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维生素 D 联合肺泡灌洗对机械通气重症肺炎患者血清 CHE、PA 的影响 *

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摘要 目的:探讨维生素 D 联合肺泡灌洗对机械通气重症肺炎患者血清胆碱酯酶(Cholinesterase, CHE)、前白蛋白(Prealbumin, PA)的影响。**方法:**2018 年 8 月到 2021 年 2 月选择在本院重症监护病房(Intensive Care Unit, ICU)诊治的重症肺炎患者 78 例作为研究对象,根据随机信封 1:1 抽签原则将患者分为联合组与对照组各 39 例。对照组给予肺泡灌洗治疗,联合组在对照组治疗基础上给予外源性维生素 D 治疗,两组均给予机械通气治疗,且治疗观察 2 周。**结果:**治疗后联合组的总有效率为 97.4%,高于对照组的 84.6% ($P<0.05$)。所有患者在治疗期间都无出现窒息、气胸、气道痉挛、心律失常等不良反应,联合组的入住 ICU 时间与 ICU 费用少于对照组 ($P<0.05$)。两组治疗后的第 1 秒 FEV₁、PaO₂ 高于治疗前 ($P<0.05$),联合组高于对照组 ($P<0.05$)。两组治疗后的血清 CHE、PA 水平高于治疗前 ($P<0.05$),联合组高于对照组 ($P<0.05$)。**结论:**维生素 D 联合肺泡灌洗在机械通气重症肺炎患者的应用能抑制血清 CHE、PA 的表达,改善血气状况与肺功能,提高治疗效果,缩短入住 ICU 时间与降低 ICU 费用。

关键词:维生素 D;肺泡灌洗;机械通气;重症肺炎;胆碱酯酶;前白蛋白

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Effect of Vitamin D Combined with Alveolar Lavage on Serum CHE and PA of Patients with Severe Pneumonia in Mechanical Ventilation*

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ABSTRACT Objective: To investigate the effect of vitamin D combined with alveolar lavage on serum cholinesterase (CHE) and prealbumin (PA) in patients with severe pneumonia from mechanical ventilation. **Methods:** From August 2018 to February 2021, 78 cases of patients with severe pneumonia diagnosed and treated in the Intensive Care Unit (ICU) of our hospital were selected as the research objects, and the patients were divided into the combination group and control groups of 39 cases in each groups accorded to the random envelope 1:1 lottery principle. The control group were given alveolar lavage treatment, the combination group were given exogenous vitamin D treatment on the basis of the control group's treatment, both groups were given mechanical ventilation treatment, and the two groups were treated for 2 weeks. **Results:** After treatment, the total effective rates of the combination group were 97.4%, which were higher than 84.6% of the control group ($P<0.05$). During the treatment, all patients had no adverse reactions such as asphyxia, pneumothorax, airway spasm, arrhythmia, and the combination group's ICU admission time and ICU cost were less than those of the control group ($P<0.05$). The forced expiratory volume in one second (FEV₁) and PaO₂ in the two groups were higher than before treatment ($P<0.05$), and the combination group were higher than the control group ($P<0.05$). The serum CHE and PA levels of the two groups after treatment were higher than those before treatment ($P<0.05$), and the combination group were higher than the control group ($P<0.05$). **Conclusion:** The application of vitamin D combined with alveolar lavage in patients with severe pneumonia on mechanical ventilation can inhibit the expression of serum CHE and PA, improve blood gas status and pulmonary function, improve the treatment effect, shorten the time of admission to the ICU and reduce the cost of ICU.

Key words: Vitamin D; Alveolar lavage; Mechanical ventilation; Severe pneumonia; Cholinesterase; Prealbumin

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前言

重症肺炎是指肺炎患者伴有低氧血症、急性呼吸道障碍与其他器官功能障碍的疾病,具有极高的致残率与死亡率^[1,2]。病理学研究表明重症肺炎患者的机体内将激活并上调酶原、炎症因子大量释放,细胞出现凋亡与死亡,特别是机体氧化/抗氧化状态失衡,使肺组织的氧化应激反应更加严重^[3,4]。常规治疗重症肺炎主要为抗炎药物治疗,但是治疗周期比较长,很难达到持续性的治疗效果^[5]。肺泡灌洗的原理为物理吸引与冲洗,主要通过使呼吸气道畅通,将局部痰栓直接稀释和清除,改善氧合,阻止炎症反应的不断扩大^[6,7]。肺泡灌洗不仅能够灌洗局部病灶,还能注入抗生素从而达到消炎作用。据报道,灌洗混合液能增强患者咳嗽反射,加快局部炎症的吸收与愈合^[8,9]。维生素D是具有多种生物活性的脂溶性类固醇衍生物,在机体循环中主要以25-羟基维生素D[25(OH)D]为主,具有抑制炎症细胞因子、调节机体钙磷代谢的作用、调节机体免疫功能等多种作用^[10]。维生素D也能诱导T细胞的产生,从而参与机体抵抗肺炎病毒或细菌感染过程^[11]。血清前白蛋白(Prealbumin, PA)主要由肝细胞合成,其变化水平能够反映机体营养情况,可评估重症疾病的疗效和预后^[12]。胆碱酯酶(Cholinesterase, CHE)由肝脏合成,其表达水平与肝细胞遭受损伤程度相关^[13,14]。本文具体探讨了维生素D联合肺泡灌洗对机械通气重症肺炎患者血清CHE、PA的影响,以明确维生素D的应用价值与机制。

1 资料与方法

1.1 一般资料

2018年8月到2021年2月选择在本院重症监护病房(Intensive Care Unit, ICU)诊治的78例重症肺炎患者作为研究对象,根据随机信封1:1抽签原则将患者分为联合组与对照组各39例。

纳入标准:(1)均符合重症肺炎的诊断标准,患者机械通气时间 ≥ 5 d;(2)年龄20-85岁;(3)患者或家属在自愿条件下签署知情同意书;(4)既往无机械通气史;(5)经本院伦理委员会批准。

排除标准:(1)传染性疾病肺炎;妊娠、哺乳期妇女;(2)合并心、脑、血管病等其他系统严重疾病;(3)表达障碍或精神疾病者;(4)凝血功能障碍且难以纠正者;(5)入院24 h内患者自动出院或死亡者;(6)合并免疫性疾病者;(7)合并其他脏器功能衰竭者;(8)合并恶性肿瘤患者。

1.2 治疗方法

对照组:给予肺泡灌洗治疗,用2%利多卡因2 mL(国药准字H20065388,中国大冢制药有限公司)雾化吸入,对咽喉部及鼻黏膜进行表面麻醉,插入纤维支气管镜至相关病变部位,向气囊(遵义市诚安医疗器械有限公司)内注入约2 mL的气体,经保护性远端导管推注少量0.9%氯化钠溶液。再用4-6支20 mL的0.9%的氯化钠溶液分别进行灌洗,反复多次吸引干净混合液后退镜。

联合组:在对照组治疗的基础上给予外源性维生素D治疗,口服维生素D软胶囊(国药准字H32023837,南京海鲸药业有限公司)0.05 mg,1次/d。

两组均给予机械通气治疗,床头抬高30°,采用小潮气量通气原则,潮气量为6~8 mL/kg;早期进行经验性、合理、足量抗感染治疗,积极给予营养支持,维持水电解质平衡,维持循环稳定、保护肝肾功能,给予吸痰、化痰治疗。以上两组均治疗观察14 d。

1.3 观察指标

1.3.1 临床疗效比较 治愈:胸部CT或X线片显示病变部位消失,临床症状消失,体温恢复正常,实验室检查血象恢复正常;好转:胸部CT或X线片显示病变部位明显缩小,临床症状减轻,体温恢复正常或稍高,实验室检查血象恢复正常。无效:未达到上述标准或恶化。总有效率=(治愈+好转)例数/总例数 $\times 100\%$ 。并观察治疗期间出现的不良反应情况。

1.3.2 入住ICU时间与ICU费用比较 记录与观察两组患者的入住ICU时间与ICU费用。

1.3.3 FEV₁和PaO₂比较 在治疗前后测定与记录患者的第1秒用力呼气末容积(Forced expiratory volume in one second, FEV₁)、动脉氧分压(PaO₂)。

1.3.4 CHE、PA含量检测 在治疗前后抽取患者的空腹静脉血2-3 mL,不抗凝,2500 r/min离心10 min,离心半径8 cm,取上层血清,采用酶联免疫法检测血清CHE、PA含量。

1.4 统计学方法

应用SPSS 22.0,使用($\bar{x} \pm s$)示计量资料,采用t检验,使用[n(%)]示计数资料,应用卡方检验, $P < 0.05$ 有统计学意义。

2 结果

2.1 一般资料对比

两组年龄、机械通气时间、体重指数、性别、急性生理学及慢性健康状况(APACHE II)评分、临床肺部感染(CPIS)评分、病程等无显著差异($P > 0.05$)。见表1。

表1 一般资料对比

Table 1 Comparison of two groups of general data

Groups	n	Body mass index (kg/m ²)	Mechanical ventilation time (d)	Apache II score (score)	CPIS score (score)	Age (years)	Gender (male/female)	Duration (d)
Joint group	39	21.33 $\pm$ 2.48	9.11 $\pm$ 0.85	23.85 $\pm$ 2.91	8.22 $\pm$ 0.84	43.11 $\pm$ 2.87	20/19	15.33 $\pm$ 2.17
Control group	39	21.98 $\pm$ 3.14	9.01 $\pm$ 0.99	23.09 $\pm$ 3.19	8.44 $\pm$ 0.22	43.93 $\pm$ 3.13	21/18	15.44 $\pm$ 1.75

2.2 临床疗效对比

治疗后联合组的总有效率为97.4%,高于对照组的84.6% ($P < 0.05$)。见表2。

2.3 入住ICU时间与ICU费用对比

所有患者在治疗期间都无出现窒息、气胸、气道痉挛、心律失常等不良反应,联合组的入住ICU时间与ICU费用都少于对照组($P < 0.05$)。见表3。

表 2 临床疗效对比(n)

Table 2 Comparison of clinical efficacy between the two groups (n)

Groups	n	Cure	Upturn	Invalid	Total effective rate
Joint group	39	34	4	1	38(97.4%)*
Control group	39	21	12	6	33(84.6%)

Note: Compared with control group, * $P<0.05$.

表 3 入住 ICU 时间与 ICU 费用对比($\bar{x}\pm s$)Table 3 Comparison of ICU stay time and ICU cost between the two groups($\bar{x}\pm s$)

Groups	n	Time of stay in ICU (d)	Cost of ICU (ten thousand Yuan)
Joint group	39	8.42 $\pm$ 0.35*	4.43 $\pm$ 0.34*
Control group	39	11.53 $\pm$ 1.12	5.11 $\pm$ 0.22

Note: Compared with control group, * $P<0.05$.

2.4 FEV₁、PaO₂ 变化对比

($P<0.05$)。见表 4。

两组治疗后的 FEV₁、PaO₂ 高于治疗前,联合组较对照组高

表 4 治疗前后 FEV₁、PaO₂ 变化对比($\bar{x}\pm s$)Table 4 Comparison of FEV₁ and PaO₂ changes between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	FEV ₁ (%)		PaO ₂ (mmHg)	
		Before the treatment	After treatment	Before the treatment	After treatment
Joint group	39	42.09 $\pm$ 0.33	73.78 $\pm$ 0.31* [#]	60.14 $\pm$ 6.78	79.14 $\pm$ 6.15* [#]
Control group	39	42.14 $\pm$ 0.25	66.09 $\pm$ 0.26 [#]	60.23 $\pm$ 6.49	72.19 $\pm$ 5.62 [#]

Note: Compared with control group, * $P<0.05$. Compared with Before treatment, [#] $P<0.05$.

2.5 血清 CHE、PA 变化对比

对照组高($P<0.05$)。见表 5。

两组治疗后的血清 CHE、PA 水平高于治疗前,联合组较

表 5 治疗前后血清 CHE、PA 变化对比($\bar{x}\pm s$)Table 5 Comparison of serum CHE and PA changes before and after treatment between the two groups ($\bar{x}\pm s$)

Groups	n	CHE(U/L)		PA(mg/dL)	
		Before the treatment	After treatment	Before the treatment	After treatment
Joint group	39	2578.10 $\pm$ 117.09	4632.33 $\pm$ 136.92* [#]	7.30 $\pm$ 0.44	12.99 $\pm$ 1.18* [#]
Control group	39	2581.55 $\pm$ 126.73	3635.55 $\pm$ 224.18 [#]	7.31 $\pm$ 0.28	10.78 $\pm$ 1.08 [#]

Note: Compared with control group, * $P<0.05$. Compared with Before treatment, [#] $P<0.05$.

3 讨论

不经治疗的肺炎,发展到一定程度会形成重症肺炎,可严重影响患者预后^[15]。现代研究表明,重症肺炎是一种以失控炎症反应为根本发病原因,以顽固性低氧血症、急性非心源性肺水肿为主要临床表现,以肺泡上皮和肺毛细血管内皮细胞的损伤为主要病理改变^[16,17]。特别是当前肺炎患者气道压力增高时,导致过低的呼气末肺容量,增加肺泡与周围血管间隙压力梯度增大,导致肺泡破裂、气体溢出,对肺泡基底膜产生"切割"作用,从而导致重症肺炎的发生^[18,19]。当前治疗该病的常规药物治疗效果不佳,且出现停药后病情恶化的现象。药物治疗主要在于口服或者静脉注射,药物不易进入肺腔,导致实际作用的药物浓度低^[20]。肺泡灌洗是一种有效、快速、直接的非创伤性的诊

疗方法,其是通过纤维支气管镜进入气管-支气管内,利用压力把 0.9%氯化钠溶液注入肺泡内,然后反复吸引干净灌洗混合液^[21,22]。特别是保护性支气管肺泡灌洗可进行亚段的肺泡灌洗,对局部病灶病原学进行采集,减少交叉感染的机会。并且肺泡灌洗可以提高脓腔内药物浓度,促使坏死脱落物质排出,可使微小肺不张的复张,从而改善肺功能。

本研究显示治疗后联合组的总有效率为 97.4%,高于对照组的 84.6%;所有患者在治疗期间都无出现窒息、气胸、气道痉挛、心律失常等不良反应,联合组的入住 ICU 时间与 ICU 费用都少于对照组,表明维生素 D 联合肺泡灌洗能提高机械通气重症肺炎患者的治疗效果,缩短入住 ICU 时间与降低 ICU 费用。这与 Kuti B 等人的研究结果一致,25-羟基维生素 D 能够提高儿童社区获得性肺炎的治愈率,他们推测该物质可能在降

低肺炎发病率方面发挥作用^[23]。从机制上分析,维生素 D 广泛分布于人体,其活性形式主要为 25-羟基维生素 D,能有效反映维生素 D 代谢及营养状态。维生素 D 在体内具有免疫、炎症及代谢调节等多种作用,可预防机体发生反复呼吸道感染,也可有效的促使肺部复张,消除呼吸道的分泌物,从而改善患者的预后^[24]。

对于重症肺炎采用常规治疗,其气道内粘液及炎性分泌物增多,抗生素到达肺组织炎症部位的浓度较低,治疗效果显著下降^[25,26]。同时大剂量药物的应用会损伤患者的肝肾功能,且容易让患者产生耐药性。本研究显示两组治疗后的 FEV₁、PaO₂ 高于治疗前,联合组较对照组高,表明经维生素 D 联合肺泡灌洗显著改善机械通气重症肺炎患者的血气状况与肺功能。这与 Han JE 等人^[27]对于肺泡灌洗联合维生素 D 的相关研究结果类似,其研究表明肺泡灌洗联合维生素 D 治疗多重耐药菌感染能增加患者的氧分压、氧饱和度,从而提高一秒用力呼气容积和用力肺活量。分析其相关机制可知,维生素 D 能影响抗原提呈,可阻止单核细胞分化为树突状细胞,从而抑制机体内的炎症反应,从而改善患者的肺功能^[28]。不过为了确保治疗效果与肺泡灌洗的顺利进行,应在无菌环境中进行,勿注入局麻药或者生理盐水,直至达到目标段支气管,对气道分泌物可予以负压吸引。灌洗液每次用量不超过 25 mL,总量不超过 150 mL,确保气囊固定良好,封堵时间不宜过长(10 min 以内)^[29,30]。

PA 可参与机体免疫调节作用,与机体多种病理状态关系密切,且起到维持酸碱平衡的作用^[31]。血清 CHE 主要来自于患者肝脏的拟胆碱酯酶,其下降程度与肝受损程度相关^[32]。当患者出现炎症反应时,均会减少 PA、CHE 的分泌,导致血清中 PA、CHE 水平下降,与病情存在相关性^[33]。本研究显示两组治疗后的血清 CHE、PA 水平高于治疗前,联合组高于对照组。从机制上进行分析,维生素 D 可抑制 Th1 免疫反应介导的炎症细胞因子分泌,从而改善呼吸道疾病患者的预后^[34]。肺泡灌洗清除并排出病变部位脓液及病原微生物,改善患者的缺氧状态,从而有利于抑制 CHE、PA 的表达^[35]。本研究也存在一定的缺陷,不过本研究是一项描述性研究,存在潜在的自我选择偏差,且选择的样本数量不足,机制分析也不够深入,将在下一步进行深入分析。

综上所述,维生素 D 联合肺泡灌洗在机械通气重症肺炎患者的应用能抑制血清 CHE、PA 的表达,改善血气状况与肺功能,提高治疗效果,缩短入住 ICU 时间与降低 ICU 费用。

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