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## 维生素 D 联合异丙托溴铵治疗支气管哮喘患者的临床疗效分析 \*

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**摘要** 目的:研究维生素 D 联合异丙托溴铵治疗支气管哮喘患者的临床疗效。方法:选择 2015 年 1 月~2017 年 12 月在我院进行诊治的 81 例支气管哮喘患者并将其随机分为两组。对照组雾化吸入异丙托溴铵,观察组在对照组的基础上联合口服维生素 D。比较两组的喘憋症状消失时间、咳嗽缓解时间、肺部哮鸣音消失时间和肺部湿啰音消失时间,治疗前后的最大呼气峰流速(peak expiratory flow rate, PEF)变异率和哮喘控制测试(asthma control test, ACT)评分值。结果:观察组治疗有效率为 90.00%(36/40),较对照组[78.05%(32/41)]显著升高( $P<0.05$ );观察组的喘憋症状消失时间、咳嗽缓解时间、肺部哮鸣音消失时间和肺部湿啰音消失时间均明显短于对照组( $P<0.05$ )。治疗前,两组 PEF 变异率和 ACT 评分值比较差异无统计学意义( $P>0.05$ );治疗后,两组 PEF 变异率均较治疗前显著降低( $P<0.05$ ),ACT 评分值均较治疗前显著升高( $P<0.05$ ),且观察组 PEF 变异率显著低于对照组( $P<0.05$ ),而 ACT 评分值明显高于对照组( $P<0.05$ )。结论:与单用雾化吸入异丙托溴铵相比,维生素 D 联合雾化吸入异丙托溴铵治疗支气管哮喘的临床疗效更优,且可以有效缩短患者的症状消失时间。

**关键词:** 维生素 D; 异丙托溴铵; 支气管哮喘; 哮喘控制测试; 最大呼气峰流速

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## Analysis of the Clinical Efficacy of Vitamin D Combined with Ipratropium Bromide in the Treatment of Patients with Bronchial Asthma\*

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**ABSTRACT Objective:** To study the clinical efficacy of vitamin D combined with ipratropium bromide in the treatment of bronchial asthma. **Methods:** 81 cases of bronchial asthma diagnosed and treated in our hospital from January 2015 to December 2017 were randomly divided into two groups. The control group was inhaled ipratropium bromide, and the observation group was given oral vitamin D on the basis of control group. The disappearance time of asthma symptoms, the time of cough remission, the time of disappearance of lung wheezing sound, and the loss of lung rale, the maximum peak expiratory flow rate (PEF) and the asthma control test (ACT) score before and after treatment were compared between the two groups. **Results:** The effective rate of observation group was 90% (36/40), which was significantly higher than that of the control group ([78.05% (32/41)]). The time of disappearance of asthmatic symptoms, the time of cough remission, the disappearance time of lung wheezing sound and the loss of lung wet rale were significantly shorter in the observation group than those in the control group ( $P<0.05$ ). Before treatment, there was no significant difference in the PEF and ACT scores between the two groups ( $P>0.05$ ). After treatment, the PEF variations of both groups were significantly lower than those before the treatment ( $P<0.05$ ), and the ACT score was significantly higher than that before the treatment ( $P<0.05$ ), and the PEF variation rate in the observation group was significantly lower than that in the control group ( $P<0.05$ ), while the ACT score was significantly higher than that of the control group ( $P<0.05$ ). **Conclusion:** Compared with the inhalation of ipratropium bromide alone, vitamin D combined with ipratropium bromide was more effective in the treatment of bronchial asthma, and it could effectively promote the disappearance of symptoms.

**Key words:** Vitamin D; Ipratropium bromide; Bronchial asthma; Asthma control test; Peak expiratory flow rate

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### 前言

支气管哮喘是一种临床上极为常见的慢性呼吸系统疾病,

全球大约有 3 亿人患有支气管哮喘,发病率可高达 18%,且逐年升高<sup>[1]</sup>。支气管哮喘会引发广泛且多变的可逆性气流受限,导致反复发作性气急、喘息、咳嗽、胸闷等临床症状,严重影响患

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者的生活质量<sup>[2-4]</sup>。WHO 将哮喘与高血压、糖尿病和血脂异常归为 4 大顽固性慢性疾病。支气管哮喘不仅受遗传因素的影响,环境、气候等条件也会影响哮喘患者的症状和治疗效果<sup>[5]</sup>。气道反应性炎症是支气管哮喘生理改变和病理改变的重要机制<sup>[6]</sup>。

临床治疗支气管哮喘的首选给药方法为雾化吸入疗法,药物能迅速、直接作用于支气管和气管,从而有效控制患者的症状。异丙托溴铵可以同时作用于副交感神经以及交感神经,使小气道、中气道和大气道明显舒张,抑制气道黏液的分泌,从而有效改善患者的症状。但单纯雾化吸入异丙托溴铵治疗支气管哮喘的效果往往并不显著,因而积极寻找更为高效的治疗方案具有重要的临床意义。流行病学研究发现许多肺部疾病与维生素 D 缺乏有关<sup>[7]</sup>。本研究将维生素 D 以及异丙托溴铵联合使用,主要探讨了其对支气管哮喘患者最大呼气峰流速(peak expiratory flow rate, PEF) 变异率和哮喘控制测试 (asthma control test, ACT)评分值的影响,结果报道如下。

## 1 材料与方法

### 1.1 一般资料

选择 2015 年 1 月~2017 年 12 月在我院进行诊治的 81 例支气管哮喘患者,均符合相关的诊断标准<sup>[8]</sup>,排除合并有重要器官严重功能衰竭患者、意识障碍或者认知障碍患者、哺乳期和妊娠期女性,将其随机分为两组。观察组 40 例,男 23 例,女 17 例;年龄 21~69 岁,平均年龄(44.52± 9.73) 岁;病程 1~15 年,平均病程(4.83± 0.45)年;轻度 18 例,中度 19 例,重度 3 例。对照组 41 例,男 23 例,女 18 例;年龄 21~69 岁,平均年龄(43.79± 8.24) 岁;病程 1~15 年,平均病程(4.76± 0.53) 年;轻度 17 例,中度 20 例,重度 3 例。本研究经医院伦理委员会同意,所有患者均签署知情同意书。两组的一般资料比较差异均无统计学意义(P>0.05),具有可比性。

### 1.2 治疗方法

对照组采用异丙托溴铵气雾剂(生产厂家:Boehringer Ingelheim Pharma GmbH & Co. KG;批准文号:H20130498;20 μg/ 掀)治疗,每次 4 掀(80 μg),每天早晚各吸入一次。观察组联合口服维生素 D(生产厂家:青岛双鲸药业有限公司;批准文号:H20113033;400IU/ 粒),每天一粒。治疗一个月。

### 1.3 观察指标

临床疗效评估标准<sup>[9]</sup>: ① 临床控制:1 年内患者未发作哮喘,痰、咳、喘症状完全消失;② 显效:1 年内患者的急性发作的休止期显著增加,急性发作次数与治疗前相比降低 2/3,痰、咳、喘症状显著缓解;③ 有效:1 年内急性发作的休止期出现一定程度的增加,急性发作次数与治疗前相比降低 1/3,痰、咳、喘症状有所改善;④ 无效:1 年内急性发作的次数未出现任何改变,痰、咳、喘症状未发生任何缓解。比较两组的喘憋症状消失时间、咳嗽缓解时间、肺部哮鸣音消失时间和肺部湿啰音消失时间。记录两组治疗前后的 ACT 评分值,评分值为 25 分表示哮喘完全控制评分值为 20~24 分表示哮喘部分控制,评分值<20 分表示哮喘未控制。采用科卡峰速仪 PEF-3/2 检测两组治疗前后的 PEF 变异率。

### 1.4 统计学分析

采用 SPSS19.0 软件进行统计学分析,计量资料以( $\bar{x} \pm s$ )表示,组间和组内对比用 t 检验,组间率的比较用  $\chi^2$  检验,以 P<0.05 表明差异有统计学意义。

## 2 结果

### 2.1 两组临床疗效的对比

临床控制:观察组 11 例(27.50%),对照组 9 例(21.95%);显效:观察组 13 例(32.50%),对照组 10 例(24.39%);有效:观察组 12 例 (30.00%), 对照组 13 例 (31.71%);无效:观察组 4 例 (10.00%), 对照组 9 例 (21.95%)。观察组的有效率为 90.00% (36/40),与对照组[78.05%(32/41)]比较显著升高(P<0.05)。见表 1。

表 1 两组临床疗效的对比[例(%)]

Table 1 Comparison of the clinical efficacy between the two groups [cases (%)]

| Groups            | n  | Clinical control | Obvious effect | Effective | No effect | Effective rate |
|-------------------|----|------------------|----------------|-----------|-----------|----------------|
| Control group     | 41 | 9(21.95)         | 10(24.39)      | 13(31.71) | 9(21.95)  | 78.05          |
| Observation group | 40 | 11(27.50)        | 13(32.50)      | 12(30.00) | 4(10.00)  | 90.00*         |

Note: compared with the control group, \*P<0.05.

### 2.2 两组临床症状消失时间的对比

观察组的喘憋症状消失时间、咳嗽缓解时间、肺部哮鸣音

消失时间和肺部湿啰音消失时间均明显短于对照组(P<0.05),见表 2。

表 2 两组临床症状消失时间对比( $\bar{x} \pm s, d$ )

Table 2 Comparison of the disappearance time of clinical symptoms between two groups( $\bar{x} \pm s, d$ )

| Groups            | n  | Disappearance time of asthmatic symptoms | Coughing time | Lung wheeze disappearance time | Pulmonary rale disappearance time |
|-------------------|----|------------------------------------------|---------------|--------------------------------|-----------------------------------|
| Control group     | 41 | 6.75± 1.32                               | 7.29± 1.03    | 5.63± 1.48                     | 4.89± 1.24                        |
| Observation group | 39 | 4.13± 1.16*                              | 5.34± 1.28*   | 3.21± 1.09*                    | 3.15± 0.73*                       |

Note: compared with the control group, \*P<0.05.

### 2.3 两组治疗前后 PEF 变异率和 ACT 评分值对比

治疗前, 两组 PEF 变异率和 ACT 评分值比较差异无统计学意义(P>0.05)。治疗后,两组 PEF 变异率均较治疗前显著降

低(P<0.05),ACT 评分值均较治疗前显著升高(P<0.05),且观察组 PEF 变异率显著低于对照组, 而 ACT 评分值明显高于对照组(P<0.05),见表 3。

表 3 两组治疗前后 PEF 变异率和 ACT 评分值的对比( $\bar{x} \pm s$ )Table 3 Comparison of the PEF and ACT scores between two groups before and after treatment ( $\bar{x} \pm s$ )

| Groups            | n  |                  | PEF variation rate (%)         | ACT Score (Score)              |
|-------------------|----|------------------|--------------------------------|--------------------------------|
| Control group     | 41 | Before treatment | 35.42 $\pm$ 7.49               | 12.39 $\pm$ 2.45               |
|                   |    | After treatment  | 30.27 $\pm$ 6.42 <sup>#</sup>  | 17.53 $\pm$ 3.19 <sup>#</sup>  |
| Observation group | 40 | Before treatment | 34.58 $\pm$ 6.93               | 12.17 $\pm$ 2.38               |
|                   |    | After treatment  | 19.65 $\pm$ 5.61 <sup>*#</sup> | 22.54 $\pm$ 3.25 <sup>*#</sup> |

Note: compared with the control group, \*P<0.05; compared with before treatment, <sup>#</sup>P<0.05.

### 3 讨论

支气管哮喘是多种结构细胞及肥大细胞、T 淋巴细胞、嗜酸性粒细胞、平滑肌细胞、中性粒细胞等炎症细胞以及细胞组分参与的一种气道慢性炎症性疾病<sup>[9,10]</sup>。支气管哮喘的发作是因为支气管粘液分泌增加、平滑肌痉挛和粘膜肿胀,导致气急、喘息、咳嗽或者胸闷等临床症状和缺氧引发的一系列并发症<sup>[11-13]</sup>。支气管哮喘患者的病理改变主要包括微血管通透性升高、气道粘膜下组织发生水肿、支气管内分泌物滞留、露出基底膜、纤毛细胞发生脱落、气道上皮炎性细胞浸润和杯状细胞增殖。其病因复杂,目前关于该病的发病机制主要有气道炎症形成机制、气道神经受体失衡机制和免疫反应机制等,主要是遗传因素、环境因素以及孕期母亲的健康状态、营养状况和生活方式等多种因素共同作用的结果<sup>[14-17]</sup>。

临床上治疗支气管哮喘患者的目标主要包括:(1)使患者可以正常开展日常的活动;(2)达到且维持临床症状的控制;(3)维持患者的肺功能,并且尽可使其恢复正常水平;(4)预防治疗支气管哮喘的药物所引发的不良反应;(5)避免哮喘急性发作;(6)预防支气管哮喘引发的死亡<sup>[18-20]</sup>。目前,主要采用 $\beta$ 受体激动剂、口服或吸入糖皮质激素、抗白三烯类以及茶碱类等药物治疗支气管哮喘,但仍有部分患者无法有效控制病情<sup>[21]</sup>。研究显示乙酰胆碱在呼吸道的作用还与哮喘的气道重塑相关<sup>[22]</sup>。异丙托溴铵通过阻断气道内 M 胆碱受体,拮抗乙酰胆碱收缩支气管,达到预防气道重塑和扩张支气管的目的<sup>[23]</sup>。该药主要作用为减少黏液分泌,扩张大、中气道,药物生物利用度高且局部作用疗效好<sup>[24]</sup>。由于生活习惯改变光照时间大大减少,饮食不均衡、反复糖皮质激素的应用使维生素 D 的分解代谢增加及大气污染等各种原因,哮喘患者大多数都有维生素 D 缺乏现象<sup>[25]</sup>。维生素 D 是一组脂溶性的类固醇衍生物,具有激素样特征,可通过调节参与哮喘炎症反应的细胞因子影响机体的免疫应答<sup>[26]</sup>。本研究结果显示观察组有效率达 90.00%,与对照组比较显著升高,其喘憋症状消失时间、咳嗽缓解时间、肺部哮鸣音消失时间和肺部湿啰音消失时间均明显短于对照组,表明维生素 D 联合异丙托溴铵可以显著改善支气管哮喘患者的症状,缓解病情,提高治疗有效率。这可能与维生素 D 具有介导单核细胞进一步分化成熟为吞噬细胞的免疫调节作用有关<sup>[27,28]</sup>。

肺功能检测可以早期检出肺、气道阻塞和病变情况,也是判断哮喘治疗效果的重要指标。PEF 测定能够良好的反应肺容量、呼吸肌强度、肺组织弹力回缩力以及评估气道阻力,在生理及临床上所表达的意义与用力呼气量(FEV)、最大通气量相似,

能较好的评估气道阻塞情况尤其是小气道,而哮喘的气道炎症也主要发生在小气道内,是临床上判断机体肺功能的一个重要指标。PEF 变异率能反映机体的气流受限程度以及气道高反应性,从而有效评估哮喘的控制情况。与肺功能仪相比,PEF 的检测方法较为经济、简单、极易掌握,可以作为监测和评估哮喘控制水平的一项客观检测指标<sup>[29]</sup>。而峰流速仪体积小、便于携带,其进行 PEF 监测比较方便。ACT 是目前临床上公认的评估以及监测支气管哮喘患者病情的简单有效的工具,能准确判断哮喘患者病情的控制程度,方便支气管哮喘患者长期管理与监测<sup>[30]</sup>。ACT 由于不需要检测患者的肺功能,有利于简化哮喘控制的判断方法,增强患者和临床医师之间的交流,极为适合进行推广使用,特别是基层医疗单位。本研究中,两组治疗后 PEF 变异率均较治疗前显著降低,ACT 评分值均较治疗前显著升高,且观察组 PEF 变异率和 ACT 评分值变化更为明显,表明维生素 D 联合异丙托溴铵可以控制支气管哮喘患者的病情,改善肺功能。但由于本研究样本量较小,后期还需进一步对维生素 D 辅助治疗哮喘的用药剂量进一步研究。

综上所述,与单用雾化吸入异丙托溴铵相比,维生素 D 联合雾化吸入异丙托溴铵治疗支气管哮喘的临床疗效更优,且可以有效缩短患者的症状消失时间。

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