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老年支气管哮喘患者血清 25-羟维生素 D3 浓度与免疫功能及肺功能的相关性研究

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摘要 目的:研究老年支气管哮喘患者血清 25-羟维生素 D3[25-(OH)D3]浓度与免疫功能及肺功能的关系。**方法:**选取 2016 年 1 月至 2017 年 12 月我院收治的老年支气管哮喘患者 96 例作为研究组,根据肺功能检查结果分为轻度哮喘组(n=30)、中度哮喘组(n=38)和重度哮喘组(n=28),另选取同期在我院进行体检的健康老年人 40 例作为对照组。比较各组血清 25-(OH)D3 浓度、第一秒最大呼气量占用力肺活量百分比(FEV1/FVC)、FEV1 占预计值百分比(FEV1%pred)、CD4⁺、CD8⁺、CD4⁺/CD8⁺以及血清免疫球蛋白 A(IgA)、免疫球蛋白 M(IgM)、免疫球蛋白 G(IgG)水平,并分析血清 25-(OH)D3 与免疫功能指标及肺功能指标的相关性。**结果:**研究组血清 25-(OH)D3 浓度、FEV1%pred 水平均低于对照组(P<0.05),两组 FEV1/FVC 水平比较差异无统计学意义(P>0.05)。研究组 CD4⁺、CD4⁺/CD8⁺、血清 IgA、IgM、IgG 水平均低于对照组,CD8⁺ 水平高于对照组(P<0.05)。重度哮喘组血清 25-(OH)D3、IgA、IgM、IgG 水平、FEV1%pred、CD4⁺、CD4⁺/CD8⁺ 均低于中度哮喘组和轻度哮喘组,中度哮喘组又低于轻度哮喘组(P<0.05),重度哮喘组 CD8⁺ 水平高于中度哮喘组和轻度哮喘组,中度哮喘组又高于轻度哮喘组(P<0.05)。经 Pearson 相关性分析可得:老年支气管哮喘患者血清 25-(OH)D3 与 FEV1%pred、CD4⁺、CD4⁺/CD8⁺、IgA、IgM、IgG 均呈正相关(P<0.05),与 CD8⁺ 呈负相关(P<0.05)。**结论:**老年支气管哮喘患者的血清 25-(OH)D3 浓度显著降低,且与肺功能和免疫功能相关,25-(OH)D3 浓度的检测可用于评估患者病情严重程度。

关键词:支气管哮喘;老年;25-羟维生素 D3;免疫功能;肺功能;相关性

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Correlation of Serum 25- Hydroxyvitamin D3 Concentration with Immune Function and Pulmonary Function in Elderly Patients with Bronchial Asthma

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ABSTRACT Objective: To study the Correlation of serum 25- hydroxyvitamin D3 [25-(OH)D3]concentration with immune function and pulmonary function in elderly patients with bronchial asthma. **Methods:** 96 elderly patients with bronchial asthma who were treated in our hospital from January 2016 to December 2017 were selected as the research group, the patients were divided into mild asthma group (n=30), moderate asthma group (n=38) and severe asthma group (n=28) according to the pulmonary function test results, 40 healthy elderly people who have been examined in our hospital for the same period as the control group. The serum 25- (OH) D3, maximum expiratory volume in first second (FEV1/FVC), FEV1 account for the percentage of estimated value (FEV1%pred), CD4⁺, CD8⁺, CD4⁺/CD8⁺, serum immunoglobulin A (IgA), immunoglobulin M (IgM) and immunoglobulin G (IgG) level were compared, the correlation between serum 25- (OH) D3 and the immune function index and pulmonary function index were analyzed. **Results:** The serum levels of 25- (OH) D3 and FEV1% pred in the research group were lower than those in the control group (P<0.05), there was no significant difference between the two groups of FEV1/FVC levels (P>0.05). The level of CD4⁺, CD4⁺/CD8⁺, serum IgA, IgM and IgG in the research group were all lower than those in the control group, and the level of CD8⁺ was higher than that of the control group (P<0.05). The levels of serum 25- (OH) D3, IgA, IgM, IgG, FEV1%pred, CD4⁺ and CD4⁺/CD8⁺ in severe asthma group were lower than those in moderate asthma group and mild asthma group, while those in moderate asthma group were lower than those in mild asthma group (P<0.05), the level of CD8⁺ in severe asthma group was higher than that in moderate asthma group and mild asthma group, and the moderate asthma group was higher than that of mild asthma group (P<0.05). Pearson correlation analysis showed that the serum 25- (OH) D3 was positively correlated with FEV1%pred, CD4⁺, CD4⁺/CD8⁺, IgA, IgM and IgG in elderly patients with bronchial asthma (P<0.05), and negatively correlated with CD8⁺ (P<0.05). **Conclusion:** The serum 25- (OH) D3 concentration of the elderly patients with bronchial asthma is significantly lower, and it is related to the pulmonary function and immune function, the detection of 25- (OH) D3 concentration can be used to assess the severity of the patient's condition.

Key words: Bronchial asthma; Elderly; 25- hydroxyvitamin D3; Immune function; Pulmonary function; Correlation

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前言

支气管哮喘是呼吸系统常见的慢性疾病,患者以反复发作的咳嗽、喘息、气短等为主要临床表现,严重影响患者的生活质量^[1,2]。近年来,随着空气质量的下降,我国哮喘发病率呈逐年升高趋势,有报道显示,自2004年到2013年十年间,我国哮喘发病率从0.97%上升至1.97%,其中50%以上为老年患者,哮喘防治形势非常严峻^[3]。目前研究认为支气管哮喘是由多种细胞和细胞组分共同参与的慢性气道炎症性疾病,患者免疫功能改变在疾病的发生、发展中起到了重要作用^[4,6]。维生素D是重要的类固醇激素,具有维持体内钙磷代谢的功能^[7]。近年来有学者发现,维生素D还具有调节免疫、抑制变应原诱导的细胞因子释放等功能,在支气管哮喘发病中可能起到重要作用^[8,9]。25-羟维生素D3[25-hydroxyvitamin D3, 25-(OH)D3]是维生素D的体内主要存在形式,其在体内的浓度稳定,可以用于疾病的诊断^[10]。鉴于此,本文通过研究老年支气管哮喘患者血清25-(OH)D3浓度与免疫功能及肺功能的关系,目的在于为临床老年支气管哮喘的早期诊断、治疗、预后评估提供依据,现作如下报道。

1 资料与方法

1.1 临床资料

选取2016年1月至2017年12月我院收治的老年支气管哮喘患者96例作为研究组,纳入标准:(1)所有患者均符合2008年制定的《支气管哮喘防治指南》中支气管哮喘诊断标准^[11];(2)患者均为初次诊断,年龄 ≥ 60 岁;(3)入院前6个月内未服用激素类药物及免疫类药物。排除标准:(1)钙磷代谢异常患者;(2)合并严重的肝、肾等脏器功能障碍者;(3)合并免疫系统及全身炎症性疾病者。其中男性38例,女性58例;年龄60-78岁,平均 (69.78 ± 6.34) 岁;身高156-182 cm,平均 (166.42 ± 7.84) cm;体重45-85 kg,平均 (68.67 ± 10.34) kg。另选取同期在我院进行体检的健康老年人40例作为对照组,其中男性15例,女性25例,年龄60-80岁,平均年龄 (70.24 ± 6.88) 岁;身高155-180 cm,平均 (165.78 ± 7.56) cm;体重43-84 kg,平均

(67.12 ± 9.78) kg。两组受试者一般资料比较无统计学差异($P > 0.05$),具有可比性。所有受试者对研究知情同意,研究经医院伦理委员会批准。

1.2 方法

研究组于入院后采集清晨空腹静脉血10 mL,对照组于体检当日采集空腹静脉血10 mL,取其中5 mL静置10 min,经4000 r/min离心10 min,离心半径6 cm,分离血清,采用酶联免疫吸附法检测受试者血清25-(OH)D3浓度,试剂盒购自美国IDS有限公司,具体操作严格按照试剂盒说明书进行。另5 mL置于EDTA抗凝试管中,应用IMK2-Lymphocyte细胞分离试剂盒将EDTA抗凝管中的血液进行分离,应用美国贝克曼库尔特公司生产的流式细胞仪测定CD4⁺、CD8⁺、CD4⁺/CD8⁺水平。应用德国西门子公司生产的全自动蛋白质分析仪检测血清免疫球蛋白A(Immunoglobulin A, IgA)、免疫球蛋白M(Immunoglobulin M, IgM)、免疫球蛋白G(Immunoglobulin G, IgG)水平。应用德国JAEGER公司生产的Master Screen肺功能检测仪检测受试者肺功能,包括用力肺活量(Forced vital capacity, FVC)、第一秒最大呼气量(First second maximum expiratory volume, FEV1),计算FEV1/FVC、FEV1占预计值百分比(FEV1%pred)。根据FEV1/FVC、FEV1%pred水平将研究组分组^[12]:(1)轻度哮喘组:FEV1/FVC $>70\%$,FEV1%pred $\geq 80\%$,30例;(2)中度哮喘组:FEV1/FVC $>70\%$, $60\% \leq$ FEV1%pred $<80\%$,38例;(3)重度哮喘组:FEV1/FVC $>70\%$,FEV1%pred $<60\%$,28例。

1.3 统计学方法

使用SPSS20.0进行统计分析,计量资料以 $(\bar{x} \pm s)$ 表示,实施t检验,多组数据比较应用单因素方差分析,血清25-(OH)D3与各项指标的关系予以Pearson相关性分析,将 $P < 0.05$ 记作差异有统计学意义。

2 结果

2.1 两组血清25-(OH)D3浓度以及肺功能指标比较

研究组血清25-(OH)D3浓度、FEV1%pred水平均低于对照组($P < 0.05$),两组FEV1/FVC水平比较差异无统计学意义($P > 0.05$),见表1。

表1 两组血清25-(OH)D3以及肺功能指标比较 $(\bar{x} \pm s)$

Table 1 Comparison of serum 25-(OH)D3 and pulmonary function of the two groups $(\bar{x} \pm s)$

Groups	n	25-(OH)D3(μ g/L)	FEV1pred(%)	FEV1/FVC(%)
Research group	96	15.44 $\pm$ 4.16	70.23 $\pm$ 8.97	82.37 $\pm$ 3.42
Control group	40	23.12 $\pm$ 3.43	88.12 $\pm$ 4.38	83.82 $\pm$ 3.24
t		16.937	28.937	0.257
P		0.000	0.000	0.839

2.2 两组免疫细胞和免疫球蛋白水平比较

研究组CD4⁺、CD4⁺/CD8⁺、血清IgA、IgM、IgG水平均低于对照组,CD8⁺水平高于对照组($P < 0.05$),见表2。

2.3 不同严重程度老年支气管哮喘患者血清25-(OH)D3浓度以及肺功能指标比较

重度哮喘组血清25-(OH)D3浓度、FEV1%pred水平均低于中度哮喘组和轻度哮喘组,中度哮喘组又低于轻度哮喘组,

各组血清25-(OH)D3浓度、FEV1%pred水平比较差异有统计学意义($P < 0.05$),各组FEV1/FVC水平比较差异无统计学意义($P > 0.05$),见表3。

2.4 不同严重程度老年支气管哮喘患者免疫细胞和免疫球蛋白水平比较

重度哮喘组CD4⁺、CD4⁺/CD8⁺、血清IgA、IgM、IgG水平均低于中度哮喘组和轻度哮喘组,中度哮喘组又低于轻度哮喘组,

组,重度哮喘组 CD8⁺ 水平高于中度哮喘组和轻度哮喘组,中度哮喘组又高于轻度哮喘组,各组 CD4⁺、CD8⁺、CD4⁺/CD8⁺、血清 IgA、IgM、IgG 水平比较有统计学意义($P<0.05$),见表 4。

表 2 两组免疫细胞和免疫球蛋白水平比较($\bar{x} \pm s$)Table 2 Comparison of immune cells and immunoglobulin levels of two groups($\bar{x} \pm s$)

Groups	n	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺	IgA(g/L)	IgM(g/L)	IgG(g/L)
Research group	96	28.67± 6.23	30.55± 5.28	0.94± 0.08	1.84± 0.10	0.82± 0.15	6.25± 0.88
Control group	40	36.10± 7.29	25.85± 4.88	1.39± 0.13	2.33± 0.21	1.07± 0.31	8.62± 1.05
t		19.037	13.932	10.893	7.082	6.843	10.782
P		0.000	0.000	0.000	0.008	0.012	0.000

表 3 不同严重程度老年支气管哮喘患者血清 25-(OH)D3 浓度以及肺功能指标比较($\bar{x} \pm s$)Table 3 Comparison of serological 25-(OH)D3 and pulmonary function in elderly patients with bronchial asthma in different severity($\bar{x} \pm s$)

Groups	n	25-(OH)D3(μg/L)	FEV1%pred(%)	FEV1/FVC(%)
Mild asthmatic group	30	18.35± 3.45	82.33± 4.23	83.12± 2.87
Moderate asthma group	38	14.65± 3.54*	68.56± 5.45*	82.32± 2.76
Severe asthma group	28	10.76± 3.86**	48.43± 4.54**	81.84± 2.89
F		22.874	45.246	1.546
P		0.000	0.000	0.758

Note: compared with mild asthma group, * $P<0.05$; compared with Moderate asthma group, ** $P<0.05$.

表 4 不同严重程度老年支气管哮喘患者免疫细胞和免疫球蛋白水平比较($\bar{x} \pm s$)Table 4 Comparison of immune cells and immunoglobulin levels in elderly patients with bronchial asthma in different severity($\bar{x} \pm s$)

Groups	n	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺	IgA(g/L)	IgM(g/L)	IgG(g/L)
Mild asthmatic group	30	32.57± 4.65	28.65± 4.65	1.14± 0.06	2.03± 0.11	0.95± 0.12	7.87± 0.82
Moderate asthma group	38	27.76± 4.76*	30.87± 4.26*	0.89± 0.08*	1.84± 0.12*	0.80± 0.13*	6.13± 0.78*
Severe asthma group	28	23.54± 4.54**	33.12± 4.23**	0.71± 0.08**	1.61± 0.11**	0.71± 0.11**	5.28± 0.75**
F		7.743	7.265	8.876	6.382	6.453	8.978
P		0.012	0.021	0.000	0.030	0.028	0.000

Note: compared with mild asthma group, * $P<0.05$; compared with Moderate asthma group, ** $P<0.05$.

2.5 老年支气管哮喘患者血清 25-(OH)D3 与免疫功能及肺功能的相关性分析

经 Pearson 相关性分析可得:老年支气管哮喘患者血清 25-(OH)D3 与 FEV1%pred、CD4⁺、CD4⁺/CD8⁺、IgA、IgM、IgG 均呈正相关,与 CD8⁺ 呈负相关($P<0.05$),与 FEV1/FVC 无相关性($P>0.05$)。见表 5。

表 5 老年支气管哮喘患者血清 25-(OH)D3 与免疫功能及肺功能的相关性分析

Table 5 Correlation analysis of serum 25-(OH)D3 with immune function and pulmonary function in elderly patients with bronchial asthma

Related factors	25-(OH)D3	
	r	P
FEV1%pred	0.545	0.000
FEV1/FVC	0.078	0.912
CD4 ⁺	0.442	0.025
CD8 ⁺	-0.311	0.032
CD4 ⁺ /CD8 ⁺	0.445	0.009
IgA	0.409	0.015
IgM	0.442	0.011
IgG	0.487	0.008

3 讨论

维生素 D 是一类开环的类固醇衍生物,广泛存在于各类食物中,当人体摄取天然维生素 D 后,皮肤经日光照射后体内的天然维生素 D 可转变为 25-(OH)D3,并经肾脏代谢最终形成 1,25-(OH)2D3,起到维持钙磷代谢、促进骨骼矿化的作用^[13-15]。近年来研究发现,维生素 D 除与维持钙磷代谢平衡有关外,还与 2 型糖尿病、心血管疾病、感染、癌症和呼吸系统疾病的发生和发展有关^[16,17]。Panek M 等研究发现维生素 D 在体内可以起到抑制 B 淋巴细胞、T 淋巴细胞、树突状细胞增殖、诱导凋亡和分化的作用^[18]。而目前研究认为免疫功能紊乱是支气管哮喘发病的重要原因,提示维生素 D 可能与支气管哮喘的发病有关^[19,20]。已有流行病学调查发现支气管哮喘儿童血清 25-(OH)D3 水平低于健康儿童,但老年支气管哮喘患者 25-(OH)D3 浓度如何仍存在一定争议^[21,22]。

本研究结果显示,研究组血清 25-(OH)D3 浓度、FEV1%pred 水平均低于对照组($P<0.05$),两组 FEV1/FVC 水平比较差异无统计学意义($P>0.05$)。表明老年支气管哮喘患者血清 25-(OH)D3、FEV1%pred 呈低表达,其主要原因是由于 FEV1%pred 是反映气流阻塞严重程度的可靠指标,而 FEV1/FVC 是反

映阻塞性通气功能障碍的敏感指标^[23,24]。而支气管哮喘是一种可逆的、发作性的小气道呼气性障碍疾病,并未出现阻塞性通气功能障碍。此外,研究组 CD4⁺、CD4⁺/CD8⁺、血清 IgA、IgM、IgG 水平均低于对照组,CD8⁺ 水平均高于对照组 ($P<0.05$),提示免疫功能失调在支气管哮喘发病中起到重要作用。CD4⁺、CD8⁺ 是机体两种重要的 T 淋巴细胞,CD4⁺ 被称为辅助性 T 淋巴细胞,发挥调节免疫应答和免疫反应的功能,而 CD8⁺ 被称为抑制性 T 淋巴细胞,主要发挥抑制免疫功能的作用,CD4⁺/CD8⁺ 是反映体液细胞免疫功能的重要指标^[25,26]。IgA、IgM、IgG 主要由 B 淋巴细胞产生并分泌,是体液免疫的重要组成部分。本研究结果还显示,重度哮喘组血清 25-(OH)D3 浓度、FEV1%pred 水平均低于中度哮喘组和轻度哮喘组,中度哮喘组又低于轻度哮喘组($P<0.05$),提示血清 25-(OH)D3 浓度可以反映支气管哮喘严重程度,其水平可能与 FEV1%pred 有关。同时不同严重程度老年支气管哮喘患者 CD4⁺、CD8⁺、CD4⁺/CD8⁺、血清 IgA、IgM、IgG 水平比较差异有统计学意义($P<0.05$),随着疾病的加重患者 CD4⁺、CD4⁺/CD8⁺、血清 IgA、IgM、IgG 水平逐渐降低,CD8⁺ 逐渐升高,证实免疫功能失调在支气管哮喘的发展中起到重要作用。此外,老年支气管哮喘患者血清 25-(OH)D3 与 FEV1%pred、CD4⁺、CD4⁺/CD8⁺、IgA、IgM、IgG 均呈正相关,与 CD8⁺ 呈负相关($P<0.05$),推测其机制可能是 25-(OH)D3 可以激发辅助性 T 淋巴细胞增殖,抑制抑制性 T 淋巴细胞增殖,诱导抑制性 T 淋巴细胞凋亡,影响细胞免疫功能^[27,28]。25-(OH)D3 增加抗原呈递细胞的耐受性,提高 IgA、IgM、IgG 水平。而支气管哮喘患者由于机体 25-(OH)D3 浓度降低,免疫功能抑制,导致疾病进一步发展^[29,30]。

综上所述,老年支气管哮喘患者的血清 25-(OH)D3 浓度显著降低,且与肺功能和免疫功能相关,血清 25-(OH)D3 浓度的检测可用于评估患者病情严重程度,可作为患者预后评估的辅助指标。

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