗生素以及住院时间 ≥ 15 d

($P<0.05$)。见下表 3。

3 讨论

临床上,肺癌为目前比较高发的恶性肿瘤之一,其发病率以及死亡率均呈快速增长趋势,严重威胁人们的生命健康与安全。当前对于肺癌的治疗,通常以化疗方式为主。即使是对于错失最佳治疗时机的晚期肺癌患者,给予化疗治疗仍可以延长生存期以及改善患者的生活质量^[7,8]。但近年来的临床研究^[9,10]发

表 2 晚期肺癌化疗患者发生医院感染的单因素分析及感染率(%)

Table 2 Single factor analysis and infection rate of nosocomial infection in patients with advanced lung cancer underwent chemotherapy(%)

Related indexes		Investigation cases	Infection cases	Infection rate	χ^2	P
Gender	Male	142	42	29.58	0.660	0.417
	Female	93	23	24.73		
Age (years)	< 60	121	26	21.49	4.749	0.029
	≥ 60	114	39	34.21		
Pathologic types	Central type	127	34	26.77	0.109	0.741
	Peripheral type	108	31	28.70		
Clinical staging	III	132	20	15.15	23.548	0.000
	IV	103	45	43.69		
Radiation therapy	Yes	65	29	44.62	12.910	0.000
	NO	170	36	21.18		
Anemia	Yes	128	47	36.72	11.530	0.001
	NO	107	18	16.82		
Use of antibiotics	Yes	133	50	37.59	15.114	0.000
	NO	102	15	14.71		
Length of stay(d)	< 15	149	14	9.40	67.874	0.000
	≥ 15	86	51	59.30		

表 3 晚期肺癌化疗患者发生医院感染的多因素分析

Table 3 Multivariate analysis of nosocomial infection in patients with advanced lung cancer underwent chemotherapy

Related indexes	Regression coefficient	Standard error	P	OR	95%CI
Age≥ 60 years old	4.238	2.707	0.002	4.592	1.128~8.396
Clinical stage IV	4.561	3.216	0.000	3.448	1.085~6.562
Radiotherapy	6.388	4.104	0.000	1.509	1.233~5.949
Anemia	5.205	3.233	0.000	2.682	1.105~10.244
Using antibiotics	4.139	2.689	0.003	1.069	2.197~8.237
Hospitalization time≥ 15 days	4.954	3.572	0.000	4.256	1.268~9.431

现,晚期肺癌化疗患者免疫机能逐步降低,使医院感染的发生率不断上升,较大程度地影响治疗及预后效果,甚至危及患者生命。因此,医院感染可作为缩短晚期肺癌患者生存期的一项关键性因素,需予以高度重视。

本文通过研究发现,造成晚期肺癌化疗患者发生医院感染的主要致病菌中,革兰阴性菌 41 株,占 54.67%,以肺炎克雷伯菌为主,分别占 20.00%及 14.67%;革兰阳性菌 26 株,占 34.67%,以金黄色葡萄球菌为主,占 25.33%;真菌 8 株,占 10.67%,以白色假丝酵母菌为主,占 8.00%。提示导致晚期肺癌化疗患者发生医院感染的病原菌主要是肺炎克雷伯菌以及金黄色葡萄球菌。符合 Qu J 等人^[11-13]关于癌症化疗患者发生院内感染的报道结果。究其原因,可能是因为医院内不合理使用抗菌药物,致使上述致病菌大量增殖,既增大了医院内感染发生率,又增加了治疗难度^[14]。分析上述主要病原菌的耐药率发现,肺炎克雷伯菌对氨苄西林的耐药率最高,为 80.00%,对万古霉素的敏感率最高,为 100.00%;金黄色葡萄球菌对青霉素的耐

药率最高,为 94.74%,对利奈唑胺的敏感率最高,为 100.00%,临床可参考选择万古霉素和利奈唑胺治疗晚期肺癌化疗发生医院感染的患者。

本研究将单因素筛选出的可能影响晚期肺癌化疗患者发生医院感染因素带入多因素的 Logistic 回归方程,结果显示,年龄≥ 60 岁、临床分期为Ⅳ期、接受放疗、存在贫血、使用抗生素以及住院时间≥ 15d 均为影响晚期肺癌化疗患者发生医院感染的危险因素。分析原因主要有以下几点:年龄≥ 60 岁患者机体免疫力较低,对于医院内致病菌的抵抗力也较小,相对而言更易引起医院感染;放疗虽然对肿瘤细胞具有杀伤作用,同时也会对机体正常细胞造成损伤,主要体现在各类放射性炎症,并使患者血液中白细胞以及血小板等含量下降,对机体免疫机制造成严重影响,降低免疫力且增大感染几率^[15-17];肺癌晚期特别是临床病理分期Ⅳ期的患者,其身体长期受到肿瘤消耗,整体情况较差,营养摄入欠缺导致营养不良,极易引发贫血。而贫血会使机体抵抗力进一步降低,机体防御机制受到破

坏,进而成为医院感染易感者^[18,19];抗生素的过度开发和滥用,使患者机体内菌群失衡,耐药性增加。而住院时间越长,患者接触外源性致病菌的几率则越大,均可加大医院感染风险。Zhao Y 等报道证实^[20],癌症化疗患者住院时间超过 15d 时发生医院感染的几率更大,甚至是住院时间低于 15d 的 2 倍以上,对患者的预后具有不利影响。

综上所述,导致晚期肺癌化疗患者发生医院感染的主要致病菌为肺炎克雷伯菌以及金黄色葡萄球菌,年龄 ≥ 60 岁、临床分期为Ⅳ期、接受放疗、存在贫血、使用抗生素以及住院时间 ≥ 15 d 均为影响晚期肺癌化疗患者发生医院感染的危险因素,值得临床重视。

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