

高水平呼气末正压通气与标准呼气末正压通气对重症急性胰腺炎伴急性呼吸窘迫综合征的疗效比较

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【摘要】目的:探讨高水平呼气末正压通气(PEEP)与标准PEEP对重症急性胰腺炎(SAP)伴急性呼吸窘迫综合征(ARDS)疗效的影响。**方法:**选取2013年12月至2016年12月期间阳山县人民医院确诊治疗的SAP伴ARDS患者100例,依据随机分配原则分为高P组和标P组,每组50例,标P组患者给予标准PEEP治疗,高P组患者给予高水平PEEP治疗。统计分析所有患者机械通气、住重症加护病房(ICU)时间、住院时间、呼吸机相关性肺炎(VAP)、死亡、治疗前和治疗后6、12 h氧利用率(O_2UC)、治疗前后血清肿瘤坏死因子- α (TNF- α)、白介素-6(IL-6)水平。**结果:**高P组患者机械通气、住ICU时间、住院时间、VAP发生率、死亡率明显低于标P组,差异有统计学意义($P<0.05$)。高P组和标P组患者治疗后6、12 h的 O_2UC 水平均较治疗前升高,但前者较后者升高更显著,差异有统计学意义($P<0.05$)。高P组和标P组患者治疗后血清TNF- α 、IL-6水平均较治疗前下降,但前者较后者下降更显著,差异有统计学意义($P<0.05$)。**结论:**与标准PEEP比较,高水平PEEP治疗可有效改善SAP伴ARDS患者的氧利用率和炎症状态,有效缩短机械通气、住ICU时间,有利于改善患者预后,值得临床进一步推广。

【关键词】重症急性胰腺炎;急性呼吸窘迫综合征;高水平;呼气末正压通气

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High-level positive end expiratory pressure and standard positive end expiratory pressure on severe acute pancreatitis combined with acute respiratory distress syndrome: an efficacy comparison

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Abstract: Objective To compare the therapeutic effect of high-level positive end expiratory pressure (PEEP) and standard PEEP on severe acute pancreatitis (SAP) combined with acute respiratory distress syndrome (ARDS). **Methods** One hundred patients with SAP combined with ARDS, selected from patients admitted to Yangshan People's Hospital from December 2013 to December 2016, were randomly divided into high-level P group and standard P group, 50 cases in each group. The patients in standard P group received standard PEEP treatment, while those in high-level P group received high-level PEEP treatment. The mechanical ventilation, intensive care unit (ICU) stay, hospital stay, the incidence of ventilator associated pneumonia (VAP), mortality, oxygen utilization (O_2UC) before treatment and that at 6 and 12 h after treatment, the serum tumor necrosis factor alpha (TNF alpha) and interleukin 6 (IL-6) levels before and after treatment were statistically analyzed. **Results** The mechanical ventilation, ICU stay, hospital stay, the incidence of VAP and mortality in high-level P group were significantly lower than those in standard P group, with statistical differences ($P<0.05$). The O_2UC levels at 6, 12 h after treatment in high-level P group and standard P group were higher than those before treatment, but the increase of the former was higher than that of the latter, with statistical differences ($P<0.05$). The serum TNF alpha, IL-6 levels after treatment in high-level P group and standard P group were lower than those before treatment, but the decrease of the former was more significant than that of the latter, with statistical differences ($P<0.05$). **Conclusion** Compared with standard PEEP, high-level PEEP therapy can effectively improve the oxygen utilization and the inflammatory state in patients with SAP combined with ARDS, and significantly shorten the time for mechanical ventilation, ICU stay, which are beneficial to the prognosis of patients. High-level PEEP therapy is worth for further clinical promotion. **Keywords:** severe acute pancreatitis; acute respiratory distress syndrome; high-level; positive end expiratory pressure

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前言

重症急性胰腺炎(Severe Acute Pancreatitis, SAP)是临床上常见的一种消化系统疾病,由胰蛋白酶的自身消化胰腺所致,常导致全身炎症反应综合征和多脏器功能衰竭,具有病情危急、进展快等特点,严重影响患者的身体健康^[1-2]。而急性呼吸窘迫综合征(Acute Respiratory Distress Syndrome, ARDS)则是一种以顽固性低氧血症为主要特征的临床综合征,具有起病急、病情进展迅速且凶险等特点,其病因繁多,也是SAP常见的并发症之一,由SAP致全身炎症反应而使炎性介质过度生成并损伤肺组织所致,可导致呼吸急促、呼吸窘迫等症状,严重时可导致患者多个器官衰竭,严重者可导致死亡的发生^[3-4]。目前,SAP伴ARDS的主要治疗方法为机械通气,其中呼气末正压通气(Positive End Expiratory Pressure, PEEP)是近年来新型的通气技术,通过其吸气末正压使陷闭的支气管和闭合的肺泡张开,可使萎陷的肺泡复张并使其维持在开放状态,可有效解除患者呼吸窘迫症状,挽救其生命^[5-6]。而多数研究表明,PEEP已成为治疗ARDS的主要措施,但其水平控制尚无统一标准,不同水平间的疗效存在差异,其中临床上标准水平为 ≤ 10 cm H₂O,高水平为 >15 cm H₂O,且选择高水平或标准的PEEP治疗仍存在较大的争议^[7-8]。此外,肿瘤坏死因子TNF- α 是一种可参与炎症反应的肿瘤坏死因子,白介素(IL)-6则是一种可介导和参与炎症反应的白介素,在机体发生炎症反应时,在血浆中的含量会显著升高,故可有效反映机体的炎症状态^[9-10]。对此,本研究通过给予患者高

水平PEEP与标准PEEP治疗,探讨二者对患者疗效的影响。

1 资料与方法

1.1 一般资料

选取2013年12月至2016年12月期间阳山县人民医院确诊治疗的SAP伴ARDS患者100例。纳入标准:(1)经临床症状、实验室、血常规、超声或CT等检查证实为SAP伴ARDS^[11-12];(2)经抗心力衰竭、激素等治疗后呼吸困难症状和顽固性低氧血症经机械通气后无法改善、就诊时间 <48 h、年龄18~70岁;(3)无精神病史或沟通交流障碍;(4)患者或其家属签署知情同意书。排除标准:(1)妊娠期、哺乳期、恶性肿瘤等特殊人群;(2)有慢性呼吸衰竭、血液、免疫等系统严重性疾病者;(3)拒绝或中途退出本次研究者;(4)有心、肝、肾等原发性严重性疾病。本研究经阳山县人民医院伦理委员会审批通过。依据随机分配原则,患者分为高P组和标P组,每组50例,其中,高P组:年龄26~69岁、就诊时间4~44 h、体质指数 $29.45\sim 31.61$ kg/m²、呼吸频率21~30次/min、心率89~112次/min、平均动脉压84~114 mmHg、急性生理和慢性健康状况评分系统得分(APACHE II)15~22分;标P组:年龄27~68岁、就诊时间3~42 h、体质指数 $29.36\sim 31.48$ kg/m²、呼吸频率21~30次/min、心率88~112次/min、平均动脉压83~113 mmHg、APACHE II 15~22分,两组患者在性别、年龄、就诊时间、体质指数、呼吸频率、心率、平均动脉压、APACHE II等资料上比较无显著差异($P>0.05$),具有可比性,具体数据见表1。

表1 两组一般资料比较($n=50$)
Tab.1 Comparison of general data in two groups ($n=50$)

Group	Gender[cases(%)]		Age/years	Clinic time/h	BMI/kg·m ²	RR(times/min)	HR(times/min)	MAP/mmHg	APACHE II/scores
	Male	Female							
Standard P	27(54.00)	23(46.00)	52.57 \pm 8.24	25.77 \pm 5.43	24.57 \pm 4.32	26.72 \pm 3.58	103.45 \pm 10.45	92.23 \pm 9.68	18.43 \pm 3.21
High-level P	29(58.00)	21(42.00)	52.22 \pm 8.52	26.12 \pm 5.50	24.98 \pm 4.41	27.02 \pm 3.62	102.87 \pm 10.39	92.82 \pm 9.73	18.01 \pm 3.18
χ^2/t value	0.162		0.167	0.137	0.202	0.179	0.118	0.130	0.213
P value	7.786		7.707	7.954	7.229	7.567	8.137	8.004	7.101

Standard P group: Standard positive end expiratory pressure group; High-level P group: High-level positive end expiratory pressure group; BMI: Body mass index; RR: Respiratory rate; HR: Heart rate; MAP: Mean arterial pressure; APACHE: Acute physiology and chronic health evaluation

1.2 方法

1.2.1 治疗方法 高P组患者给予高水平PEEP治疗,

即给予禁食、禁水、心电监护、质子泵抑制剂、持续胃肠减压、生长抑素、抗炎、抗生素、全身营养等常规

SAP 对症支持治疗, 完毕后气管切开、连接德国 PB840 呼吸机, 参数设置: 调节通气模式为同步间歇指令通气、潮气量 6~8 mL/kg、PEEP 为 15~25 cm H₂O、吸气上升时间为 25%、暂停时间为 0.2 s、呼吸频率为 12~18 次/min、指脉氧饱和度为 90%~100%, 通气至呼吸窘迫、腹痛、呕吐、体温、水电解质等缓解或正常, PEEP 应用时间 ≤3 d, 以患者脱离危险期转出 ICU 为标准。标 P 组患者给予标准 PEEP 治疗, 即在高 P 组治疗中的其他参数不变的基础上, 将呼吸窘迫缓解前的 PEEP 降为 ≤10 cm H₂O, 其余均同高 P 组。呼吸窘迫缓解标准为^[6]: (1) 患者神志清楚、可自行排痰; (2) 白细胞计数 <10×10⁹/L, 流体动力指数正常; (3) 体温 <38 ℃; (4) 潮气量在 3.8~4.2 mL/kg、呼吸频率 <30 次/min, 氧合指数 (PaO₂/FiO₂) >250 mmHg; (5) 呼吸机参数可更改为: 同步间歇指令通气频率为 8~12 次/min, PEEP 为 6~8 cm H₂O。

1.2.2 指标观察和标准 所有患者通过电话、复诊等方式随访 3 个月。于治疗前、治疗后 6、12 h 时行常规血气分析测定血氧饱和度 (SaO₂)、中心静脉血氧饱和度 (ScvO₂) 等; 于治疗前后抽取静脉血 4 mL 置入无菌抗凝

试管中, 常规分离血清 (3 000 r/min, 10 min) 后, 取上清液采用酶联免疫吸附法检测血清 TNF-α、IL-6 水平, 试剂盒均购自南京森贝伽生物科技有限公司。统计分析所有患者机械通气、住重症加强护理病房 (ICU) 时间、住院时间、呼吸机相关性肺炎 (Ventilator Associated Pneumonia, VAP)、死亡和治疗前、后 6、12 h 氧利用率 (O₂UC)、治疗前、治疗后 TNF-α、IL-6 水平, 其中 O₂UC = (SaO₂-ScvO₂)/SaO₂^[13]。

1.3 统计学分析

采用 SPSS 16.0 统计软件处理数据, 对计数资料比较采用 χ^2 检验, 对计量资料采用 t 检验, 用均数 ± 标准差表示, 对多组资料采用重复测量方差分析, 在 $P < 0.05$ 时, 差异有统计学意义。

2 结果

2.1 两组机械通气、住 ICU 时间、住院时间、VAP、死亡情况比较

高 P 组患者机械通气、住 ICU、住院时间、VAP 发生率、死亡率明显低于标 P 组, 差异有统计学意义 ($P < 0.05$), 见表 2。

表 2 两组机械通气、住 ICU、住院时间、VAP、死亡情况比较 ($n=50$)

Tab.2 Comparison of mechanical ventilation, ICU stay, hospital stay, the incidence of VAP, mortality in two groups ($n=50$)

Group	Mechanical ventilation time/d	ICU stay/d	Hospital stay/d	VAP [cases(%)]	Mortality [cases(%)]
Standard P	15.24±2.38	21.51±3.04	27.51±3.67	13(26.00)	8(16.00)
High-level P	11.52±2.01	15.68±2.62	20.67±3.28	4(8.00)	2(4.00)
t/χ^2 value	3.369	4.129	4.004	5.741	4.000
P value	0.003	<0.001	<0.001	0.025	0.038

ICU: Intensive care unit; VAP: Ventilator associated pneumonia

2.2 两组治疗前后 O₂UC 水平比较

治疗前, 高 P 组和标 P 组患者 O₂UC 水平基本相同, 差异无统计学意义 ($P > 0.05$)。高 P 组和标 P 组患

者治疗后 6、12 h 的 O₂UC 水平均较治疗前升高, 但前者较后者升高更显著, 差异有统计学意义 ($P < 0.05$), 见表 3。

表 3 两组治疗前后 O₂UC 水平比较 ($n=50$, %)

Tab.3 Comparison of O₂UC levels before and after treatment ($n=50$, %)

Group	Before treatment	6 h after treatment	12 h after treatment	F value	P value
Standard P	26.38±2.67	28.75±2.82	31.72±2.24	34.672	<0.001
High-level P	26.81±2.72	31.42±3.12	36.67±2.57	45.124	<0.001
t value	0.343	2.249	4.414		
P value	5.954	0.014	<0.001		

2.3 两组治疗前后血清TNF- α 、IL-6水平比较

治疗前,高P组和标P组患者血清TNF- α 、IL-6水平基本相同,差异无统计学意义($P>0.05$),高P组和

标P组患者治疗后血清TNF- α 、IL-6水平均较治疗前下降,但前者较后者下降更显著,差异有统计学意义($P<0.05$),见表4。

表4 两组治疗前后血清TNF- α 、IL-6水平比较($n=50$, pg/mL)

Tab.4 Comparison of TNF- α , IL-6 levels before and after treatment ($n=50$, pg/mL)

Group	TNF- α				IL-6			
	Before treatment	After treatment	<i>t</i> value	<i>P</i> value	Before treatment	After treatment	<i>t</i> value	<i>P</i> value
Standard P	123.72 \pm 13.24	96.42 \pm 10.24	4.464	<0.001	232.45 \pm 31.52	152.68 \pm 20.64	5.516	<0.001
High-level P	122.67 \pm 13.15	75.84 \pm 8.84	10.810	<0.001	234.71 \pm 31.58	120.11 \pm 15.29	14.313	<0.001
<i>t</i> value	0.169	4.901	-	-	0.153	4.407	-	-
<i>P</i> value	7.685	<0.001	-	-	7.826	<0.001	-	-

TNF: Tumor necrosis factor; IL: Interleukin

3 讨论

本研究通过给予患者高水平PEEP与标准PEEP治疗,发现高P组患者机械通气、住ICU时间、住院时间明显低于标P组($P<0.05$)。两组治疗后6、12 h的O₂UC水平均较治疗前升高,但高P组较标P组升高更显著,表明高水平PEEP可有效改善患者的O₂UC,有利于缩短机械通气、住ICU时间,这可能是由于标P组虽可在呼吸末时避免肺泡的再次塌陷,进而有效提高功能残气量,使肺内静动血分流降低、改善通气/血流比例和弥散功能,从而改善肺功能和促进氧合改善,但可能是由于患者合并SAP,其全身炎症反应剧烈,导致肺内渗出较多、肺表面活性物质缺乏,使肺泡塌陷较为严重^[14],进而导致部分患者未能有效复张肺泡,影响对肺功能、氧合的改善作用,从而延长患者的治疗时间和康复。而在高水平PEEP中,其可能通过升高PEEP而更有效复张患者塌陷的小气道、肺泡,进而有效改善肺顺应性、降低气道压力降低、增加肺泡通气量等,有利于降低由肺泡反复关闭、开放产生剪切力所致的肺损伤^[15]。同时研究中PEEP应用时间限定在 ≤ 3 d内,以避免PEEP过高可能会使肺泡过度扩张而降低肺顺应性,阻碍静脉回流而造成CO₂潴留而导致未能真正改善组织缺氧状态的发生^[16-17],故可确保对肺功能、氧合的改善作用,最终达缩短通气和康复时间的作用。

此外,本研究还发现高P组和标P组患者治疗后血清TNF- α 、IL-6水平均较治疗前下降,但前者较后者下降更显著,前者VAP发生率、死亡率明显低于后者,表明高水平PEEP可有效改善患者的炎症状态,有利于改善患者预后,这可能是由于其有效减少了

患者的通气时间,有利于降低长时间人工气道使肺黏膜组织丢失使病原体侵袭所致VAP的发生^[18],同时其有效确保了对肺功能、氧合的改善作用,可有效改善患者机体的缺血缺氧状态,进而可缓解其所致肺部局部炎症反应对肺组织的损伤^[19],并有利于避免炎症介质进一步加重SAP对全身多个器官损伤^[20],从而进一步降低患者死亡的风险。

综上所述,高水平PEEP治疗可有效改善SAP伴ARDS患者的O₂UC和炎症状态,有效缩短机械通气、住ICU时间,有利于改善患者预后,值得临床作进一步推广。

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