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重症慢性阻塞性肺病急性发作期患者血清 PCT, hs-CRP 及 D-D 的表达及意义

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摘要 目的:探究重症慢性阻塞性肺病(COPD)急性发作期患者血清降钙素原(PCT)、超敏 C 反应蛋白(hs-CRP)和 D- 二聚体(D-D)的表达及意义。**方法**:选取 2014 年 9 月 -2016 年 9 月我院收治的 146 例 COPD 患者作为研究对象,其中 73 例 COPD 急性发作期(AECOPD)患者纳入急性期组,73 例 COPD 缓解期患者纳入缓解期组,另选取同期来我院体检的 40 例健康者作为对照组。比较三组研究对象的血清 PCT、hs-CRP 和 D-D 水平,同时比较急性期组细菌感染与无细菌感染患者、不同肺功能分级的患者血清 PCT、hs-CRP 和 D-D 水平的差异。**结果**:急性期组与缓解期组患者的血清 PCT、hs-CRP 和 D-D 水平较对照组显著升高(P＜0.05),急性期组的血清 PCT、hs-CRP 和 D-D 水平较缓解期组显著升高,差异有统计学意义(P＜0.05)。合并细菌感染组血清 PCT、hs-CRP 水平均显著高于无细菌感染组(P＜0.05),而 D-D 水平则无统计学差异(P＞0.05)。不同肺功能分级患者间的血清 PCT、hs-CRP 和 D-D 水平比较差异显著(P＜0.05),且肺功能分级越高水平越高(P＜0.05)。**结论**:AECOPD 患者的血清 PCT、hs-CRP 和 D-D 水平均显著的升高,三者联合检测能够有效反映患者病情严重程度,并有利于诊断患者是否存在有细菌感染。

关键词:慢性阻塞性肺病;急性加重期;血清降钙素原;超敏 C 反应蛋白;D- 二聚体

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Chronic Obstructive Pulmonary Disease: Expression and Significance of Serum PCT, hs-CRP and D-D of Patients in Acute Exacerbation

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ABSTRACT Objective: To explore the expression and significance of serum procalcitonin (PCT), high sensitive C reaction protein (hs-CRP) and D-dimer (D-D) in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD). **Methods:** A total of 146 patients with COPD, who were treated in First Hospital of Qinhuangdao from September 2014 to September 2016, were selected as research subjects, in which, 73 patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) were enrolled in acute stage group, 73 patients with remission of chronic obstructive pulmonary disease, in remission group, and 40 healthy persons inspected in the hospital during the same period, control group. The levels of serum PCT, hs-CRP and D-D were compared among the three groups.The levels of serum PCT, hs-CRP and D-D were compared in bacterial infection and non bacterial infection, different pulmonary function grade of the patients with AECOPD. **Results:** The levels of serum PCT, hs-CRP and D-D in the acute stage group and the remission group were significantly higher than those in the control group (P<0.05). The levels of serum PCT, hs-CRP and D-D in the acute stage group were significantly higher than those in the remission group, the differences were statistically significant (P<0.05). The levels of serum PCT and hs-CRP in the bacterial infection group were significantly higher than those in the non bacterial infection group (P<0.05), there was no significant difference in D-D level (P>0.05). The levels of serum PCT, hs-CRP and D-D were significantly different among the patients with different pulmonary function grades (P<0.05), the level increased with the increase of pulmonary function grade (P<0.05). **Conclusion:** The levels of serum PCT, hs-CRP and D-D are significantly increased in the patients with AECOPD, and three joint detection can effectively reflect the severity of patients and be helpful for the diagnosis of bacterial infection.

Key words: Chronic obstructive pulmonary disease; Acute exacerbation;Procalcitonin; High sensitive C reaction protein; D-dimer

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前言

慢性阻塞性肺病（Chronic obstructive pulmonary disease，COPD)是临床呼吸科常见疾病,可逐渐发展为肺心病和呼吸衰

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竭,临床上以不完全可逆性气流受限为主要特点[1,2]。COPD 患者可出现慢性咳嗽、气短、咳痰、呼吸困难等症状[3]。近年来,随着人们生活习惯以及环境的变化,COPD 的发病率与死亡率持续上升[4,5]。有研究表明[6],COPD 患者由于急性发作期感染、二氧化碳潴留等原因,凝血功能常出现异常,血液呈高凝状态,这导致了 COPD 的进一步发展。由于 COPD 的肺部损害呈慢性进展,当出现临床症状时病情常常已经不可逆转,全世界每年有几百万人死于 COPD,目前 COPD 已经成为全球范围内的主要公共卫生问题[7,8]。目前的研究表明[9],细菌感染会导致 COPD 急性加重期(AECOPD)的发生,这一时期患者的肺功能持续下降,COPD 病情不断加重,最终会出现呼吸衰竭,生命安全受到严重威胁。因此,寻找能够有效监测 AECOPD 病情的指标对及时救治患者有重要意义。本研究分析并探讨了血清降钙素原(Procalcitonin,PCT)、超敏 C 反应蛋白 (High sensitive C reaction protein,hs-CRP)和 D- 二聚体(D-dimer,D-D)在 AECOPD 患者中的表达情况及临床意义, 旨在为 AECOPD 的诊治提供参考,现报道如下。

1 资料与方法

1.1 一般资料

将 2014 年 9 月 -2016 年 9 月我院收治的 146 例 COPD 患者作为本次研究的对象,纳入标准:① COPD 患者均符合我国 2013 年修订的 " 慢性阻塞性肺疾病诊治指南 " 中的诊断标准[10];② 其他脏器如肝、肾等均无功能障碍者;③ 入院前半个月内未用抗菌药物治疗;④ 患者及家属均对本研究知情,并签署知情同意书。排除标准:① 肺部以外发生感染者;② 合并有肺结核等其他肺部疾病者;③ 存在精神疾病或无法配合研究者;④ 合并有原发或继发性肿瘤者。

其中 73 例 COPD 急性发作期患者纳入急性期组,73 例 COPD 缓解期患者纳入缓解期组,病程分期标准为[11]:① 急性期:在患病后,短期内出现咳嗽、咳痰、呼吸急促和(或)喘息加重、呼吸道分泌痰量增多,可伴有发热等症状;② 缓解期:咳嗽、咳痰、气短等症状稳定或症状轻微。急性期组男 48 例,女 25 例,年龄 45~66 岁,平均(55.42± 9.45)岁;病程 3~9 年,平均(6.21± 2.12)年。缓解期组男 45 例,女 28 例,年龄 43~65 岁,平均(55.21± 9.14)岁;病程 4~9 年,平均(6.32± 2.24)年。另选取同期来我院体检的 40 例健康者作对照组,男 26 例,女 14 例,年龄 45~67 岁,平均(54.93± 9.12)岁。三组患者的一般资料差异无统计学意义(P>0.05),可行组间对比。

1.2 检测方法

所有研究对象于清晨抽取空腹状态下外周静脉血 5 mL,置于抗凝试管中,于常温下 2000 r/min 离心 15 min,将血浆分离,再以 1500 r/min 离心 10 min。hs-CRP 采用免疫透射比浊法检测,D-D 采用酶联免疫吸附测定法进行检测,仪器均使用 HITACHI 日立 7600 全自动生化分析仪检测,hs-CRP 试剂盒由北京九强生物技术股份有限公司提供,D-D 试剂盒由南京基蛋生物科技有限公司;PCT 采用电化学发光法检测, 仪器使用德国罗氏 cobase 601 电化学发光仪,试剂盒由深圳市新产业生物医学工程有限公司提供。所有指标检测均严格按照试剂盒配套说明书进行。

1.3 观察方法

首先比较急性期组、缓解期组和对照组间血清 PCT、hs-CRP 和 D-D 的差异, 而后比较急性期存在细菌感染患者与无细菌感染患者间的血清 PCT、hs-CRP 和 D-D 的差异。此外,依据肺功能分级,将急性期患者分为肺功能Ⅰ级组、Ⅱ级组和Ⅲ级组,比较不同肺功能分级患者的血清 PCT、hs-CRP 和 D-D 的差异。肺功能分级标准[12]:Ⅰ级:轻度气流受限,一秒用力呼气容积(FEV1)/ 用力肺活量(FVC)<70%但 FEV1≥ 80%预计值;Ⅱ级:加重的气流受限,50%≤ FEV1<80%预计值,以活动后气急的症状的进展为特征; Ⅲ级: 进一步加重的气流受限,30%≤ FEV1<50%预计值,气急加重,反复急性发作。细菌感染诊断标准[13]:患者出现寒战、皮疹、关节痛及肝脾肿大等症状,部分患者有急性全身性感染、感染性休克、紫绀、呼吸增速等症状。

1.4 统计学方法

使用 SPSS18.0 统计学软件进行计算, 计量资料用均数± 标准差($\bar{x}\pm s$)表示,组间两两比较采用 t 检验,多组间比较采用 F 检验,若 P<0.05,则说明差异具有统计学意义。

2 结果

2.1 三组血清 PCT、hs-CRP 和 D-D 的水平比较

三组间血清 PCT、hs-CRP 和 D-D 水平比较,差异有统计学意义(P<0.05);急性期组与缓解期组患者的血清 PCT、hs-CRP 和 D-D 水平较对照组显著升高,差异有统计学意义(P<0.05)。急性期组的血清 PCT、hs-CRP 和 D-D 水平较缓解期组显著升高,差异有统计学意义(P<0.05)。详见表 1。

2.2 AECOPD 合并细菌感染与无细菌感染患者血清 PCT、hs-CRP 和 D-D 的水平比较

73 例 AECOPD 患者中,40 例合并细菌感染,33 例无细菌

表 1 三组血清 PCT、hs-CRP 和 D-D 的水平比较

Table 1 Comparison of levels of serum PCT, hs-CRP and D-D in the three groups

Groups	n	PCT(ng/mL)	hs-CRP(mg/L)	D-D(μg/L)
Acute stage group	73	5.82± 1.72*#	39.28± 3.23*#	1927.37± 83.38*#
Remission group	73	1.83± 1.24*	16.37± 3.37*	314.21± 69.23*
Control group	40	0.37± 0.14	3.82± 1.48	235.72± 58.47
F	-	6.754	11.267	35.486
P	-	0.005	0.001	0.000

Note: Compared with the control group, *p <0.05; Compared with the remission group, #p < 0.05.

感染。合并细菌感染组血清 PCT、hs-CRP 水平均显著高于无细菌感染组(P<0.05),而两组 D-D 水平比较无统计学差异(P>0.05),详见表 2。

2.3 不同肺功能分级 AECOPD 患者血清 PCT、hs-CRP 和 D-D 的水平比较

73 例 AECOPD 患者中,肺功能分级为Ⅰ级 17 例,Ⅱ级 20 例,Ⅲ级 36 例。不同肺功能分级患者间的血清 PCT、hs-CRP 和 D-D 水平比较,差异有统计学意义(P<0.05),且肺功能分级越高,PCT、hs-CRP 和 D-D 水平越高(P<0.05),详见表 3。

表 2 AECOPD 合并细菌感染与无细菌感染患者血清 PCT、hs-CRP 和 D-D 的水平比较

Table 2 Comparison of levels of serum PCT, hs-CRP and D-D in patients with AECOPD combined with bacterial infection and non bacterial infection

Groups	n	PCT(ng/mL)	hs-CRP(mg/L)	D-D(μg/L)
Bacterial infection group	40	6.43± 1.38	41.37± 1.73	1905.34± 84.28
No bacterial infection group	33	5.02± 1.05	36.28± 1.24	1937.74± 83.91
t	-	4.468	16.542	2.842
P	-	0.012	0.000	0.065

表 3 不同肺功能分级 AECOPD 患者血清 PCT、hs-CRP 和 D-D 的水平比较

Table 3 Comparison of levels of serum PCT, hs-CRP and D-D in different pulmonary function grades of patients with AECOPD

Pulmonary function grade	n	PCT(ng/mL)	hs-CRP(mg/L)	D-D(μg/L)
Ⅰ	17	1.25± 0.64	10.58± 3.24	1523.48± 67.28
Ⅱ	20	3.44± 0.97	29.46± 10.38	1727.29± 71.32
Ⅲ	36	6.15± 1.25	63.81± 19.46	2083.47± 88.26
F	-	6.568	15.489	34.494
P	-	0.019	0.001	0.000

3 讨论

近年来，我国老龄人口数量不断增加,COPD 的发病率也因此急剧升高,严重威胁了老年人的生命健康[14,15]。COPD 的发病机制目前仍未完全阐明,大多数学者认为 COPD 的主要特征为气道、肺实质和肺血管出现慢性炎症,在肺中各个部位均出现肺泡巨噬细胞、T 淋巴细胞等的数量增多，部分患者存在嗜酸性粒细胞增多 [16]。炎症细胞在被激活后将会释放出许多因子,包括白介素 6、肿瘤坏死因子等,这些因子会对机体肺组织结构产生较大破坏,同时加重炎症反应。除此之外,肺内的蛋白酶与抗蛋白酶失衡、神经系统功能紊乱等也将对 COPD 的发病起到促进作用[17]。吸入某些有害气体或颗粒则会使肺部发生炎症,吸烟也会导致肺部炎症并对肺脏造成损害,大多数 COPD 的危险因素都可导致相似的炎症过程，进而促使 COPD 发生[18]。AECOPD 是 COPD 反复发作后引起的，同时也是造成 COPD 患者病情进一步恶化、肺功能急剧下降,最终导致患者病死的重要原因。许多患者在罹患 COPD 后常合并有感染症状,而其中细菌感染占 40%~50%[19,20]。合并细菌感染的患者临床上一般表现为发热、白细胞异常升高、黄绿色痰液等,也有患者会出现失眠、下肢水肿、疲乏抑郁等症状[21,22]。早期的检查并诊断是避免患者病情进一步恶化,同时进行对症治疗的必要手段,但由于 COPD 患者多属中老年人群,具有免疫力差、营养状况不良等特点,因此在检查时患者的血清白细胞、血沉等指标并无较大变化,缺乏有效的诊断方法,这为 AECOPD 的治疗带来了较大的困难[23]。

hs-CRP 是一种非特异性的免疫组分物质，在机体中广泛存在,在正常生理情况下含量较低,但当机体出现损伤或有微生物入侵后肝细胞会大量释放 hs-CRP 入血，并刺激炎症因子的释放，进一步加剧炎症效应 [24]。本次研究中，三组间血清 hs-CRP 水平差异显著,合并与未合并细菌感染、不同肺功能分级患者间的血清 hs-CRP 水平也有显著差异。由此可见 hs-CRP 能够有效反映患者的病情程度,且对于合并细菌感染有较好的诊断效果。既往研究表明,hs-CRP 的水平与机体炎症反应和感染程度密切相关,并且具有较高的敏感性,不受年龄、药物等因素影响,因此应用于 AECOPD 的检测效果理想[25]。PCT 是降钙素的前肽糖蛋白,由甲状腺 C 细胞分泌并释放,在正常人机体中含量极低,且不受激素影响,但在细菌感染时会大量释放入血,其水平会随着感染进展而升高[26]。本次研究中,三组间血清 PCT 水平差异显著,合并与未合并细菌感染、不同肺功能分级患者间的血清 PCT 水平也有显著差异。由此可见,PCT 参与了 COPD 加重期的炎症反应,且在细菌感染后水平升高,在 AECOPD 病情的诊断中具有重要的参考价值。D-D 是纤溶酶水解纤维蛋白后形成的产物，其水平反映了机体内部的纤溶过程,当其含量增加时说明机体纤溶系统存在异常[27]。我们在研究中发现,三组间血清 D-D 水平差异显著,不同肺功能分级患者间的血清 D-D 水平也有显著差异，而合并与未合并细菌感染者的 D-D 水平则无显著性差异。结果提示,AECOPD 患者较 COPD 患者机体内的纤溶 - 凝血系统发生了较大改变,血液处在高凝状态。由于 AECOPD 患者会出现缺氧、二氧化碳潴留等症状,血液中的红细胞数量增加,从而导致患者的血液粘稠度

增加，再加上血管内皮损伤，极易造成血管栓塞[28]。有研究[29-30]表明 COPD 患者在缺氧的条件下气道炎症反应严重程度与凝血活性呈正相关，约 10%的 AECOPD 患者的死因为肺栓塞，D-D 是机体中高凝与纤溶亢进的主要标记物，其含量的增加意味着机体中可能会形成血栓，故严密监测 D-D 水平对患者血栓形成的早期诊断有重要意义，这与本研究结果一致。通过检查并检测患者的 D-D 水平有助于尽早对患者的病情严重程度进行诊断并治疗，避免血栓形成。

综上所述，AECOPD 患者的血清 PCT、hs-CRP 和 D-D 水平血清含量均显著的升高，三者联合检测能够有效反映患者病情严重程度，并有利于诊断患者是否存在有细菌感染。

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