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乌司他丁联合痰清宁雾化吸入对重症肺炎患者肌钙蛋白水平及心肌酶谱的影响*

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摘要 目的:探讨乌司他丁联合痰清宁雾化吸入对重症肺炎患者肌钙蛋白水平、心肌酶谱的影响。**方法:**收集 2014 年 3 月至 2016 年 3 月于我院治疗的 104 例重症肺炎患者,52 例行常规治疗患者作为对照组,52 例于常规治疗基础上行乌司他丁联合痰清宁雾化吸入患者作为观察组,比较两组体征及症状消失时间、肌钙蛋白[心肌肌钙蛋白 T(cTnT)、心肌肌钙蛋白 I(cTnI)]、心肌酶谱[谷草转氨酶(AST)、乳酸脱氢酶(LDH)、氢丁酸脱氢酶(HBDH)、肌酸激酶同工酶(CK-MB)]、临床症状积分、临床疗效及不良反应的发生情况。**结果:**观察组体征及症状消失时间明显短于对照组($P<0.05$);治疗后,观察组 cTnT、cTnI 低于对照组,差异有统计学意义($P<0.05$);观察组 AST、LDH、HBDH、CK-MB 低于对照组,差异有统计学意义($P<0.05$);观察组临床症状积分低于对照组($P<0.05$);观察组有效率 96.15%高于对照组 82.69%($P<0.05$);两组不良反应发生率比较无统计学差异($P>0.05$)。**结论:**乌司他丁联合痰清宁雾化吸入治疗重症肺炎的临床疗效好,且可有效降低肌钙蛋白及心肌酶谱水平,减轻心肌损伤。

关键词:重症肺炎;肌钙蛋白;心肌酶谱;乌司他丁;痰清宁

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The Influence of Ulinastatin Combined with Tanqingning Aerosol Inhalation on the Troponin Levels and Myocardial Enzyme Spectrum of Patients with Severe Pneumonia*

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ABSTRACT Objective: To study the influence of ulinastatin combined with phlegm qing ning aerosol inhalation on the troponin levels and myocardial enzyme spectrum of patients with severe pneumonia. **Methods:** 104 cases of patients with severe pneumonia from March 2014 to March 2016 were collected in our hospital, 52 cases with routine treatment as control group, 52 cases with the conventional treatment based on ulinastatin combined phlegm qing ning aerosol inhalation were selected as the observation group, the signs and symptoms disappearance time, troponin [myocardial troponin T (cTnT), cardiac troponin I (cTnI)], myocardial enzyme spectrum [aspartate aminotransferase (AST), lactate dehydrogenase (LDH), hydrogen butyric acid dehydrogenase (HBDH), creatine kinase isoenzyme (CK-MB)], clinical symptoms integral, clinical efficacy and adverse reaction of two groups were compared. **Results:** The signs and symptoms disappearance time of observation group was shorter than that of control group ($P<0.05$). After treatment, the cTnT and cTnI levels of observation group were lower than the those of control group ($P<0.05$); the AST, LDH, HBDH and CK-MB levels of observation group were lower than those of the control group ($P<0.05$); The clinical symptom score of the observation group was lower than that of the control group ($P<0.05$); The effective rate of observation group was 96.15%, which was higher than 82.69% of the control group ($P<0.05$); There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Ulinastatin combined with sputum qing ning aerosol inhalation therapy have good clinical curative effect on severe pneumonia, which could reduce the troponin and myocardial enzyme levels, improve the myocardial injury.

Key words: Severe pneumonia; Troponin; Myocardial enzyme spectrum; Ulinastatin; Tanqingning

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前言

重症肺炎为呼吸内科的常见感染性疾病,患者可出现胸

痛、发热、咳嗽、寒战等临床症状,还可发生肾脏、神经系统、心脏损伤等并发症,其中心肌损伤多见,是导致患者死亡的主要因素^[1]。相关研究显示肌钙蛋白及心肌酶谱水平变化能够一定

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程度反映心肌状态,是心肌损伤的敏感标志物^[2]。重症肺炎临床上治疗多以解痉、平喘、化痰、抗感染为主,然而抗生素的反复使用容易出现耐药性,加剧病情进展^[3]。临床研究表明中西医结合治疗能够明显提高重症肺炎的临床效果^[4]。乌司他丁为一种蛋白酶抑制剂,能够使肺损伤减轻,起到肺保护作用^[5]。痰清宁具有宣肺止咳、化痰清热之功效。目前临床上鲜有关于二者联合治疗重症肺炎的报道,本研究主要探讨了乌司他丁联合痰清宁雾化吸入对重症肺炎患者肌钙蛋白水平、心肌酶谱及临床疗效的影响,现报道如下。

1 材料与方法

1.1 一般资料

收集 2014 年 3 月至 2016 年 3 月于我院治疗的 104 例重症肺炎患者:入选标准:① 符合《社区获得性肺炎诊断和治疗指南》标准^[6](满足 a~d 中任 1 项,同时满足 e 项):a:基础呼吸道疾病的症状加剧或者咳嗽、咳痰新近出现,且出现脓性痰液,可见胸痛;b:肺部可闻及湿啰音或者可见实变体征;c:白细胞在 $4 \times 10^9/L$ 以下或者在 $10 \times 10^9/L$ 以上,可见细胞核左移;d:发热;e:胸部 X 线平片可见片状、斑片状的浸润性阴影或者间质性变化,可见胸腔积液。② 符合重症肺炎标准^[7](满足 a~b 任 1 项或者同时满足 c~j 中任 3 项):a:感染性休克,需血管升压类药物;b:需予以机械通气;c:呼吸频率在 30 次/分以上;d:氧合指数在 250 mmHg 以下;e:意识或定向障碍;f:多肺叶可见浸润现象;g:体温在 $36^\circ C$ 以下;h:低血压,需予以强力液体复苏;i:血小板在 $10 \times 10^9/L$ 以下;j:白细胞在 $4 \times 10^9/L$ 以下;③ 未行其他相关治疗。排除标准:① 过敏体质;② 妊娠或者哺乳期;③ 伴药物、酒精滥用史。本研究已签署家属和患者同意书,且征得我院伦理委员会许可,52 例行常规治疗患者作为对照组,52 例于常规治疗基础上行乌司他丁联合痰清宁雾化吸入患者作为观察组。男性有 58 例,女性有 46 例;年龄 18~65 岁,平均 (43.57 ± 2.56) 岁。观察两组性别、年龄等无差异($P>0.05$),有比较性。

1.2 治疗方法

对照组行常规治疗,参照患者病情制定基础治疗方案,依据痰培养情况选择对应抗生素抗感染治疗,同时联合机械通气、维持电解质平衡、营养支持、免疫调节、化痰、接痉等对症治疗。观察组在对照组基础上行乌司他丁联合痰清宁雾化吸入治疗,使 20 U 乌司他丁(西南药业股份有限公司,10 IU/盒,20140227)与 100 mL 氯化钠注射液(重庆福安药业有限公司,250 mL/瓶,20140223)稀释予以患者静脉滴注,早晚各 1 次,1

个疗程为 7 d。痰清宁[®](川贝、桔梗、半夏、双花、桑白皮各 15 g,甘草 10 g)煎 2 次,取 200 mL 药汁,常规灭菌,采用超声波雾化器,以 3 mL/分钟生成起雾,指导患者佩戴面罩接受治疗,每次 20 min,每日 4 次,每次 50 mL,1 个疗程为 7 d。两组均持续治疗 2 个疗程,并定期复查患者心电图、肝肾功能等,记录不良反应情况,于治疗结束时进行临床疗效评估。

1.3 血清指标测定

收集患者治疗前及治疗结束时的空腹外周静脉血 4 mL,肝素抗凝后分离血清。采用化学发光免疫法检测肌钙蛋白[心肌肌钙蛋白 T(Cardiac troponin T,cTnT),心肌肌钙蛋白 I(Cardiac troponin I,cTnI)]水平。采用酶联免疫吸附法检测心肌酶谱[谷草转氨酶(Aspartate aminotransferase,AST),乳酸脱氢酶(Lactate dehydrogenase,LDH),氢丁酸脱氢酶(Hydrogen butyric acid dehydrogenase,HBDH),肌酸激酶同工酶(Creatine kinase isoenzyme,CK-MB)]水平。

1.4 观察指标

比较两组体征及症状消失时间、肌钙蛋白水平、心肌酶谱、临床疗效及不良反应情况。

临床症状积分评估^[8]:参照《中药新药临床研究指导原则》进行,症状、体征(发热、咳嗽、咯痰、乏力)依据程度计为 0、2、3、4 分,肺部啰音计为 0、1、2 分,胸壁 X 线变化、痰培养检查计为 0、2 分,脉、舌象异常计为 1 分,临床症状积分与病情程度呈正比。临床疗效评估^[9]:按照《中医病证诊断疗效标准》分作痊愈、显效、有效、无效 4 个等级,痊愈:主要症状、体征得到完全或者基本的改善,客观评估指标已恢复正常,治疗后临床症状积分减少多于 90%;显效:主要症状、体征得到显著改善,客观评估指标基本正常,治疗后临床症状积分减少在 70%至 89%;有效:主要症状、体征有所缓解、客观评估指标有一定缓解,治疗后临床症状积分减少在 30%至 69%;无效:症状、体征未见改变,客观评估指标改变不显著或者加重,治疗后临床症状积分减少。有效率=(痊愈+显效+有效)/总例数 $\times 100\%$ 。

1.5 统计学分析

选用 SPSS18.0 行统计学分析,计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用 t 检验比较;计数资料以[例(%)]表示,并选用 χ^2 检验比较,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组重症肺炎患者体征、症状消失时间的比较

观察组症状、体征消失时间均明显短于对照组,差异有统计学意义($P<0.05$),见表 1。

表 1 两组重症肺炎患者体征、症状消失时间的比较($\bar{x} \pm s$)

Table 1 Comparison of the signs and symptoms disappearance time between two groups

Groups	n	Antifebrile time(d)	Respiratory failure to correct time(d)	Wet rale disappearing time (d)
Control group	52	5.89 $\pm$ 1.34	8.23 $\pm$ 1.36	10.27 $\pm$ 1.65
Observation group	52	4.56 $\pm$ 1.15	6.25 $\pm$ 1.23	8.74 $\pm$ 1.38
t		5.431	7.786	5.129
P		0.000	0.000	0.000

2.2 两组重症肺炎患者治疗前后肌钙蛋白水平的比较

治疗前,两组肌钙蛋白水平比较无差异($P>0.05$);治疗后,

两组肌钙蛋白水平均有降低,观察组下降更为明显,差异有统计学意义($P<0.05$)。

表 2 比较两组重症肺炎患者治疗前后肌钙蛋白水平变化的比较($\bar{x} \pm s$)

Table 2 Comparison of the change of troponin level before and after treatment between two groups

Groups	n	cTnT($\mu\text{g/L}$)		t	P	cTnI($\mu\text{g/L}$)		t	P
		Before treatment	After treatment			Before treatment	After treatment		
Control group	52	1.06 $\pm$ 0.24	0.25 $\pm$ 0.07	23.364	0.000	0.26 $\pm$ 0.08	0.19 $\pm$ 0.04	5.644	0.000
Observation group	52	1.05 $\pm$ 0.25	0.12 $\pm$ 0.03	26.634	0.000	0.25 $\pm$ 0.06	0.13 $\pm$ 0.01	14.226	0.000
t		0.208	12.309			0.721	10.494		
P		0.836	0.000			0.473	0.000		

2.3 两组重症肺炎患者治疗前后心肌酶谱水平变化的比较 两组心肌酶谱水平均有下降,观察组下降更为显著,差异有统计学意义($P<0.05$);治疗前,两组心肌酶谱水平比较无差异($P>0.05$);治疗后,统计学意义($P<0.05$),见表 3。

表 3 两组重症肺炎患者治疗前后心肌酶谱水平变化的比较($\bar{x} \pm s$)

Table 3 Comparison of the changes of myocardial enzyme levels before and after the treatment between two groups

Groups	n	AST(U/L)		t	P	LDH(U/L)		t	P
		Before treatment	After treatment			Before treatment	After treatment		
Control group	52	56.84 $\pm$ 12.37	43.62 $\pm$ 9.10	6.208	0.000	421.23 $\pm$ 57.85	248.17 $\pm$ 41.60	17.514	0.000
Observation group	52	56.75 $\pm$ 12.32	38.59 $\pm$ 8.67	8.693	0.000	420.38 $\pm$ 57.81	203.39 $\pm$ 35.12	23.133	0.000
t		0.037	2.886			0.075	5.931		
P		0.970	0.005			0.940	0.000		

Groups	n	HBDH(U/L)		t	P	CK-MB(U/L)		t	P
		Before treatment	After treatment			Before treatment	After treatment		
Control group	52	223.39 $\pm$ 15.41	176.32 $\pm$ 11.81	17.483	0.000	7.36 $\pm$ 2.17	3.28 $\pm$ 0.51	13.199	0.000
Observation group	52	225.50 $\pm$ 15.47	163.47 $\pm$ 10.28	24.082	0.000	7.38 $\pm$ 2.14	1.63 $\pm$ 0.34	19.136	0.000
t		0.697	5.918			0.047	19.412		
P		0.488	0.000			0.962	0.000		

2.4 两组重症肺炎患者治疗前后临床症状积分比较 两组临床症状积分均降低,观察组低于对照组,差异有统计学意义($P<0.05$);治疗前,两组临床症状积分比较无差异($P>0.05$);治疗后,意义($P<0.05$),见表 4。

表 4 两组重症肺炎患者治疗前后临床症状积分比较($\bar{x} \pm s$)

Table 4 Comparison the clinical symptom integral of before and after treatment in two groups of patients with severe pneumonia

Groups	n	Clinical symptoms integral		t	P
		Before treatment	After treatment		
Control group	52	11.58 $\pm$ 1.19	7.68 $\pm$ 1.3	17.869	0.000
Observation group	52	11.60 $\pm$ 1.14	4.60 $\pm$ 1.02	32.998	0.000
t		0.087	15.321		
		0.930	0.000		

2.5 两组重症肺炎患者临床疗效的比较 义($P<0.05$),见表 4。

治疗后,观察组临床有效率高于对照组,差异有统计学意义

表 5 两组重症肺炎患者临床疗效的比较[(例(%))]

Table 5 Comparison two groups of clinical curative effect in patients with severe pneumonia between two groups[n(%)]

Groups	n	Cure	Markedly	Effective	Invalid	Effective rate
Control group	52	19(36.54)	13(25.00)	11(21.15)	9(17.31)	43(82.69)
Observation group	52	28(53.84)	18(34.62)	4(7.69)	2(3.85)	50(96.15)
χ^2		2.652				4.981
P		0.008				0.026

3 讨论

肺炎是一种发生于肺泡、肺间质、终末气道的炎症,可由理化因素、免疫损伤、病原微生物等所致^[10]。重症肺炎属肺炎的危重类型,具有发病迅速、治疗难度大等特点,不仅能够造成多个器官的损害,还可出现少尿、休克、昏迷等严重症状^[11,12]。临床研究显示重症肺炎患者由于酸中毒、低氧血症等导致体内生成过度炎症因子和氧自由基,与病原体释放的酶类、毒素等一起作用于心肌细胞,导致心肌损伤,进而加剧病情,增加治疗难度,影响预后^[13]。

肌钙蛋白是由 cTnT、cTnI 等组成的复合物,cTnT 能够参与心肌收缩,多存在于心肌细胞,其水平能够于心肌损伤后几小时内上升,在受损半天或一天时血水平最多,研究表明临床制造的单克隆抗体能够特异性辨别 cTnT,明显增加其对心肌损伤诊断的特异性;cTnI 仅存在于机体心肌组织中,能够参与心肌收缩与舒张过程,肌钙蛋白系统中不存在交叉反应,一旦心肌受损,则会使心肌细胞膜的通透性增加,进而使 cTnT、cTnI 等水平上升^[14]。AST、LDH、HBDH、CK-MB 是心肌细胞的常见酶,统称为心肌酶谱,心肌细胞受到炎症、缺氧等损伤因素时能够使多种心肌酶释放入血,导致心肌酶浓度增加^[15]。本研究结果显示,患者治疗后肌钙蛋白、心肌酶谱水平均明显低于治疗前,提示重症肺炎患者多合并心肌损伤。而乌司他丁联合痰清宁雾化吸入可改善重症肺炎患者的心肌损伤。

目前,重症肺炎的治疗多以抗生素为主,但抗生素的广泛使用能够引起患者出现一定的耐药性,以至于肺部感染无法得到有效控制,疗效欠佳^[16,17]。乌司他丁为一种蛋白酶抑制剂,是由人体尿液中所提取的糖蛋白,能够抑制炎症因子的释放,缓解机体微循环,使组织损伤减轻^[18]。中医学认为肺炎属“咳嗽”、“哮喘”、“喘证”等范畴,多因外邪犯肺、脾失健运、痰浊内蕴、情致失调、久病劳欲所致,应以宣肺止咳、清热化痰为主^[19]。痰清宁方中以川贝为君,主润化燥痰、清热化痰之功;桔梗、半夏为臣,一升一降,能够起到降逆止呕、燥湿化痰、理气止咳之功;金银花、桑白皮为佐,可具清热解毒、宣散肺热之功;甘草具祛咳止痰,且调和诸药之功。经雾化吸入能够使不良反应明显降低,且存在吸收率高、避免肝脏首过效应等优势^[20]。本研究结果显示:乌司他丁联合痰清宁治疗的重症肺炎患者体征、症状消失时间均优于常规治疗组,提示二者联合治疗更能迅速、有效缓解患者体征、症状。两组治疗后肌钙蛋白、心肌酶谱水平均有下降,乌司他丁联合痰清宁组下降更为明显,表明二者联合治疗更能有效改善心肌损伤,考虑可能与乌司他丁能够使溶酶体膜稳定,使其释放受到抑制,进而组织心肌抑制因子的生成、释放;且痰清宁能够起到清热消毒、消炎之功,使炎症因子对心肌细胞的损伤降低,进而保护心肌细胞,减轻心肌损伤^[21]。同时,乌司他丁联合痰清宁组临床症状评分及有效率明显优于常规治疗组,表明二者联合治疗更能改善临床症状,提高临床疗效,考虑可能与二者联合治疗具有协同作用,且经雾化吸入能够减少药物于其他组织中的分布,增加药效。此外,两组安全性均较高,治疗期间未见明显不良反应。

综上,乌司他丁联合痰清宁雾化吸入治疗重症肺炎的临床疗效肯定,能够使肌钙蛋白及心肌酶谱水平降低,减轻心肌损伤。

参考文献(References)

- [1] Yang Cong-qin, Guo Shuan. Severe pneumonia in children with the clinical analysis of myocardial damage [J]. China disabled medicine, 2014, 22 (8): 22
- [2] Xu Zhi-you, Dong Zhan-ling. Serum cTnI and CK - MB in children with severe pneumonia value for early diagnosis of myocardial injury [J]. Modern preventive medicine, 2011, 38(24): 5073-5074
- [3] Salih KM, Bilal JA, Eldouch W, et al. Assessment of Treatment of Community Acquired Severe Pneumonia by Two Different Antibiotics[J]. J Clin Diagn Res. 2016, 10(5): SC06-SC09
- [4] Fang Zhi-cheng, Zhou Chan-ge, Zheng Xiang, et al. The blood will net joint of ulinastatin in the treatment of severe pneumonia study [J]. Journal of clinical and laboratory medicine, 2013, 12(4): 268-270
- [5] Wang Ji-feng, Qi Gang, Zhang Hua. Ulinastatin in patients with severe pneumonia lung protection experience [J]. Journal of clinical lung, 2011, 16(4): 645-646
- [6] The Chinese medical association respiratory disease diagnosis and treatment of community-acquired pneumonia guide [J]. Chinese tuberculosis and respiratory journal, 2006, 29(10): 651-655
- [7] Lu Zai-ying, Zhong Nan-shan. Internal medicine [M]. Beijing: people's medical publishing house, 2009: 19
- [8] Zhang Hong-wei. The curative effect of sputum qing ning atomization inhalation in The treatment of severe pneumonia in Chinese traditional medicine and its correlation research on serum level of substance P [D]. Heilongjiang university of Chinese medicine, 2009
- [9] Zheng Xiao-ying. Chinese medicine new medicine clinical research guiding principles (trial) [M]. Beijing: China medical science and technology publishing house, 2002: 54-58
- [10] PrayGod G, Mukerebe C, Magawa R, et al. Indoor Air Pollution and Delayed Measles Vaccination Increase the Risk of Severe Pneumonia in Children: Results from a Case-Control Study in Mwanza, Tanzania [J]. PLoS One, 2016, 11(8): e0160804
- [11] Phua J, Dean NC, Guo Q, et al. Severe community-acquired pneumonia: timely management measures in the first 24 hours [J]. Crit Care, 2016, 28(20): 237
- [12] Welte T. Severe pneumonia in the intensive care unit [J]. Med Klin Intensivmed Notfmed, 2016, 111(4): 279-289
- [13] Yang Xiao-guang, Wang Guo-ping. Children with severe pneumonia myocardial damage of 58 cases of clinical analysis [J]. Journal of bengbu medical college, 2013, 38(11): 1450-1452
- [14] Yu Zhi-xi, n Hua Feng, Zhang Qing-xiu. Blood troponin and myocardial enzyme spectrum detection for the early prediction of severe pneumonia in children clinical research [J]. China medical innovation, 2015, 12(32): 30-32
- [15] Shen Guofang. Myocardial enzyme spectrum and cTnI levels and the relationship between the children with severe pneumonia study [J]. Journal of preventive medicine, 2014, 21(9): 1106-1107
- [16] Naucier P, Strålin K. Routine atypical antibiotic coverage is not necessary in hospitalised patients with non-severe community-acquired pneumonia[J]. Int J Antimicrob Agents, 2016, 48(2): 224-225
- [17] Su TY, Shie SS, Chia JH, et al. Case Report of Low Virulence Francisella tularensis Presented as Severe Bacteremic Pneumonia. Medicine (Baltimore), 2016, 95(19): e3390 (下转第 2165 页)

- cardium and epicardium from multielectrode intrachamber and intravenous catheter: a computer stimulation-based validation[J]. *Electrocardiol*, 2010, 43(1): 56-62
- [11] Armour JA, Murphy DA, Yuan BX, et al. Gross and microscopic anatomy of the human intrinsic cardiac nervous system [J]. *Anat Rec*, 1997, 247: 289-298
- [12] Murakawa Y. Role of purkinje fibers in the maintenance of ventricular fibrillation[J]. *Cir J*, 2009, 73(10): 1793-1794
- [13] Bonilla I M, Vargas-Pinto P, Nishijima Y, et al. Ibuprofen and Ventricular Arrhythmia Risk [J]. *Journal of cardiovascular electrophysiology*, 2014, 25(3): 299-306
- [14] Folino AF, Bobbo F, Schiraldi C, et al. Ventricular arrhythmias and autonomic profile in patients with primary pulmonary hypertension [J]. *Lung*, 2003, 181(6): 321
- [15] Gintant GA, Antzelevich C. Ionic bases for electrophysiological distinction among epicardial, midmyocardial and endocardial myocytes from the free wall of the canine left ventricle [J]. *Circ Res*, 1993, 72(3): 671-687
- [16] Folino AF, Bobbo F, Schiraldi C, et al. Ventricular arrhythmias and autonomic profile in patients with primary pulmonary hypertension [J]. *Lung*, 2003, 181(6): 321
- [17] Tabatabaei N, Asirvatham S J. Supraventricular arrhythmia: identifying and ablating the substrate[J]. *Circulation Arrhythmia and electrophysiology*, 2009, 2(3): 316-326
- [18] Behling A, Moraes RS, Rohde LE, et al. Cholinergic stimulation with pyridostigmine reduces ventricular arrhythmia and enhances heart rate variability in heart failure[J]. *Am Heart J*, 2003, 146(3): 494
- [19] Billman GE. Heart rate response to onset of exercise: evidence for enhanced cardiac sympathetic activity in animals susceptible to ventricular fibrillation[J]. *Am J Physiol Heart Circ Physiol*, 2006, 291(1): H429
- [20] 郭继鸿. β 受体阻滞剂应当成为快速心律失常治疗的基础用药[J]. *中国心脏起搏与心电生理杂志*, 2006, 19(5): 331-334
- Guo Ji-hong. β receptor blockers should be basic treatment of rapid arrhythmia treatment, [J]. *China Journal of Cardiac pacing and Electrophysiology*, 2006, 19(5): 331-334
- [21] Lowe D, Hendry S, McLeod K. catecholamine-induced arrhythmia in children[J]. *Emerg Med J*, 2013, 30(11): 951-953
- [22] Kovach JA, Nearing BD, Verrier RL. Anger like behavioral state potentiates myocardial ischemia induced T wave alternans in canines [J]. *J Am Coll Cardio*, 2001, 37(6): 1719-1725
- [23] Cuparencu B, Horak J. Effects of 4'-chloridiazepam on glycemia and serum lipids in hyperlipidemic rats: interactions with PK 11195 and flumazenil [J]. *Research communications in molecular pathology and pharmacology*, 1995, 89(1): 57-66
- [24] Verrier R L, Josephson M E. Impact of sleep on arrhythmogenesis[J]. *Circulation: Arrhythmia and Electrophysiology*, 2009, 2(4): 450-459
- [25] Pierre B, Babuty D, Poret P, et al. Abnormal nocturnal heart rate variability and QT dynamics in patients with Brugada syndrome [J]. *PACE*, 2007, 30(Suppl 11): S188
- [26] Tsai CF, Ueng KC, Wu DJ, et al. Remodeled left ventricular myocardium remote to infarctions sites is the arrhythmogenic substrate for the sudden cardiac death[J]. *Med Hypotheses*, 2010, 75(4): 368-371
- [27] 郭红阳, 王玉堂, 单兆亮, 等. 山羊应激性心律失常发生中交感神经信号的细胞传递机制[C]. *中华医学会心电生理和起搏分会第八次全国学术年会论文集*, 2008
- Guo hong-yang, Wang yu-tang, Shan zhao-liang, et al. The mechanism of stress induce arrhythmia in goat in sympathetic nerve cell transfer [C]. *The Chinese society of pacing and electrophysiology Eighth National Symposium*, 2008
- [28] Passariello G, Peluso A, Moniello G, et al. Effect of autonomic nervous system dysfunction on sudden death in ischemic patients with anginal syndrome died during electrocardiographic monitoring in Intensive Care Unit[J]. *Minerva Anestesiologica*, 2007, 73(4): 207
- [29] Butera G, Bonnet D, Sidi D, et al. Patients operated for tetralogy of fallot and with nonsustained ventricular tachycardia have reduced heart rate variability[J]. *Herz*, 2004, 29(3): 304
- [30] Wei F, Wang TZ, Zhang J, et al. Mesenchymal stem cells neither fully acquire the electrophysiological properties of mature cardiomyocytes nor promote ventricular arrhythmias in infarcted rats [J]. *Basic Res Cardiol*, 2012, 107(4): 274

(上接第 2126 页)

- [18] Wang Zhi, Wu Han-bing. Ulinastatin pulmonary surfactant protein in patients with severe pneumonia and the effects of anti-inflammatory and proinflammatory medium [J]. *Chinese journal of biochemical drugs*, 2016, 4(3): 43-45
- [19] Yu Da-xing, Qi Wen-sheng. Research progress of traditional Chinese medicine in the treatment of severe pneumonia [J]. *Journal of henan traditional Chinese medicine*, 2015, 35(7): 1712-1714
- [20] Nemec A, Pavlica Z, Nemec-Svete A, et al. Aerosolized clindamycin is superior to aerosolized dexamethasone or clindamycin-dexamethasone combination in the treatment of severe *Porphyromonas gingivalis* aspiration pneumonia in an experimental murine model. *Exp Lung Res*, 2012, 38(1): 9-18
- [21] Sun Xiao-hui, Zhang Huo. Ulinastatin myocardial injury in patients with severe pneumonia protection study [J]. *Journal of trauma and emergency electronic journal*, 2014, 2(1): 34-36