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血必净联合利奈唑胺注射液对老年重症肺炎患者血清肺表面活性蛋白、基质金属蛋白酶及其组织抑制剂水平的影响*

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摘要 目的：探讨血必净联合利奈唑胺注射液治疗老年重症肺炎患者的临床疗效及对患者血清肺表面活性蛋白(Pulmonary surfactant protein，SP)、基质金属蛋白酶 (Matrix metalloproteinases，MMPs) 及其组织抑制剂 (Matrix metalloproteinases tissue inhibitor，TIMPs)水平的影响。**方法：**选择我院 2015 年 6 月 ~2017 年 12 月收治的 101 例老年重症肺炎患者，按随机数字表法分为对照组(n=48)和研究组(n=53)。对照组采用利奈唑胺注射液治疗，研究组在对照组基础上采用血必净治疗。比较两组临床疗效，细菌清除情况，症状缓解时间，治疗前后血清 SP、MMPs、TIMPs 水平的变化，动脉血气，肺功能，不良反应的发生情况和 28 天内病死率。**结果：**治疗后，研究组有效率、细菌清除率均显著高于对照组(均 P<0.05)，发热消失、血常规恢复、痰液颜色改变及胸部影像明显吸收时间均明显短于对照组(P<0.05)；两组血清 SP-A、SP-B、SP-C、SP-D、MMP-2、MMP-9 及 TIMP-1 及 TIMP-2、血氧饱和度(blood oxygen saturation，SaO_2)、动脉血二氧化碳分压(arterial blood，$PaCO_2$)、动脉血二氧化碳分压(arterial blood CO_2 partial pressure of CO_2 partial pressure，$PaCO_2$)、峰流速 (peak velocity of flow，PEF) 水平均较治疗前显著下降，而血氧饱和度 (blood oxygen saturation，SaO_2)、氧分压(oxygen partial pressure，PaO_2)、最大呼气中段流量(maximum tidal midexpiratory flow，MMF)、用力肺活量(forced vital capacity，FVC)均较治疗前明显上升，且研究组以上指标变化较对照组更明显(均 P<0.05)。两组不良反应的发生情况比较差异无统计学意义(P>0.05)，而研究组在 28 天内病死率显著低于对照组(P<0.05)。**结论：**血必净联合利奈唑胺注射液对老年重症肺炎患者的疗效优于单用利奈唑胺注射液治疗，可能与其显著降低患者血清 SP、MMPs 及 TIMPs 水平，改善肺功能，降低病死率有关。

关键词：老年重症肺炎；血必净；利奈唑胺注射液；肺表面活性蛋白；基质金属蛋白酶；基质金属蛋白酶组织抑制剂

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Effects of Xuebijing Combined with Linazolamide Injection on the Serum Lung Surface Active Proteins, Matrix Metalloproteinases and Tissue Inhibitors Levels in the Elderly Patients with Severe Pneumonia*

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ABSTRACT Objective: To analyze the clinical efficacy of xuebijing combined with linazolamide injection in the treatment of elderly patients with severe pneumonia and its effect on serum levels of pulmonary surface active protein (SP), matrix metalloproteinase (MMPs) and tissue inhibitor (TIMPs). **Methods:** 101 cases of elderly severe pneumonia who treated from June 2015 to December 2017 in our hos-pital, according to the random number table method, those patients were divided into the control group (n=48) and the research group (n=53). The control group was treated with linazolamide injection, and the research group was treated with xuebijing based on the control group. Then clinical efficacy, bacterial clearance, symptom relief time, changes of SP, MMPs and TIMPs levels before and after treatment, the occurrence of adverse reactions and mortality within 28 days in both group were compared. **Results:** After treatment, effective rate in research group was significant higher than that of the control group (P<0.05). disappearance of fever, restoration of blood routine, change of sputum color, and apparent absorption time of chest image in research group were significant lower than that in the control group (P<0.05). After treatment, serum levels of SP-A, SP-B, the SP-C, SP-D, MMP-2, MMP-9 and TIMP-1 and TIMP-2, blood oxygen saturation(SaO_2), arterial blood($PaCO_2$), arterial blood CO_2 partial pressure of CO_2 partial pressure($PaCO_2$), peak velocity of flow (PEF) in both group was significant reduction than before the treatment, and blood oxygen saturation(SaO_2), oxygen partial pressure(PaO_2), maximum tidal midexpiratory flow(MMF) and forced vital capacity(FVC) was significant increase than before the treatmen, the changes of the above indexes in the research group were more obvious than those in the control group, and the differences were statistically significant (all P<0.05). adverse reactions in both group was no significant difference(P>0.05). Fatality rate with 28 days in research group was lower

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than that of the control group (P<0.05). **Conclusion:** The curative effect of xuebijing combined with linezolid injection on elderly patients with severe pneumonia is better than that of linezolid injection alone, which may be related to significantly reducing the serum levels of SP, MMPs and TIMPs, improving lung function and reducing the mortality of patients.

Key words: Elderly Severe Pneumonia; Xuebijing; Linazolamide Injection; Lung Surface Active Protein; Matrix Metalloproteinase; Matrix Metalloproteinase Tissue Inhibitor

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前言

重症肺炎主要是因病原微生物入侵肺组织后导致机体分泌多种炎性介质所致的全身炎症反应综合征，病情进展快速，病死率较高[1]。老年重症肺炎患者多合并一定程度的基础疾病，容易出现多脏器功能衰竭，且可并发低蛋白血症、呼吸衰竭、心律失常等严重并发症，增加临床治疗难度[2,3]。临床治疗指南建议[4,5]老年重症肺炎的治疗应首选强力抗菌的广谱抗生素，并按足量给药。利奈唑胺注射液作为一种唑烷酮类抗生素，对耐药葡萄糖球菌、肺炎链球菌、青霉素易感等病原菌有良好的抗菌作用，在临床中对革兰氏阳性感觉感染的治疗中有明显优势[6]。近年来，随着抗生素的滥用，耐药菌明显增加，也在一定程度上影响影响了重症肺炎患者的临床疗效。

血必净注射液为中药制剂，具有拮抗炎症介质、内毒素作用，且可降低血液黏稠度，改善血液循环。临床试验证实[7]血必净在防治全身炎症反应综合征及脓毒症等方面的效果明显，但血必净联合利奈唑胺注射液治疗老年重症肺炎作用机制尚不完全明确。相关研究表明[8,9]肺表面活性蛋白(SP)、机制金属蛋白酶(MMP)及其组织抑制剂(TIMP)和重症肺炎患者损伤状态有显著相关性，可反映肺部局部纤维化。因此，本研究主要探讨了血必净联合利奈唑胺注射液对老年重症肺炎患者的治疗效果，并分析了其对肺表面活性蛋白、基质金属蛋白酶及其组织抑制剂的影响，以期为重症肺炎的临床治疗提供更多的参考依据。

1 资料与方法

1.1 一般资料

101 例老年重症肺炎患者的纳入标准：符合重症肺炎相关诊断标准[10]：含 1 项主要标准：需感染性休克，血管升压类药物或者予以机械通气，并含 3 项以上次要标准：呼吸频率在 30 次 / 分以上，体温在 36℃以上，血小板在 10× 10^9/L 以下，白细胞在 4× 10^9/L 以下，意识或定向障碍，氧合指数在 250 mmHg 以下，低血压，需予以强力液体复苏，多肺叶可见浸润现象；符合中医痰热蕴肺证型；病原菌检测呈阳性；非过敏体质者或者恶性肿瘤；无药物或者酒精依赖；年龄在 60 岁以上。排除标准：其他急慢性疾病史；肝肾功能明显异常；肺结核；入组前接受糖皮质激素等药物治疗，已知凝血功能或者血液异常。

按随机数字表法将所有患者分为对照组(n=48)和研究组(n=53)。对照组中，男 26 例，女 22 例；年龄 60~79 岁，平均(70.42± 7.95)岁；急性生理学和慢性健康状况评分(APACHE)平均(24.11± 3.76)分；双肺病变 27 例，单肺病变 21 例；合并症：高血压 18 例，糖尿病 14 例，呼吸衰竭 20 例。研究组中，男 30 例，女 23 例；年龄 61~80 岁，平均(70.85± 6.33)岁；急性生理学和慢性健康状况评分(APACHE)平均(25.30± 2.95)分；双肺病变 28 例，单肺病变 25 例；合并症：高血压 20 例，糖尿病 17 例，呼吸衰竭 24 例。两组患者的一般基础资料比较差异均无统计学意义(P>0.05)，具有可比性。

1.2 治疗方法

对照组采用利奈唑胺注射液治疗，静脉滴注 600 mg 利奈唑胺注射液(生产厂家：Fresenius Kabi Norge AS，规格：100 mL: 200 mg，批号：150112)，每天 2 次。研究组在对照组基础上联合血必净治疗，将 50 mL 血必净注射液(生产厂家：天津红日药业股份有限公司，规格：10 mL/ 支，批号：141023)和 100 mL 0.9% 氯化钠注射液 (生产厂家：四川美大康佳乐药业有限公司，规格：100 mL:0.9 g，批号：140819)稀释，给予患者静脉滴注，每天 2 次。两组均持续治疗 14 天，入院后均接受营养支持、化痰、退热、补液、吸氧等对症支持治疗。于用药结束时评估疗效，并观察症状缓解时间及治疗期间的不良反应的发生情况和 28 天内病死率。

1.3 观察指标

1.3.1 临床疗效 体征及症状全部消退，实验室及胸部 X 线平片未见异常为治愈；体征及症状显著缓解，实验室指标显著改善，胸部 X 线平片提示肺部纹理、阴影显著减轻为显效；体征及症状有一定缓解，部分实验室指标异常，胸部 X 线平片提示肺部纹理、阴影有减轻为有效；体征及症状缓解不明显，实验室指标无减轻，胸部 X 线平片提示肺部纹理及阴影增粗为无效。痊愈、显效及好转均评定为总有效[10]。

1.3.2 细菌清除情况 病原菌全部消失且未见新生病原菌为清除；病原菌减少为部分清除；病原菌未见改变为未清除；可见新生病原菌，但无需处理为菌群交替；可见新生病原菌，并出现相应临床表现，需处理为再感染。清除及部分清除均视作清除。

1.3.3 指标测定 于用药前及结束时抽取患者 2 mL 空腹静脉血，以血清分离机常规分离后保存待检。采用酶联免疫吸附法检测 SP-A、SP-B、SP-C、SP-D、MMP-2、MMP-9 及 TIMP-1 及 TIMP-2 水平。采用 BXY4 型血气分析仪测定血氧饱和度(SaO_2)、动脉血二氧化碳分压($PaCO_2$)、氧分压(PaO_2)。采用 AS-507 型肺功能检测仪测定峰流速(PEF)、最大呼气中段流量(MMF)、用力肺活量(FVC)。

1.4 统计学分析

选用 SPSS18.0 软件进行数据分析，计量资料以()表示，组间比较选用独立样本 t 检验，计数资料以[例(%)]表示，组间比较用 x^2 检验，以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组临床疗效比较

治疗后，研究组有效率为 90.56%，较对照组显著升高 (75%,P<0.05),见表 1。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison of the clinical curative effect between two groups[n(%)]

Groups	n	Cure	Significantly effective	Effective	Invalid	Efficient rate
Control group	48	6(12.50)	13(27.08)	17(35.42)	12(25.00)	36(75.00)
Research group	53	13(24.53)	20(37.74)	15(28.30)	5(9.43)	48(90.56)[a]

Note: Compared with the control group [a]P<0.05.

2.2 两组细菌清除情况比较

治疗后，研究组细菌清除率为 83.01%，显著高于对照组 (64.58%,P<0.05),见表 2。

表 2 两组细菌清除情况比较[例(%)]

Table 2 Comparison of the bacterial clearance between two groups[n(%)]

Groups	n	Cleared completely	Partially cleared	Not cleared	Replacement	Reinfection	clearance rate
Control group	48	26(54.17)	5(10.42)	12(25.00)	3(6.25)	2(4.16)	31(64.58)
Research group	53	42(79.25)	2(3.77)	8(1.50)	1(1.88)	0(0.00)	44(83.01)[a]

Note: Compared with the control group [a]P<0.05.

2.3 两组症状缓解时间比较

研究组发热消失、血常规恢复、痰液颜色改变及胸部影像明显吸收时间均明显短于对照组(P<0.05),见表 3。

表 3 两组症状缓解时间比较($\bar{x}\pm s$)

Table 3 Comparison of the symptom relief time between two groups($\bar{x}\pm s$)

Groups	n	Fever disappears	Blood recovery	Sputum color change	Obvious absorption of chest image (>50%)
Control group	48	3.10± 0.42	5.81± 0.73	6.48± 0.69	11.70± 2.19
Research group	53	2.74± 0.30[a]	4.12± 0.62[a]	5.03± 0.55[a]	9.84± 1.38[a]

Note: Compared with the control group [a]P<0.05.

2.4 两组治疗前后血清肺表面活性蛋白水平比较

治疗前,两组血清肺表面活性蛋白比较差异无统计学意义(P>0.05);治疗后,两组肺表面活性蛋白水平均较治疗前显著下降，且研究组血清肺表面活性蛋白水平明显低于对照组(P<0.05),见表 4。

表 4 两组治疗前后血清肺表面活性蛋白水平比较($\bar{x}\pm s$,ng/mL)

Table 4 Comparison of the serum lung surface active protein levels between two groups before and after the treatment($\bar{x}\pm s$, ng/mL)

Groups	n	Time	SP-A	SP-B	SP-C	SP-D
Control group	48	Before treatment	39.27± 4.50	43.10± 5.28	59.88± 7.42	80.57± 12.59
		After treatment	19.55± 3.17[#]	20.77± 3.65[#]	26.40± 3.91[#]	50.52± 7.40[#]
Research group	53	Before treatment	38.33± 5.21	42.51± 6.39	51.03± 6.20	81.36± 10.27
		After treatment	12.30± 1.64[a#]	13.94± 1.55[a#]	17.85± 2.44[a#]	41.64± 5.20[a#]

Note: Compared with the control group [a]P<0.05; Compared with before treatment [#]P<0.05.

2.5 两组治疗前后血清基质金属蛋白酶及其组织抑制剂水平比较

治疗前,两组血清基质金属蛋白酶及其组织抑制剂水平比较差异无统计学意义(P>0.05);治疗后,两组血清基质金属蛋白酶及其组织抑制剂水平均较治疗前显著下降,且研究组以上指标均明显低于对照组(P<0.05),见表 5。

2.6 两组治疗前后动脉血气、肺功能比较

治疗前,两组动脉血气、肺功能指标比较差异均无统计学意义(P>0.05);治疗后,两组 SaO_2、PaO_2、MMF 及 FVC 均较治疗前明显上升,$PaCO_2$、PEF 均较治疗前显著下降，研究组 SaO_2、PaO_2、MMF 及 FVC 均明显高于对照组,而 $PaCO_2$、PEF 均显著低于对照组(P<0.05),见表 6。

2.7 两组随访情况比较

研究组 28 天死亡率为 7.55%(4/53)，显著低于对照组[25.00%(12/48)],组间比较有统计学差异(P<0.05)。

3 讨论

老年重症肺炎为肺炎的危重类型,多缺乏典型的呼吸系统表现,症状无特异性,进展快速,严重威胁患者的生命健康[11,12]。老年患者机体抵抗力较低下,并发症多,病情复杂,是临床治疗

表 5 两组治疗前后血清基质金属蛋白酶及其组织抑制剂水平的比较($\bar{x}\pm s$,ng/mL)

Table 5 Comparison of the serum matrix metalloproteinase and its tissue inhibitor levels between two groups before and after the treatment($\bar{x}\pm s$, ng/mL)

Group	n	Time	MMP-2	MMP-9	TIMP-1	TIMP-2
Control group	48	Before treatment	438.10± 60.11	187.45± 25.95	58.60± 7.41	158.30± 18.15
		After treatment	268.09± 31.09#	130.18± 15.20#	40.72± 6.33#	105.70± 15.77#
Research group	53	Before treatment	432.97± 65.38	184.20± 27.33	60.17± 5.90	154.08± 21.39
		After treatment	193.42± 25.77a#	99.54± 11.54a#	30.59± 4.21a#	84.29± 11.40a#

Note: Compared with the control group aP<0.05; Compared with before treatment #P<0.05.

表 6 两组治疗前后动脉血气、肺功能比较($\bar{x}\pm s$)

Table 6 Comparison of the arterial blood gas, lung function between two groups before and after the treatment($\bar{x}\pm s$)

Group	n	Time	SaO_2(%)	$PaCO_2$(mmHg)	PaO_2(mmHg)	PEF(mL/s)	MMF(L/s)	FVC(L)
Control group	48	Before treatment	88.33± 13.70	59.17± 6.50	63.10± 6.69	113.27± 13.59	0.58± 0.02	1.90± 0.18
		After treatment	93.20± 14.29#	42.19± 5.70#	90.05± 12.37#	88.42± 13.05#	1.12± 0.16#	2.33± 0.42#
Research group	53	Before treatment	89.60± 11.65	57.83± 8.43	61.99± 8.11	110.83± 16.30	0.57± 0.04	1.87± 0.23
		After treatment	98.74± 16.01a#	36.12± 3.40a#	98.75± 15.40a#	79.50± 10.23a#	1.60± 0.23a#	2.71± 0.55a#

Note: Compared with the control group aP<0.05; Compared with before treatment #P<0.05.

的一大难点。合理应用抗生素是老年重症肺炎治疗的重要手段[13]。万古霉素是老年重症肺炎的常用抗生素,抗菌谱广泛。有研究显示[14,15]万古霉素对肺部细胞组织的穿透性欠佳,部分患者可存在耐药性,导致杀菌效果并不理想。利奈唑胺注射液是细菌蛋白质合成抑制剂,通过抑制核糖体及 mRNA 连接,减少 70S 起始复合物产生,抑制细菌蛋白质形成[16]。利奈唑胺注射液的组织穿透性较强,可于短时间内分布于不同器官组织,加上其作用及结构较独特,不容易出现交叉耐药现象[17]。体外试验表明[18]利奈唑胺注射液对多种病原菌均有较强抗菌活性。Liu P 等[19]研究发现老年重症肺炎患者单用利奈唑胺注射液的效果不甚理想,仍有待提高。

老年重症肺炎为中医学“喘证、痰饮”等范畴,肺为娇脏,外邪可经皮毛犯肺,致肺热上升、毒气瘀阻,加上老年正气大虚,容出阳气欲脱之危症,因此去除病邪为其治疗之关键[20]。相关研究报道[21]血必净中当归化痰润肺,赤芍行血中之滞,川芎、丹参主活血化瘀,红花可消痰、化毒,诸药共奏溃散毒邪、通络止痛、活血祛瘀等功效。药理研究表明[22,23]当归通过减轻心肌缺血,可改善外周循环,减轻机体炎症及缺氧反应;赤芍能够抑制血小板聚集,改善肺部循环;红花能够降低血管通透性,改善血管内液体渗出。其在抗氧化、抗炎、增强免疫功能等方面的作用已得到临床证实。Hou SY 等[24]研究表明血必净能够诱导蛋白 C 表达,抑制转录因子 -kB、肿瘤坏死因子 -α 等刺激物质的表达,抑制失控的炎症反应。本研究结果显示血必净联合利奈唑胺注射液的有效率、细菌清除率及临床症状缓解时间均明显优于单用利奈唑胺注射液,说明二者联合应用在老年重症肺炎治疗上有明显优势,利于病原菌的清除,从而为其治疗创造良好条件。

SP 是来自于肺泡Ⅱ型上皮细胞的蛋白质复合物,能够降低肺泡的表面张力,影响肺部通气及换气功能,导致呼吸功能不全[25]。相关研究报道[26]重症肺炎发生后 SP 的表达明显上调,参与肺部细胞状态的调节。国外研究显示[27]重症肺炎与细胞外基质(ECM)过度降解有着密切联系,其降解程度过大可导致器官纤维化,MMPs 可调节相关黏膜上皮损伤和修复。MMP-2 能够破坏细胞组织成分,诱导新生血管形成,MMP-9 可能够介导肺部组织的基质重构、生长等生理病理过程[28]。TIMP-1 及 TIMP-2 为 MMPs 的抑制因子,可下调多种 MMPs 活性,于呼吸系统细胞外基底膜及细胞外基质修复中起到主要作用[29]。目前动物试验显示[30]重症肺炎小鼠 TIMPs 及 MMPs 表达均明显上调,且以 MMPs 上调更为明显。本研究结果显示患者治疗后 SP、MMPs 及 TIMPs 水平均显著下降,但血必净联合利奈唑胺注射液能显著下调肺表面活性蛋白水平,考虑与二者的作用途径不同,可起协同作用,改善机体状态,这也可能是二者联合治疗疗效更佳的作用机制。一项荟萃分析显示[31]肺部炎症及充血可引起肺泡通气和血流量紊乱,降低动脉血气指标,影响肺部功能。本研究中,血必净联合利奈唑胺注射液治疗能更有效改善患者肺部通气状态,促进肺功能的恢复。治疗期间,血必净联合利奈唑胺注射液质量均未引起严重不适,但患者 28 天死亡率显著降低,提示其在改善短期生存方面有明显优势,但远期效果仍有待更多大规模、多中心明确。

综上所述,血必净联合利奈唑胺注射液对老年重症肺炎患者的疗效优于单用利奈唑胺注射液治疗,可能与其显著降低患者血清 SP、MMPs 及 TIMPs 水平,改善肺功能,降低病死率有关。

参考文献(References)

[1] Jwa H, Beom JW, Lee JH. Predictive Factors of Methicillin-Resistant Staphylococcus aureus Infection in Elderly Patients with Community-Onset Pneumonia[J]. Tuberc Respir Dis (Seoul), 2017, 80(2): 201-209

[2] Morley D, Torres A, Cillóniz C, et al. Predictors of treatment failure and clinical stability in patients with community acquired pneumonia [J]. Ann Transl Med, 2017, 5(22): 443

[3] Jeon K, Yoo H, Jeong BH, et al. Functional status and mortality prediction in community-acquired pneumonia [J]. Respirology, 2017, 22 (7): 1400-1406

[4] Kanungo R, Anandhalakshmi S S, Sheeladevi C, et al. Fatal infection in adults by pneumolysin & autolysin producing, non-vaccine

serotype Streptococcus pneumonia [J]. Indian J Med Res, 2016, 143 (4): 514-517

[5] Montravers P, Harpan A, Guivarch E. Current and Future Considerations for the Treatment of Hospital-Acquired Pneumonia [J]. Adv Ther, 2016, 33(2): 151-166

[6] Yang W, Liu J, Blažeković B, et al. In vitro antibacterial effects of Tanreqing injection combined with vancomycin or linezolid against methicillin-resistant Staphylococcus aureus [J]. BMC Complement Altern Med, 2018, 18(1): 169

[7] Wang Y, Ji M, Wang L, et al. Xuebijing injection improves the respiratory function in rabbits with oleic acid-induced acute lung injury by inhibiting IL-6 expression and promoting IL-10 expression at the protein and mRNA levels[J]. Exp Ther Med, 2014, 8(5): 1593-1598

[8] Yamaguchi M, Nakata M, Sumioka R, et al. Zinc metalloproteinase ZmpC suppresses experimental pneumococcal meningitis by inhibiting bacterial invasion of central nervous systems[J]. Virulence, 2017, 8(8): 1516-1524

[9] Li YT, Wang YC, Lee HL, et al. Elevated Plasma Matrix Metalloproteinase-9 and Its Correlations with Severity of Disease in Patients with Ventilator-AssociatedPneumonia[J]. Int J Med Sci, 2016, 13(8): 638-645

[10] Sparham S, Charles PG. Controversies in diagnosis and management of community-acquired pneumonia [J]. Med J Aust, 2017, 206(7): 316-319

[11] Perrone T, Quaglia F. Lung US features of severe interstitial pneumonia: case report and review of the literature[J]. J Ultrasound, 2017, 20(3): 247-249

[12] Hendriks SA, Smalbrugge M, van Gageldonk-Lafeber AB, et al. Pneumonia, Intake Problems, and Survival Among Nursing Home Residents With Variable Stages of Dementia in the Netherlands: Results From a Prospective Observational Study[J]. Alzheimer Dis Assoc Disord, 2017, 31(3): 200-208

[13] Akhter S, Rizvi N, Bhura S, et al. Management of community acquired pneumonia by Family Physicians [J]. Pak J Med Sci, 2017, 33 (4): 783-787

[14] Barber KE, Bell AM, Stover KR, et al. Intravenous Vancomycin Dosing in the Elderly: A Focus on Clinical Issues and Practical Application[J]. Drugs Aging, 2016, 33(12): 845-854

[15] van Beurden YH, Nieuwdorp M, van de Berg PJEJ, et al. Current challenges in the treatment of severe Clostridium difficile infection: early treatment potential of fecal microbiota transplantation[J]. Therap Adv Gastroenterol, 2017, 10(4): 373-381

[16] Schweizer M, Richardson K, Sarrazin MV, et al. Improving Definitive Therapy Among Patients with Methicillin-resistant Staphylococcus aureus Bloodstream Infections: Predictors of Early Therapeutic Switch to Linezolid or Daptomycin[J]. Open Forum Infect Dis, 2017, 4(1): S289-S289

[17] Dupont J, Prat D, Sztrymf B. Linezolid versus vancomycin in Methicillin Resistant Staphylococcus aureus nosocomial pneumonia in the elderly[J]. Am J Emerg Med, 2017, 35(8): 1197-1198

[18] Ferrone V, Carlucci M, Cotellese R, et al. Development of a dried blood spot HPLC-PDA method for the analysis of linezolid and ciprofloxacin in hospital-acquired pneumoniapatients [J]. Drug Test Anal, 2017, 9(10): 1611-1619

[19] Liu P, Capitano B, Stein A, et al. Clinical outcomes of linezolid and vancomycin in patients with nosocomial pneumonia caused by methicillin-resistant Staphylococcus aureus stratified by baseline renal function: a retrospective, cohort analysis [J]. BMC Nephrol, 2017, 18 (1): 168

[20] Li DM, Tang SH, Liao Q, et al. Literature study on prevention and treatment of community acquired pneumonia by traditional Chinese medicine[J]. Zhongguo Zhong Yao Za Zhi, 2017, 42(8): 1418-1422

[21] Yuxi Q, Zhang H, Baili Y, et al. Effects of Xuebijing Injection for Patients With Sepsis-induced Acute Kidney Injury After Wenchuan Earthquake[J]. Altern Ther Health Med, 2017, 23(2): 36-42

[22] Li A, Li J, Bao Y, et al. Xuebijing injection alleviates cytokine-induced inflammatory liver injury in CLP-induced septic rats through induction of suppressor of cytokine signaling 1 [J]. Exp Ther Med, 2016, 12(3): 1531-1536

[23] Cheng C, Lin JZ, Li L, et al. Pharmacokinetics and disposition of monoterpene glycosides derived from Paeonia lactiflora roots (Chishao) after intravenous dosing of antiseptic XueBiJing injection in human subjects and rats [J]. Acta Pharmacol Sin, 2016, 37(4): 530-544

[24] Hou SY, Feng XH, Lin CL, et al. Efficacy of Xuebijing for coagulopathy in patients with sepsis[J]. Saudi Med J, 2015, 36(2): 164-169

[25] Smith NM, Wasserman GA, Coleman FT, et al. Regionally compartmentalized resident memory T cells mediate naturally acquired protection against pneumococcal pneumonia [J]. Mucosal Immunol, 2017, 11(1): 220-235

[26] Schneider-Futschik EK, Paulin OKA, Hoyer D, et al. Sputum Active Polymyxin Lipopeptides: Activity against Cystic Fibrosis Pseudomonas aeruginosa Isolates and Their Interactions with Sputum Biomolecules[J]. ACS Infect Dis, 2018, 4(5): 646-655

[27] Park JW, Kim YJ, Shin IS, et al. Affects Matrix Metalloproteinase 12 (MMP-12) and MMP-13 Expression via Nuclear Factor κB Signaling in Human Carcinoma Epithelial Cells and a Pneumonia Mouse Model[J]. J Infect Dis, 2016, 214(6): 962-969

[28] Puntorieri V, McCaig LA, Howlett CJ, et al. Lack of matrix metalloproteinase 3 in mouse models of lung injury ameliorates the pulmonary inflammatory response in female but not in male mice[J]. Exp Lung Res, 2016, 42(7): 365-379

[29] Ordonez AA, Tasneen R, Pokkali S, et al. Mouse model of pulmonary cavitary tuberculosis and expression of matrix metalloproteinase-9[J]. Dis Model Mech, 2016, 9(7): 779-788

[30] White ES, Xia M, Murray S, et al. Plasma Surfactant Protein-D, Matrix Metalloproteinase-7, and Osteopontin Index Distinguishes Idiopathic Pulmonary Fibrosis from Other Idiopathic Interstitial Pneumonias[J]. Am J Respir Crit Care Med, 2016, 194(10): 1242-1251

[31] Gutbier B, Schönrock SM, Ehrler C, et al. Sphingosine Kinase 1 Regulates Inflammation and Contributes to Acute Lung Injury in Pneumococcal Pneumonia via the Sphingosine-1-Phosphate Receptor 2[J]. Crit Care Med, 2018, 46(3): e258-e267