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神经外科重症监护病房耐万古霉素肠球菌感染的流行特征及危险因素研究

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摘要 目的:探讨神经外科重症监护病房(ICU)耐万古霉素肠球菌(VRE)感染的流行特征及危险因素,为临床防控提供参考依据。**方法:**选择2014年1月至2016年1月在我院接受手术治疗的神经外科ICU住院患者420例为研究对象。比较VRE感染患者在感染前抗生素的应用情况,并分别应用单因素及多因素 Logistic 回归分析分析 VRE 感染患者的危险因素,提出防控措施。**结果:**420例ICU住院患者中,VRE感染者58例,占13.81%。VRE感染患者在感染前应用的抗生素以三代头孢最多,占37.93%,以四代头孢最少,占6.90%。由单因素及多因素 Logistic 回归分析显示,ICU住院时间 ≥ 14 d、留置尿管 ≥ 14 d、格拉斯哥昏迷量表(GCS)评分 <8 分以及附近存在VRE感染者均为VRE感染患者的危险因素($P<0.05$)。**结论:**VRE感染患者在感染前应用的抗生素以三代头孢最多,ICU住院时间 >14 d、留置尿管 >14 d、GCS评分 <8 分以及附近存在VRE感染者均为VRE感染患者的危险因素,临床上应合理应用抗生素,采取相应的防控措施,降低VRE感染的发生。

关键词:神经外科;重症监护病房;耐万古霉素肠球菌;感染;危险因素

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Epidemiological Characteristics and Risk Factors of Vancomycin Resistant Enterococcus Infection in Intensive Care Unit of Department of Neurosurgery

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ABSTRACT Objective: To investigate the epidemiological characteristics and risk factors of vancomycin resistant enterococcus (VRE) infection in intensive care unit (ICU) of department of neurosurgery, and to provide reference for clinical prevention and control. **Methods:** A total of 420 patients, who underwent surgery in the ICU of department of neurosurgery in Taizhou Hospital of Traditional Chinese Medicine from January 2014 to January 2016, were chosen as subjects. The application of antibiotics before infection in the patients with VRE infection was compared, and univariate and multivariate Logistic regression analysis were used to analyze the risk factors of VRE infection to propose the prevention and control measures. **Results:** Among the 420 inpatients in ICU, there were 58 cases of VRE infection, accounted for 13.81%. The most common antibiotics used before VRE infection was three generation cephalosporin, accounted for 37.93%, and four generation cephalosporin was least, accounted for 6.90%. Single factor and Logistic regression analysis showed that the ICU hospitalization time ≥ 14 d, indwelling catheter ≥ 14 d, Glasgow Coma Scale (GCS) score <8 and patients infected by VRE nearby were the risk factors of VRE infection($P<0.05$). **Conclusion:** The most common antibiotics used before VRE infection is three generation cephalosporin. ICU hospitalization time ≥ 14 d, indwelling catheter ≥ 14 d, GCS score <8 and patients infected by VRE nearby are the risk factors of VRE infection. Rational use of antibiotics and taking corresponding prevention and control measures are necessary in the clinical practice to reduce the incidence of VRE infection.

Key words: Department of Neurosurgery; Intensive care unit; Vancomycin resistant enterococcus; Infection; Risk factors

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前言

耐万古霉素肠球菌 (Vancomycin resistant enterococcus, VRE)感染在临床住院患者中比较常见,其在不同医院中的感

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染发生率也具有较大差异,大约为1.5%~32%^[1,2]。由于神经外科重症病房(Intensive care unit, ICU)住院患者的病情通常较为严重,此类病房中患者发生VRE感染的几率相对更大。患者在形成VRE感染后,常会引发反复性高热和脑膜炎,以及败血症和多器官衰竭等严重症状,若不及时进行干预治疗,则可能直接危及生命安全^[3,4]。有研究发现,若患者合并有VRE感染,则发生进一步严重感染的几率将增加5至10倍,从而直接加大了治疗难度^[5]。既往报道指出^[6,7],VRE的感染可能与糖尿病和

移植等因素有关。神经外科 ICU 住院患者中突发性疾病占据的比例较大,引发 VRE 感染的危险因素常规研究存在一定的区别。本文通过分析我院神经外科 ICU 病房中住院患者 VRE 感染的流行特征及危险因素,并由此探讨对应的防控措施,从而更好地辅助临床治疗,现报道如下。

1 资料和方法

1.1 临床资料

选择 2014 年 1 月至 2016 年 1 月在我院接受手术治疗的神经外科 ICU 住院患者 420 例进行研究,纳入标准:(1)均为 ICU 患者;(2)年龄 ≥ 40 岁;(3)感染者均经过血液检测出 VRE;(4)研究经医学伦理委员会批准,所有患者及家属均知情同意并签署知情同意书。排除标准:(1)患有其他类型感染者;(2)合并机体其他部位严重骨折者;(3)有心、肝、肾等器官的严重性功能衰竭者。其中,发生 VRE 感染者 58 例,其中男 39 例,女 19 例;年龄 40~75 岁,平均 (58.23 ± 3.25) 岁,未感染者 362 例,其中男 323 例,女 39 例;年龄 40~77 岁,平均 (60.23 ± 2.76) 岁。按疾病类型:重型颅脑损伤 287 例,急性出血性脑卒中 121 例,颅内肿瘤 12 例。

1.2 研究方法

1.2.1 资料收集 统计所有患者人口学资料,记录基础性合并疾病、留置导管或者插管的情况以及格拉斯哥昏迷量表(Glasgow Coma Scale, GCS)评分,统计抗生素应用情况及呼吸机的通气时间以及 ICU 住院时间。

1.2.2 标本检测 在患者的住院期间,为其每周采集 1 次检测标本,主要包含大便、痰液、尿液和创面脓液,全部标本均送至我院检测实验室实施病原菌培养检测。其中上述标本的检测结果 ≥ 1 次出现 VRE 感染即可认为已发生 VRE 感染。针对 VRE 感染者在隔离到其他单独病房内治疗至标本转阴之后 3 周即可解除隔离。

1.3 观察指标

(1)比较 VRE 感染患者在感染前抗生素应用情况;(2)分

别应用单因素及多因素 Logistic 回归分析分析 VRE 感染患者的危险因素。

1.4 统计学方法

通过 SPSS20.0 统计软件分析,计数资料以率(%)的形式表示,比较采用卡方检验,VRE 感染的危险因素应用单因素分析及多因素 Logistic 回归分析法进行分析评价, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 VRE 感染患者在感染前抗生素应用情况

420 例 ICU 住院患者中,VRE 感染者 58 例,占 13.81%;未感染者 362 例,占 86.19%。VRE 感染患者在感染前应用的抗生素以三代头孢最多,占 37.93%,以四代头孢最少,占 6.90%,见表 1。

表 1 VRE 感染患者在感染前抗生素应用情况的比较(n,%)

Table 1 Comparison of application of antibiotic before infection in VRE infected patients(n, %)

Antibiotic	Cases(n=58)	Percentage
Three generation cephalosporin	22	37.93
Vancomycin	13	22.41
Metronidazole	5	8.62
Four generation cephalosporin	4	6.90
Two types of antibiotic	6	10.34
Antibiotic $\geq$ Three types	8	13.79

2.2 VRE 感染患者的单因素分析

单因素分析显示,VRE 感染与 ICU 住院时间、留置尿管、GCS 评分以及附近是否存在 VRE 感染者等因素有关,见表 2。

表 2 VRE 感染患者的单因素分析(n,%)

Table 2 Single factor analysis of VRE infected patients(n, %)

Items		Total cases (n=420)	Infection cases (n=58)	Infection rate(%)	χ^2	P
Gender	Male	228	26	11.40	1.831	0.176
	Female	192	32	16.67		
Age (years old)	≥ 60	236	28	11.86	1.291	0.256
	< 60	184	30	16.30		
Mechanical ventilation time (d)	> 14 d	233	31	13.30	0.085	0.771
	≤ 14 d	187	27	14.44		
ICU hospital stay (d)	> 14 d	306	52	16.99	7.648	0.006
	≤ 14 d	114	6	5.26		
Indwelling catheter time (d)	> 14 d	294	49	16.67	5.274	0.022
	≥ 14 d	126	9	7.14		
Whether or not associated with diabetes	Yes	127	11	8.66	3.154	0.076
	No	293	47	16.04		

Whether or not associated with nephropathy	Yes	12	2	16.67	0.063	0.802
	No	408	56	13.73		
Whether or not associated with hepatopathy	Yes	9	2	22.22	0.386	0.534
	No	411	56	13.63		
Whether or not associated with hepatopathy pneumonia	Yes	15	3	20.00	0.360	0.548
	No	405	55	13.58		
Number of indwelling pipe (number)	>4	49	5	10.20	0.472	0.492
	≤ 4	371	53	14.29		
GCS scores (scores)	≥ 8 scores	173	7	4.05	18.410	0.000
	<8 scores	247	51	20.65		
Whether or not had VRE infected nearby	Yes	218	39	17.89	4.822	0.028
	No	202	19	9.41		

2.3 VRE 感染患者的危险因素分析

由 Logistic 回归分析危险因素显示,ICU 住院时间 >14 d、

留置尿管 >14 d、GCS 评分 <8 分以及附近存在 VRE 感染者均为 VRE 感染患者的危险因素,见表 3。

表 3 VRE 感染患者的危险因素分析
Table 3 Analysis of risk factors in patients with VRE infection

Risk factors	B	SE	Wald	P	OR	95%CI
ICU hospital stay>14 d	4.285	3.221	5.272	0.000	2.296	1.011~7.386
Indwelling catheter time>14 d	6.211	4.078	3.989	0.012	1.412	1.212~6.941
GCS scores<8	5.039	3.204	3.624	0.042	1.387	1.106~11.219
There are VRE infected nearby	4.106	2.215	4.001	0.002	2.039	1.237~8.240

3 讨论

VRE 定植于肠道而不引起感染症状,VRE 不引起腹泻且 VRE 定植或感染高危险性的患者,尤其是 ICU、免疫抑制、接受腹腔或心胸手术、中心静脉导管留置、延长住院时间或近期使用广谱抗生素治疗及接受口服或静脉万古霉素等的患者^[8-10]。据调查发现^[11],导致 VRE 感染的原因主要可能是抗生素应用的泛滥,特别是头孢类药物和万古霉素等药物的普遍使用,其不但降低了患者的免疫力和中性粒细胞数目,甚至导致肝肾功能不全等症状的出现。有报道显示^[12,13],神经外科 ICU 住院患者中,诸多无意识的患者常需连接各类生命支持管及引流管,此类患者常会引发 VRE 感染。因此,了解 ICU 患者感染前抗生素的应用情况及分析发生 VRE 感染的危险因素对临床治疗具有重要意义^[14]。

本文研究结果显示,VRE 感染患者在感染前应用的抗生素中三代头孢最多,占 37.93%,四代头孢最少,占 6.90%,提示头孢对 VRE 感染的发生有重要影响,尤其是三代头孢,同样说明,人们可能对一代和二代头孢产生了耐药性,分析其原因可

能是神经外科 ICU 病房内的多数患者均需应用 7d 左右的三代头孢,这有助于患者 VRE 感染继续发展,而当患者在此阶段中发生全身感染,常会进一步联合使用万古霉素或者其他抗厌氧菌类抗生素^[15-17],这也提示在以后的临床治疗中应用抗生素时应进行合理评估,可以考虑从控制头孢类药物及万古霉素的剂量方面尽可能地减少 VRE 定植和感染^[18]。

此外,本研究单因素分析及多因素 Logistic 回归分显示,ICU 住院时间 >14 d、留置尿管 >14 d、GCS 评分 <8 分以及附近存在 VRE 感染者均为 VRE 感染患者的危险因素,提示上述危险因素均可能导致 VRE 感染,临床上应尽可能地规避此类因素^[19,20]。究其原因可能是 ICU 较医院其他病房存在相对更多的病原菌,在这样复杂的环境下随着 ICU 住院时间的延长,大大增加了患者感染的几率,加之各类抗生素的应用,容易造成耐药病原菌的形成,最终导致患者感染 VRE^[21-23]。若留置尿管的时间越长,则增加了尿管与身体尿道的接触时间,使病原菌更易通过尿管进入机体,从而引发 VRE 感染。Adrie C 等人报道指出^[24,25],神经外科 ICU 住院患者常会留置较多导管,包括中心静脉管和鼻饲管,及引流管和导尿管等导管,并因此而产生

皮肤污染或者二次感染。临床上可合理地早期拔除引流管,同时确保医师及护理人员触摸管时进行无菌操作,其可有利于降低此类导管性感染的发生率^[26,27]。而 GCS 评分 <8 分的患者由于病情较为严重,甚至可能较长时间地处于昏迷状态,机体免疫力也相对较低,因此较易造成 VRE 感染^[28]。附近存在 VRE 感染者则可能由于交叉感染而致使相同耐药病原菌在患者的机体发生定植和感染。为避免此种现象的发生,临床可将 VRE 感染阳性的患者给予隔离到单独病房,从而有效预防交叉感染。薄天慧等人也报道证实^[29,30],两例或者多例患者共用病房则可能增大互相感染的风险。

综上,VRE 感染患者在感染前应用的抗生素以三代头孢最多,ICU 住院时间 >14 d、留置尿管 >14 d、GCS 评分 <8 分以及附近存在 VRE 感染者均为 VRE 感染患者的危险因素,临床上应合理应用抗生素,采取相应的防控措施,降低 VRE 感染的发生。

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