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中重度支气管哮喘急性发作期患儿 Fe NO 表达水平与肺功能的相关性研究 *

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摘要 目的:探究中重度支气管哮喘急性发作期患儿呼出气一氧化氮(Fe NO)表达水平与肺功能的相关性。**方法:**选择 2016 年 3 月-2019 年 3 月来我院就诊的中重度支气管哮喘急性发作期患儿 69 例为观察组,其中,中度支气管哮喘急性发作期患儿 58 例,重度支气管哮喘急性发作期患儿 11 例;另选取同期来我院体检的 69 例正常健康儿童作为对照组,对比观察组中中度、重度支气管哮喘急性发作期患儿 Fe NO 表达水平、用力肺活量(forced vital capacity, FVC)、最大呼气流量占预计值百分比(Maximum expiratory flow as a percentage of expected value, PEF%)、第一秒用力呼气容积占预计值的百分比(FORCED EXPIRATORY VOLUME AS A PERCENTAGE OF EXPECTED VALUE IN THE FIRST SECOND, FEV₁%)与对照组健康儿童的差异,并对观察组患儿 Fe NO 表达水平与肺功能的相关性进行分析。**结果:**观察组患儿的 Fe NO 表达水平均高于对照组,且重度组患儿的 Fe NO 表达水平明显高于中度组($P<0.05$);观察组患儿的 PEF%、FEV₁%、FVC 水平均高于对照组,且重度组患儿的 PEF%、FEV₁%、FVC 水平均高于中度组($P<0.05$);观察组患儿 Fe NO 表达水平与 FVC、PEF%、FEV₁%指标均呈负相关关系($r=-0.503$ 、 -0.551 、 -0.532 , P 均 <0.05)。**结论:**中重度支气管哮喘急性发作期患儿 Fe NO 表达水平与肺功能成负相关,可通过监测 Fe NO 水平间接判断炎症程度。

关键词:中重度支气管哮喘;急性发作期;Fe NO 表达水平;肺功能;相关性

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Correlation between Fe NO Expression Level and Pulmonary Function in Children with Moderate to Severe Bronchial Asthma*

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ABSTRACT Objective: To investigate the correlation between the expression level of exhaled nitric oxide (Fe NO) and lung function in children with acute bronchial asthma. **Methods:** 69 children with moderate to severe bronchial asthma who were admitted to our hospital from March 2016 to March 2019 were selected as the observation group. 58 children with moderate bronchial asthma and 11 patients with severe bronchial asthma during acute attack. In addition, 69 normal healthy children who were admitted to our hospital during the same period were selected as the control group. The expressions of Fe NO, forced vital capacity (FVC), maximum expiratory flow rate as a percentage of predicted value (PEF%), forced expiratory volume in the first second as a percentage of predicted value (FEV₁%) in children with moderate and severe bronchial asthma in the acute observation group were compared with healthy children in the control group. The correlation between Fe NO expression level and lung function in the observation group was analyzed. **Results:** The expression level of Fe NO in the observation group was higher than that in the control group, and the expression level of Fe NO in the severe group was higher than that in the moderate group. The difference was statistically significant ($P<0.05$). The PEF%, FEV₁%, and FVC levels in the observation group were higher than those in the control group, and the PEF%, FEV₁%, and FVC levels in the severe group were higher than those in the moderate group ($P<0.05$). The expression of Fe NO in the observation group was negatively correlated with FVC, PEF% and FEV₁%($r=-0.503$, -0.551 , -0.532 , $P<0.05$). **Conclusion:** The expression of Fe NO in children with moderate to severe bronchial asthma is negatively correlated with lung function. The degree of inflammation can be judged indirectly by monitoring the level of Fe NO.

Key words: Moderate to severe bronchial asthma; Acute attack; Fe NO expression level; Lung function; Correlation

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前言

支气管哮喘是一种临床上常见的以可逆性气流受限、气道高反应性为特征的呼吸道慢性炎症性疾病^[1,2],如果支气管哮喘患者对自身疾病不加以重视,会导致很多身心问题也会很大程度地影响到患者的工作生活,如果治疗不规范或发病就诊不及时,病情加重或出现进展易致患者死亡^[3,4]。据流行病学资料显示,近年来,儿童哮喘的发病率有逐年增高的趋势,且多发生在学龄前期及学龄期,男童患病率高于女童^[5,7]。由于哮喘患儿急性发作时其气道炎症反应程度和临床症状表现存在差异,加之在行肺功能检查时,患儿的配合程度对肺功能指标存在影响,所以儿童哮喘常被误诊或漏诊^[8,9]。呼出气一氧化氮测定具有安全、无创、方便等优点,广泛应用于哮喘的控制评估中^[10,11]。本文通过探究中重度支气管哮喘急性发作期患儿 Fe NO 表达水平与肺功能的相关性,为临床该类疾病的诊断及治疗评估提供科学依据,具体内容报告如下。

1 对象与方法

1.1 一般资料

选择 2016 年 3 月-2019 年 3 月来我院就诊的中重度支气管哮喘急性发作期患儿 69 例为观察组,经临床诊断及病理学检查,所有患儿均符合中重度支气管哮喘急性发作的临床诊断标准,排除合并严重心肺疾病及肺部感染的患儿;其中男 42 例,女 27 例,年龄 5-11 岁,平均年龄为 8.1 ± 1.2 岁,中度支气管哮喘急性发作期患儿 58 例,重度支气管哮喘急性发作期患儿 11 例;另选取同期来我院体检的 69 例正常健康儿童作为对

照组,其中,男 44 例,女 25 例,年龄 6-11 岁,平均年龄为 8.2 ± 1.1 岁;统计学对比两组患儿的基础资料无差异($P > 0.05$),可进行对比。本研究已征得我院医学伦理委员会的支持,病例选择遵循自愿原则,所有参选患儿的家属均已签订《知情同意书》。

1.2 研究方法

采用 MastercrinePaed 型肺功能仪(德国 Jaeger 公司)检测患儿潮气呼吸肺功能,检查指标主要包括:用力肺活量(FVC)、最大呼气流量占预计值百分比(PEF%)、第一秒用力呼气容积占预计值的百分比(FEV1%)^[12]。采用 Sunvou-D100 型纳库仑一氧化氮分析仪(无锡尚沃有限公司)测定 Fe NO,测定 3 次取均值^[13]。

1.3 观察指标

对比观察组中中度、重度支气管哮喘急性发作期患儿 Fe NO 表达水平、FVC、PEF%、FEV1%指标与对照组健康儿童的差异,并对观察组患儿 Fe NO 表达水平与肺功能的相关性进行分析^[14,15]。

1.4 统计学分析

采用 SPSS 19.0 统计学方法,计数资料以例数、百分比表示,对比经卡方分析;计量资料以均数 $\pm$ 标准差表示,对比经 t 检验;利用 Pearson 积差相关分析检验, $P < 0.05$ 表示差异存在统计学意义。

2 结果

2.1 两组 Fe NO 表达水平对比

观察组患儿的 Fe NO 表达水平均高于对照组,且重度组患儿的 Fe NO 表达水平明显高于中度组($P < 0.05$),结果见表 1。

表 1 两组 Fe NO 表达水平对比($\times 10^{-9}$ mmol/L)

Table 1 Comparison of Fe NO expression levels between the two groups ($\times 10^{-9}$ mmol/L)

Groups	n	Fe NO expression level
Control group	69	14.9 ± 3.1
Observation group	Moderate	$68.4 \pm 15.8^*$
	Severe	$83.5 \pm 20.3^{* \#}$

Note: Compared with control group, $^*P < 0.05$; compared with moderate, $^{\#}P < 0.05$.

2.2 两组肺功能各指标对比

观察组患儿的 PEF%、FEV1%、FVC 水平均高于对照组,且

重度组患儿的 PEF%、FEV1%、FVC 水平均高于中度组($P < 0.05$),结果见表 2。

表 2 两组肺功能各指标对比

Table 2 Comparison of indicators of lung function between the two groups

Groups	n	FVC(L)	FEV1%(%)	PEF%(%)
Control group	69	3.9 ± 0.8	95.7 ± 13.1	7.1 ± 1.5
Observation group	Moderate	$3.4 \pm 0.7^*$	$70.8 \pm 11.8^*$	$5.7 \pm 1.1^*$
	Severe	$3.0 \pm 0.6^{* \#}$	$52.3 \pm 8.5^{* \#}$	$4.9 \pm 0.8^{* \#}$

Note: Compared with control group, $^*P < 0.05$; compared with moderate, $^{\#}P < 0.05$.

2.3 观察组患儿 Fe NO 表达水平与肺功能的相关性分析

观察组患儿 Fe NO 表达水平与 FVC、PEF%、FEV1%指标均呈负相关关系($r = -0.503$ 、 -0.551 、 -0.532 , P 均 < 0.05)。见图 1-3。

3 讨论

支气管哮喘是儿科呼吸道门诊的最常见疾病之一,近年来的环境因素使得中重度支气管哮喘急性发作期患儿的比例明

显增多,严重影响儿童的身心健康,也给家庭和社会带来沉重的经济负担^[16-18]。临床上对哮喘的治疗及管理主要是控制气道炎症反应。目前评价气道炎症的直接方法包括支气管镜下支气管内膜活检和肺泡灌洗液中嗜酸性粒细胞计数,但两种方法具有一定的创伤性,且不易重复测定,在哮喘患儿中有一定的局

限性^[19,20]。因此,积极寻找一种简单、无创、特异的在早期能监测、评估支气管哮喘急性发作期病情控制、评估炎症程度的指标,有助于在发病早期既能准确地告知,及时反应患者病情的严重程度并指导其治疗,具有重要的临床意义。

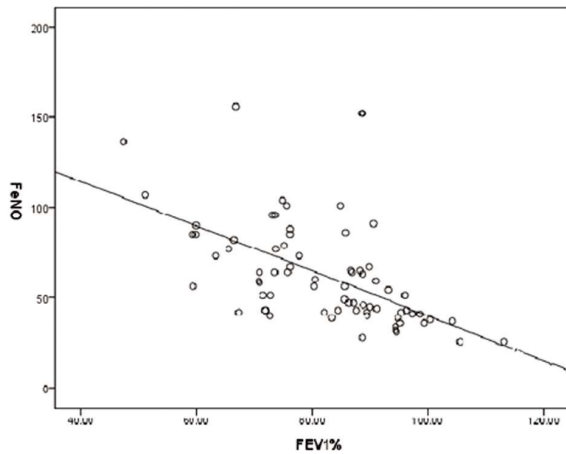


图1 观察组患儿 Fe NO 表达水平与 FEV₁% 的相关性分析

Fig.1 Correlation analysis between Fe NO expression level and FEV₁% in observation group

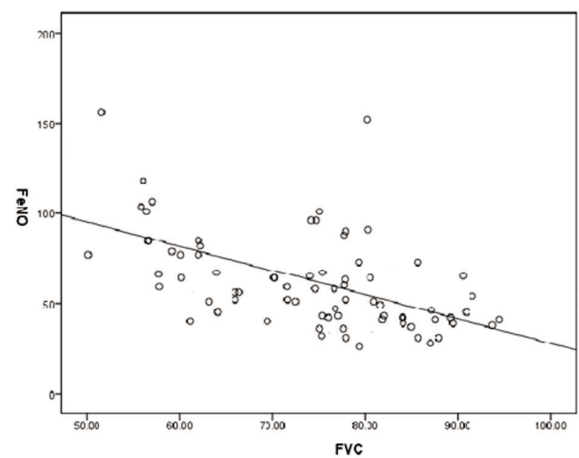


图2 观察组患儿 Fe NO 表达水平与 FVC 的相关性分析

Fig.2 Correlation analysis between Fe NO expression level and FVC in children in observation group

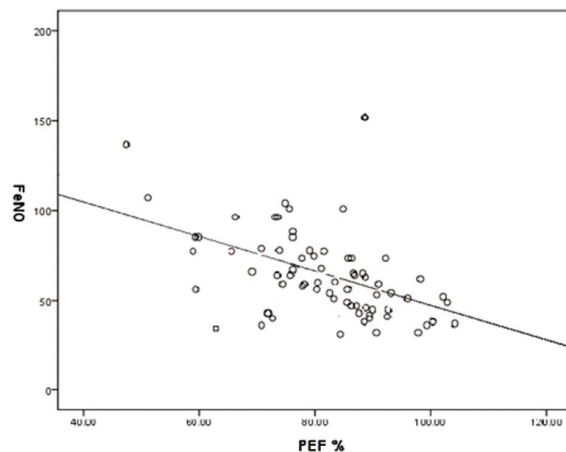


图3 观察组患儿 Fe NO 表达水平与 PEF% 的相关性分析

Fig.3 Correlation analysis between Fe NO expression level and PEF% in children in observation group

气道炎症评估是支气管哮喘诊断、治疗及管理中的关键,传统的评估方式主要根据病史、患儿症状控制情况及肺功能检测结果等进行多方面共同综合分析^[21,22],其中,肺功能检查项目包括换气功能、通气功能、呼吸调节功能及肺循环功能等,测定指标众多,且通过肺功能仪测定过程繁琐,费时费力,而且检测误差较大。目前临床上评价气道炎症治疗效率主要基于患儿的症状控制情况及肺功能测定,但是有的研究表明临床症状和肺功能测定与气道炎症之间没有显著的相关性^[23,24],而且在支气管哮喘患儿中即使有些没有突出的临床表现且肺功能检查指标是正常的,其炎性反应仍可以持续地在气道中存在,这表明临床中常用的肺功能检查,在一定程度上并不能准确地反映炎症在气道中作用的情况,敏感性差^[25,26]。

近年来,Fe NO 检测术因其无创、测定时间短、操作简便、可重复性高、对受检者的配合性要求低等特点,更受到儿科医

生的青睐^[27,28]。本文研究结果显示,观察组患儿的 Fe NO 表达水平均高于对照组,且重度组患儿的 Fe NO 表达水平高于中度组,与 Chen Feng-Jia^[29]等人对咳嗽变异性哮喘诊断的结果一致,其诊断敏感性和特异性分别为 81.3 % 和 84.0 %,说明 Fe NO 表达水平在哮喘患儿中显著升高,且随着病情的严重程度呈升高的趋势。因此,可作为哮喘患儿气道炎症的评价指标。本研究观察组患儿的 PEF%、FEV₁%、FVC 水平均高于对照组,且重度组患儿的 PEF%、FEV₁%、FVC 水平均高于中度组;与 Yin SS^[30]等人的结果一致,说明在哮喘患儿中,肺功能指标均显著升高,且随着气道慢性炎症程度的加深,患儿的 Fe NO 表达水平逐渐增高,肺功能指标均下降。但与杨梦丝^[31]的研究结果相反,通过评价 Fe NO 在社区儿童哮喘诊断价值,得到 Fe NO 与肺功能各参数 PEF%、FEV₁%、FVC 水平均未见显著的相关性,分析其原因可能是与治疗方法及病情程度有关。同时,本文研究结果还显示,观察组患儿 Fe NO 表达水平与 FVC、PEF%、FEV₁% 指标均呈负相关关系。表明,中重度支气管哮喘急性发作期患儿 Fe NO 表达水平与肺功能成负相关,可通过监测 Fe NO 水平间接判断炎症程度。因此,在中重度支气管哮喘急性发作期,对患儿 Fe NO 表达水平的检测,可以评估患儿气道阻塞程度及气道炎症,可作为哮喘规范化管理中的有效工具,能够更清晰和直观地观察到哮喘患儿各项临床指标,提高治疗效果。同时,本研究也存在一定的不足之处,如纳入的受试对象数目较少,后期应通过大样本量的深入研究,以支持本次研究结果。同时本研究没有对比 FeNO 测定方法、肺功能检测方法的检测价值,后续需要进一步的比较,为哮喘治疗提供了可靠依据。

综上所述,中重度支气管哮喘急性发作期患儿 Fe NO 表达水平与肺功能成负相关,可通过监测 Fe NO 水平间接判断炎症程度。

参 考 文 献(References)

- [1] Khaitov MR, Gaisina AR, Shilovskiy IP, et al. The Role of Interleukin-33 in Pathogenesis of Bronchial Asthma. New Experimental Data[J]. Biochemistry, 2018, 83(1): 13-25
- [2] MM Rafeeq, HAS Murad. Evaluation of drug utilization pattern for patients of bronchial asthma in a government hospital of Saudi Arabia [J]. Nigerian Journal of Clinical Practice, 2017, 20(9): 1098-1105
- [3] 马蕴蕾,宿英豪,于向艳. 固肾定喘丸对肺肾气虚型支气管哮喘慢性持续期患者血清 ECP、NO、IL-6 水平和肺功能的影响[J]. 中药药理与临床, 2018, 34(1): 161-164
- [4] Jing-bo Liang, Li-jin Liu, Qiu-hong Fang. Clinical characteristics of patients with chronic obstructive pulmonary disease overlapped with bronchial asthma [J]. Ann Allergy Asthma Immunol, 2017, 118(5): 564-569
- [5] Youroukova V M, Dimitrova D G, Valerieva A D, et al. Phenotypes Determined by Cluster Analysis in Moderate to Severe Bronchial Asthma[J]. Folia Med, 2017, 59(2): 165-173
- [6] Cao Y, Feng X, Wang Y, et al. An increased of Th17 cells and IL-23 and IL-17 in the lymph and blood of rats with bronchial asthma[J]. Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi, 2013, 29(12): 1281-1284
- [7] Li P, Yang QZ, Wang W, et al. Increased IL-4- and IL-17-producing CD8+ cells are related to decreased CD39+CD4+Foxp3+ cells in allergic asthma[J]. J Asthma, 2017, 55(1): 8-14
- [8] Yusupalieva MM, Savtchenko VM. The effectiveness of combined laser therapy for the treatment of the patients presenting with bronchial asthma and concomitant allergic rhinitis [J]. Vopr Kurortol Fizioter Lech Fiz Kult, 2017, 94(4): 14-18
- [9] Workgroup A. Chinese guideline for the prevention and management of bronchial asthma (Primary Health Care Version)[J]. J Thorac Dis, 2013, 5(5): 667-677
- [10] Zhang HQ, Zhang HQ, Zhang JJ, et al. Application of pulmonary function and fractional exhaled nitric oxide tests in the standardized management of bronchial asthma in children [J]. Zhongguo Dang Dai Er Ke Za Zhi, 2017, 19(4): 419-424
- [11] Kuan Shi, Wenzhong Wu, Lanying Liu, et al. Optimization of acupuncture application scheme in the treatment of bronchial asthma based on the orthogonal design method [J]. Chinese acupuncture & moxibustion, 2017, 37(6): 571-575
- [12] Yoshida M, Kaneko Y, Ishimatsu A, et al. Effects of tiotropium on lung function in current smokers and never smokers with bronchial asthma[J]. Pulmonary Pharmacology & Therapeutics, 2017, 42(suppl 59): 7-12
- [13] Mohan A, Arora S, Uniyal A, et al. Evaluation of plasma leptin, tumor necrosis factor- α , and prealbumin as prognostic biomarkers during clinical recovery from acute exacerbations of chronic obstructive pulmonary disease[J]. Lung India, 2017, 34(1): 3-8
- [14] Folly Messan, Albérick Tito, Polycarpe Gouthon, et al. Comparison of Catecholamine Values Before and After Exercise-Induced Bronchospasm in Professional Cyclists[J]. Tanaffos, 2017, 16(2): 136-143
- [15] Elliott M, Heltshe SL, Stamey DC, et al. Exhaled nitric oxide predicts persistence of wheezing, exacerbations, and decline in lung function in wheezy infants and toddlers [J]. Clin Exp Allergy, 2013, 43(12): 1351-1361
- [16] Marina Lluncor, Pilar Barranco, Emerson-Daniel Amaya, et al. Relationship between upper airway diseases, exhaled nitric oxide, and bronchial hyperresponsiveness to methacholine [J]. J Asthma, 2019, 56(1): 53-60
- [17] Zhang Q, Xiang XM, Song H, et al. Relationship between exposure to air pollutants during pre-pregnancy or early pregnancy and birth defects in Xi'an, 2013-2015: a case crossover study [J]. Zhonghua Liu Xing Bing Xue Za Zhi, 2017, 38(12): 1677-1682
- [18] Yin SS, Liu H, Gao X. Elevated fractional exhaled nitric oxide (FeNO) is a clinical indicator of uncontrolled asthma in children receiving inhaled corticosteroids [J]. Int J Clin Pharmacol Ther, 2017, 55(1): 66-77
- [19] Indinnimeo L, Chiappini E, Giudice M MD. Guideline on management of the acute asthma attack in children by Italian Society of Pediatrics[J]. Italian Journal of Pediatrics, 2018, 44(1): e46
- [20] Magallanes CD. Factors Associated with Failure of Emergency Department Management in Children with Acute Moderate or Severe Asthma: A Prospective, Multicenter, Cohort Study [J]. The Journal of Emergency Medicine, 2017, 52(2): 266-267
- [21] Liyan C, Ying T, Li Z, et al. Detection of interleukin-22 in peripheral blood of patients with bronchial asthma and its clinical significance [J]. Journal of Jilin University, 2017, 43(2): 349-352
- [22] Eugen Bersuch, Florian Gräf, Ellen D Renner, et al. Lung function improvement and airways inflammation reduction in asthmatic children after a rehabilitation program at moderate altitude [J]. Pediatric Allergy & Immunology, 2017, 28(8): 768-775
- [23] Malgorzata Olszowiec-Chlebna, Pawel Majak, Agnieszka Brzozowska, et al. Effect of inhaled steroid and montelukast on clinical symptoms in children with newly diagnosed asthma: A pilot study[J]. Pediatr Allergy Immunol, 2010, 21(4 Pt 2): e687-e690
- [24] Wang Xuan, Zhang Xi-rong, Li Gang. Effect of Azithromycin on Function of Peripheral Blood Dendritic Cells in Children with Bronchial Asthma[J]. Journal of International Translational Medicine, 2017, 5(1): 23-28
- [25] Tooba Momen, Hamid Ahanchian, Mohsen Reisi, et al. Comparison of Interleukin-33 Serum Levels in Asthmatic Patients with a Control Group and Relation with the Severity of the Disease [J]. Int J Prev Med, 2017, 8(1): e65
- [26] Michael D Evans, Stephane Esnault, Loren C Denlinger, et al. Sputum cell interleukin-1 receptor expression level is a marker of airway neutrophilia and airflow obstruction in asthma [J]. J Allergy Clin Immunol, 2017, 142(2): 415-423
- [27] Yang Yan, Chen Ru-hua, Wang Ceng, et al. Correlation between exhaled nitric oxide level and serum levels of IL-6, IL-8, TNF- α and respiratory function in patients with chronic obstructive pulmonary disease[J]. Journal of Tropical Medicine, 2017, 17(1): 78-80
- [28] Wang HF, Yang WL, Wang LH. Changes of exhaled nitric oxide level in patients with chronic obstructive pulmonary disease and its clinical significance [J]. Journal of Shanghai Jiaotong University(Medical Science), 2017, 37(4): 523-526
- [29] Chen Feng-Jia, Huang Xin-Yan, Lin Geng-Peng, et al. Validity of Fractional Exhaled Nitric Oxide and Small Airway Function Indices in Diagnosis of Cough Variant Asthma [J]. J Asthma, 2018, 55(7): 750-755
- [30] Yin SS, Liu H, Gao X. Elevated fractional exhaled nitric oxide (FeNO) is a clinical indicator of uncontrolled asthma in children receiving inhaled corticosteroids [J]. Int J Clin Pharmacol Ther, 2017, 55(1): 66-77
- [31] 杨梦丝. 呼出气一氧化氮水平在社区哮喘儿童诊断与管理中的价值[J]. 湖北科技学院学报(医学版), 2018, 32(3): 237-239