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序贯机械通气对肺心病患者心功能、内皮损伤程度及氧化应激反应程度的影响

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[摘要] **目的**:研究序贯机械通气对肺心病(CCP)患者心功能、内皮损伤程度及氧化应激反应程度的影响。**方法**:选择肺源性心脏病合并呼吸衰竭患者进行研究,随机分为接受序贯机械通气联合常规治疗的序贯组以及接受有创正压机械通气联合常规治疗的对照组。治疗前及治疗后3天、治疗后7天时,检测血清中心功能相关神经体液指标、内皮损伤指标、氧化应激反应指标的含量。**结果**:治疗后3天和7天时,两组血清中NT-proBNP、Copeptin、Ang-II、ALD、ET-1、vWF、sST2、8-iso-PGF2a、MDA的含量均显著低于治疗前,NO、SOD、GSH-Px、T-AOC的含量显著高于治疗前;序贯组患者治疗后3天时血清中NT-proBNP、Copeptin、Ang-II、ALD、ET-1、vWF、sST2、NO、8-iso-PGF2a、MDA、SOD、GSH-Px、T-AOC的含量与对照组比较无显著性差异;序贯组患者治疗后7天时血清中NT-proBNP、Copeptin、Ang-II、ALD、ET-1、vWF、sST2、8-iso-PGF2a、MDA的含量显著低于对照组,NO、SOD、GSH-Px、T-AOC的含量显著高于对照组。**结论**:序贯机械通气用于肺心病的治疗能够改善心功能、减轻内皮损伤程度及氧化应激反应程度。

[关键词] 肺源性心脏病;序贯机械通气;心力衰竭;内皮损伤;氧化应激
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Effect of sequential mechanical ventilation on cardiac function, endothelial injury and oxidative stress response in patients with cor pulmonale

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View from specialist: It is creative, and of certain scientific and educational value.

[ABSTRACT] Objective: To study the effect of sequential mechanical ventilation on cardiac function, endothelial injury and oxidative stress response in patients with cor pulmonale (CCP). Methods: Patients with cor pulmonale complicated by respiratory failure who were treated in Dongfeng People's Hospital were selected and randomly divided into the sequential group who received sequential mechanical ventilation combined with conventional therapy and the control group who received invasive positive pressure ventilation combined with conventional therapy. The serum levels of cardiac function-related neurohumoral indicators, endothelial injury indicators and oxidative stress response indicators were detected before treatment as well as 3 and 7 d after treatment. Results: Three and seven d after treatment, serum NT-proBNP, Copeptin, Ang-II, ALD, ET-1, vWF, sST2 levels of both groups of patients were significantly lower than those before treatment while NO, SOD, GSH-Px and T-AOC levels were significantly higher than those before treatment; serum NT-proBNP, Copeptin, Ang-II, ALD, ET-1, vWF, sST2, NO, 8-iso-PGF2a, MDA, SOD, GSH-Px and T-AOC levels of sequential group 3 d after treatment were not significantly dif-

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ferent from those of control group; serum NT-proBNP, Copeptin, Ang-II, ALDET-1, vWF, sST2, 8-iso-PGF2a and MDA levels of sequential group 7 d after treatment were significantly lower than those of control group while NO, SOD, GSH-Px and T-AOC levels were significantly higher than those of control group. **Conclusions**: Sequential mechanical ventilation for cor pulmonale can improve the cardiac function and reduce the degrees of endothelial injury and oxidative stress response.

[KEY WORDS] Cor pulmonale; Sequential mechanical ventilation; Heart failure; Endothelial injury; Oxidative stress

慢性肺源性心脏病(chronic corpulmonale, CCP)是老年人群常见的呼吸系统慢性疾病,同时存在肺功能和心功能减退。慢性阻塞性肺疾病(COPD)是造成CCP最常见的病因,COPD会造成肺间质及血管发生纤维化并造成肺动脉高压,进而增加右心室负荷、逐步引起心功能减退及心力衰竭[1,2]。呼吸道感染是导致CCP病情急性加重的主要诱因,病原菌感染会造成局部分泌物增多并加重缺血缺氧,进而增加呼吸衰竭和心力衰竭的发生风险。在临床实践中,纠正缺氧是治疗CCP的关键环节,机械通气是增加肺泡通气量、改善通气和换气功能的有效治疗手段,但有创机械通气存在脱机困难、呼吸机相关性肺炎发生风险增大等不足之处[3,4]。无创-有创序贯机械通气是近年来新发展起来的机械通气模式,适时的切换有创与无创机械通气有助于缓解呼吸肌疲劳并为下一步撤出呼吸机创造有利条件[5]。在下列研究中,我们具体分析了序贯机械通气对肺心病患者心功能、内皮损伤程度及氧化应激反应程度的影响。

1　资料及方法

1.1　一般资料

选择2014年5月～2017年2月期间在东凤人民医院接受治疗的肺源性心脏病合并呼吸衰竭患者进行研究,所有患者均符合肺源性心脏病的诊断标准及II型呼吸衰竭的诊断标准,排除合并严重心律失常、心源性休克、左心功能不全的患者以及存在机械通气禁忌症的患者。共入组98例患者,采用随机数表法分为两组,每组各49例。序贯组中男性29例,女性20例,年龄42～58岁;对照组中男性31例,女性18例,年龄44～60岁。两组患者一般资料的比较无显著性差异($P>0.05$)。

1.2　机械通气方法

两组患者均给予常规抗感染、解痉、化痰、舒张气道的药物治疗。对照组患者在常规治疗的基础上给予有创正压机械通气,方法如下:气管切开后气管插管,设置通气模式为SIM+PSV、潮气量为7～10 mL/kg、呼吸频率为6～20次/分、呼吸比为1:1.5～1:2.5。序贯组患者给予有创-无创序贯机械通气,有创机械通气方法与对照组相同,当体温下降且复查血常规提示白细胞降低时改为经面罩无创正压机械通气,设定通气模式为S/T、IPAP为4～8 cmH_2O、EPAP为2～3 cmH_2O。

1.3　血清指标检测方法

治疗前及治疗后3天、治疗后7天时,采集两组患者的外周静脉血并采用酶联免疫吸附试剂盒测定NT-proBNP、Copeptin、Ang-II、ALD、ET-1、vWF、sST2、NO的含量,采用放射免疫沉淀试剂盒测定8-iso-PGF2a、MDA、SOD、GSH-Px、T-AOC的含量。

1.4　统计学处理

采用SPSS19.0软件录入数据,对两组间的数据进行t检验,$P<0.05$为差异有统计学意义。

2　结果

2.1　血清中心功能相关神经体液指标

治疗前,两组血清中NT-proBNP、Copeptin、Ang-II、ALD的含量无显著性差异($P>0.05$);治疗后3天和7天时,两组血清中NT-proBNP、Copeptin、Ang-II、ALD的含量均显著低于治疗前($P<0.05$);序贯组患者治疗后3天时血清中NT-proBNP、Copeptin、Ang-II、ALD的含量与对照组比较无显著性差异($P>0.05$),治疗后7天时血清中NT-proBNP、Copeptin、Ang-II、ALD的含量显著低于对照组($P<0.05$)。见表1。

表1　治疗前后血清中心功能相关神经体液指标的变化($n=49, \bar{x}\pm s$)

组别	时间	NT-proBNP (ng/mL)	Copeptin (ng/mL)	Ang-II (pg/mL)	ALD (pg/mL)
序贯组	治疗前	1.84±0.22	2.85±0.42	35.54±2.24	294.52±35.61
	治疗后3天	1.33±0.14#	1.88±0.18#	23.45±3.41#	223.45±29.35##
	治疗后7天	0.78±0.08*#	1.03±0.14*#	15.62±2.03*#	154.57±20.23*#
对照组	治疗前	1.90±0.23	2.92±0.45	36.13±4.46	298.41±38.42
	治疗后3天	1.41±0.18#	1.93±0.31#	24.12±3.28#	230.11±29.34#
	治疗后7天	1.16±0.18#	1.78±0.25#	20.31±3.25#	215.62±30.25#

注:与对照组比较,*$P<0.05$;治疗前与治疗后比较,#$P<0.05$。

2.2　血清中内皮损伤指标

治疗前,两组血清中ET-1、vWF、sST2、NO的含量无显著性差异($P>0.05$);治疗后3天和7天时,两组血清中ET-1、vWF、sST2的含量均显著低于治疗前,NO的含量显著高于治疗前($P<0.05$);序贯组患者治疗后3天时血清中ET-1、vWF、sST2、NO的含量与对照组比较无显著性差异($P>0.05$),治疗后7天时血清中ET-1、vWF、sST2的含量显著低于对照组,NO的含量显著高于对照组($P<0.05$)。见表2。

表 2 治疗前后血清中内皮损伤指标的变化($n=49,\bar{x}\pm s$)

组别	时间	ET-1 (pg/mL)	vWF (ng/mL)	sST2 (pg/mL)	NO (nmol/mL)
序贯组	治疗前	68.43±8.24	2.94±0.42	2.42±0.34	75.12±8.85
	治疗后 3 天	54.21±6.72#	2.31±0.34#	1.77±0.21#	112.31±13.48#
	治疗后 7 天	38.65±5.23*#	1.73±0.22*#	1.15±0.14*#	158.42±9.35*#
对照组	治疗前	67.83±8.94	2.98±0.35	2.48±0.38	74.58±8.12
	治疗后 3 天	55.62±7.423#	2.35±0.28#	1.80±0.23#	111.52±10.45#
	治疗后 7 天	48.58±6.23#	2.11±0.32#	1.62±0.19#	116.45±13.24#

注:序贯组与对照组比较,* $P<0.05$;治疗前与治疗后比较,# $P<0.05$。

2.3 血清中氧化应激指标

治疗前,两组患者血清中 8-iso-PGF2a、MDA、SOD、GSH-Px、T-AOC 的含量无显著性差异($P>0.05$);治疗后 3 天和 7 天时,两组患者血清中 8-iso-PGF2a、MDA 的含量均显著低于治疗前,SOD、GSH-Px、T-AOC 的含量显著高于治疗前($P<0.05$);序贯组患者治疗后 3 天时血清中 8-iso-PGF2a、MDA、SOD、GSH-Px、T-AOC 的含量与对照组比较无显著性差异($P>0.05$),治疗后 7 天时血清中 8-iso-PGF2a、MDA 的含量显著低于对照组,SOD、GSH-Px、T-AOC 的含量显著高于对照组($P<0.05$)。见表 3。

表 3 治疗前后血清中氧化应激指标的变化($n=49,\bar{x}\pm s$)

组别	时间	8-iso-PGF2a (pg/mL)	MDA (μmol/L)	SOD (U/mL)	GSH-Px (U/mL)	T-AOC (mmol/L)
序贯组	治疗前	135.21±16.86	12.46±1.62	94.51±10.25	64.42±8.94	1.03±0.14
	治疗后 3 天	103.54±12.52#	10.24±1.42#	129.33±16.85#	83.25±10.25#	1.42±0.18#
	治疗后 7 天	68.34±9.35*#	7.03±0.89*#	178.94±23.25*#	125.27±14.52*#	1.98±0.25*#
对照组	治疗前	134.59±14.95	12.89±1.56	95.21±10.75	65.12±8.12	1.01±0.12
	治疗后 3 天	104.12±12.48#	10.41±1.35#	130.12±14.47#	82.93±9.35#	1.38±016#
	治疗后 7 天	92.35±10.25#	9.32±1.06#	142.12±16.96#	96.72±11.26#	1.55±0.20#

注:序贯组与对照组比较,* $P<0.05$;治疗前与治疗后比较,# $P<0.05$。

3 讨论

慢性阻塞性肺疾病(COPD)是造成慢性肺心病(CCP)的最常见病因,缺氧则是导致 COPD 患者发生 CCP 的重要病理因素。在缺氧状态下,COPD 患者的肺间质及肺动脉会发生重塑并发展为肺动脉高压,进而增加右心室的负荷及做功,逐步引起心室结构和功能变化并发展为 CCP[6]。老年人群 COPD 和 CCP 的好发人群,受到机体免疫力减退的影响,在 COPD 和 CCP 的病程中容易发生呼吸道感染,进而加重患者缺氧的状况并影响呼吸功能、心功能,严重者会发生呼吸衰竭和心力衰竭。在临床实践中,通过机械通气+呼吸机辅助呼吸来纠正缺氧是治疗 CCP 合并心力衰竭及呼吸衰竭的关键。常规的有创正压机械通气能够有效改善通气和换气功能并纠正缺氧,但存在脱机困难、呼吸机相关性肺炎发生风险增大等不足之处[7]。无创-有创序贯机械是新发展起来的机械通气模式,适时的将有创通气改为无创通气能够尽快恢复患者的自主呼吸、降低气道阻力并改善肺泡氧合功能,进而纠正缺氧并逆转心力衰竭、呼吸衰竭的病程[8,9]。

肺心病患者合并呼吸衰竭、心力衰竭时会加重机体缺氧并引起心脏代偿性做功增加,进而会引起心脏负荷加大并造成神经体液出现相应的变化。Copeptin 是 AVP 原碳末端的部分片段,NT-proBNP 是 BNP 原氮末端的部分片段[10,11],心肌负荷增加会促进 AVP 和 BNP 的生成,同时引起 Copeptin 和 NT-proBNP 生成增多[12,13]。心衰过程中心排出量减少还会激活 RAAS 系统,增加肾素的分泌并将血管紧张素原裂解为血管紧张素 I,而后在血管紧张素转化酶的作用下生成 Ang-II;Ang-II 既能促进血管收缩、又能增加 ALD 分泌并调节水钠代谢[14,15]。我们通过分析上述心功能相关神经体液指标的变化可知:两组患者治疗后血清中 NT-proBNP、Copeptin、Ang-II、ALD 的含量均显著降低且序贯组患者治疗后 3 天时血清中 NT-proBNP、Copeptin、Ang-II、ALD 的含量与对照组比较无显著性差异,而治疗后 7 天时血清中 NT-proBNP、Copeptin、Ang-II、ALD 的含量显著低于对照组。这就说明序贯机械通气以及有创正压机械通气均能有效纠正缺氧并降低心脏负荷;序贯机械通气患者平均在有创通气后 5 天改为无创通气,在改为无创通气前心脏负荷减轻的程度无明显变化,而在改为无创通气后机体心脏负荷得到了进一步减轻。

在心力衰竭的病程中,内皮功能损伤是重要的病理环节,过度的内皮损伤会加重血管痉挛及心脏负荷[16]。ET-1 是由内皮细胞合成的缩血管活性物

质，具有强大的促进血管收缩活性，在内皮损伤过程中大量释放进入血液循环并引起血管痉挛、加重心力衰竭[17]；vWF 是由血管内皮细胞及巨核细胞合成和分泌的糖蛋白，对血小板的活化和聚集具有促进作用，能够使血管内皮发生损伤并诱导血小板发生活化和聚集[18]；sST-2 是膜受体 ST-2 的可溶性形式，能够与 ST-2L 结合并拮抗其内皮保护功能，进而引起内皮功能损伤[19]；NO 是具有舒血管及内皮保护作用的气体信号分子，内皮损伤过程中 NO 的合成受到抑制并加重内皮损伤[20]。我们通过分析上述内皮损伤指标的变化可知：治疗后 3 天和 7 天时，两组患者血清中 ET-1、vWF、sST2 的含量均显著低于治疗前，NO 的含量显著高于治疗前且序贯组患者治疗后 3 天时血清中 ET-1、vWF、sST2、NO 的含量与对照组比较无显著性差异，而治疗后 7 天时血清中 ET-1、vWF、sST2 的含量显著低于对照组，NO 的含量显著高于对照组。这就说明序贯机械通气以及有创正压机械通气均能在一定程度上减轻内皮功能损伤；序贯机械通气过程中，在改为无创通气前内皮损伤的减轻程度无明显变化，而在改为无创通气后内皮损伤得到了进一步减轻。

CCP 患者合并呼吸衰竭时，肺泡氧化功能减退会引起机体缺氧，进而造成氧自由基生成增多、氧化应激反应过度激活。细胞膜结构中的花生四烯酸和脂质极易被氧自由基氧化，引起细胞膜结构破坏、细胞功能损伤的同时也生成大量的氧化产物 8-iso-PGF2a 和 MDA，通过释放进入血液循环中 8-iso-PGF2a 和 MDA 含量的评估能够自由基的生成量及氧化应激反应的程度[21,22]。SOD 和 GSH-Px 是体内重要的酶类抗氧化物，能够通过催化还原反应来清除自由基；在持续缺氧及氧自由基不断生成的过程中，酶类抗氧化物会被大量消耗并造成 T-AOC 降低。我们通过分析上述氧化应激指标的变化可知：治疗后 3 天和 7 天时，两组患者血清中 8-iso-PGF2a、MDA 的含量均显著低于治疗前，SOD、GSH-Px、T-AOC 的含量显著高于治疗前且序贯组患者治疗后 3 天时血清中 8-iso-PGF2a、MDA、SOD、GSH-Px、T-AOC 的含量与对照组比较无显著性差异，而治疗后 7 天时血清中 8-iso-PGF2a、MDA 的含量显著低于对照组，SOD、GSH-Px、T-AOC 的含量显著高于对照组。这就说明序贯机械通气以及有创正压机械通气均能在一定程度上减轻氧化应激的程度；序贯机械通气过程中，在改为无创通气前氧化应激的减轻程度无明显变化，而在改为无创通气后氧化应激的程度得到了进一步减轻。

综上所述，序贯机械通气用于肺心病的治疗能够在改为无创机械通气后改善心功能、减轻心脏负荷，同时能够减轻内皮损伤的程度及氧化应激反应的程度。

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