综 述

电子鼻检测技术在支气管哮喘诊断方面的研究进展

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摘 要: 支气管哮喘的诊断主要依靠病史及肺功能检查,但对有禁忌证、配合欠佳的患者易误诊、漏诊。对支气管哮喘患者采用电子鼻检测技术检测呼出挥发性有机化合物,用于早期快速筛查支气管哮喘、评估类固醇治疗效果以及预测类固醇反应,是一种经济、快速和高诊断率的诊断方法。

关键词: 电子鼻检测技术; 支气管哮喘; 挥发性有机化合物; 肺功能检查; 类固醇

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Research progress of electronic nose detection technology in diagnosis of bronchial asthma

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Abstract: Diagnosis of bronchial asthma mainly depends on history of disease and pulmonary function examination, but patients with contraindications and poor cooperation are easy to be misdiagnosed and missed diagnosed. Using electronic nose detection technology to detect exhaled volatile organic compounds in patients with bronchial asthma is an economic, rapid and high diagnostic method with higher diagnostic rate method for early and rapid screening of bronchial asthma, and assessment on the efficacy of steroid treatment and prediction of steroid response.

Key words: electronic nose detection technology; bronchial asthma; volatile organic compounds; pulmonary function examination; steroid

支气管哮喘表现为喘息、气短、胸闷和咳嗽,与气道高反应性和气道炎症有关,导致气道重构,随着气流受限强度和时间变化,气流受限可能持续存在[1]。挥发性有机化合物(VOC)检测通过冷却呼出挥发性气体得到冷凝液,测定冷凝物中的各种炎症介质水平来反映肺部疾病的炎症状态[2-4]。目前气相色谱-质谱是检测 VOC 灵敏度和特异性较高的标准方法,但成本昂贵、分析时间长,而电子鼻分析方法具有非侵入性、快速、便携式、经济的优点[5-6]。本文总结电子鼻检测 VOC 在支气管哮喘诊断方面的最新进展。

1 电子鼻检测原理及影响因素

1.1 电子鼻检测原理

电子鼻有 3 个系统,传感器阵列系统、数据处理系统和模式识别系统,其主要元件是气体传感器阵列部件,通常被放置在一个可控制湿度和温度的腔室中[7],通过(传感器阵列系统)模仿哺乳动物的嗅觉,对尿液、血液、呼吸道中 VOC 进行检测。当接触到 VOC 时,传感器里面的物理性质将会发生变化,从而变成可以被测量和量化的特异性呼吸信号(呼吸印记)[8]。目前,电子鼻检测已被应用于囊性纤维化、肺癌、慢性阻塞性肺疾病、胃肠道疾病、结肠癌和膀胱癌等的诊断中[9-10]。人体呼吸系统能携带多种 VOC,而电子鼻检测传感器可同时与多种 VOC 发生反应,且能通过多个传感器捕获到具有重叠的 VOC,在复杂多变的呼吸信号判定方面具有显著优势。

1.2 VOC 来源及分类

VOC主要分为外源性VOC和内源性VOC。

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外源性 VOC 通常存在于室内空气和特定的化合物中,例如建筑材料(油漆)、吸烟、杀虫剂、消毒剂等,主要包括醇类、醚类、醛类、苯类、烯类、酮类、烷类,其中以丙醇、甲醛、间二甲苯、异戊二烯、丙酮、氯甲烷等为标志物,且有报道[11-14]称其浓度变化主要与 VOC 的来源环境(室内和室外)、季节变化(寒冷)存在显著相关。内源性 VOC 则主要来自于人体的呼吸、唾液、血液、皮肤分泌物、尿液和粪便,与年龄、饮食、性别、身高、体质量、生活方式以及个体新陈代谢有关[15]。丙酮和异戊二烯是呼吸系统中最丰富的 VOC,与清洁剂和消毒剂相关的 VOC 以 1-丙醇、2-丙醇和乙醇为主,与吸烟存在高度相关性的 VOC 为氯甲烷、苯和环已二烯等,在成年男性中异戊二烯的水平更高[16]。

1.3 电子鼻检测的影响因素

电子鼻检测技术关键影响因素是检测环境(如房间空气质量、湿度和温度)和个体差异,因此在收集 VOC 前,待检测的患者应当避免吸烟、剧烈运动和使用药物等[17]。欧洲呼吸学会建议在电子鼻对呼出的 VOC 取样过程中,应当注意如食物、饮料摄入和妊娠等非疾病相关因素,对于重症监护病房的患者可以通过呼吸机管道回路进行采样。丙酮和异戊二烯在支气管哮喘中含量丰富且有节律性,16 点达到峰值,10 点出现低谷,因此建议 VOC 取样可根据节律性进行。年龄和性别并不影响电子鼻对 VOC 的检测[18]。呼出气体的体积、温度、湿度不影响电子鼻传感器的读数大小,但呼气流量与传感器读数呈线性相关[19]。改变呼气流量能显著影响电子鼻对呼吸模式的评估能力,从而体现出对 VOC 的不同分析能力[20]。但电子鼻洗气过程中呼吸节律的变化并不影响对 VOC 的分析。研究[21]表明室内和室外的空气由于缺乏通风,VOC 对肺部疾病产生中等影响,包括支气管哮喘和喘息发作,且因国家、年龄、疾病类型等有差异。

2 支气管哮喘与 VOC 的关联性

支气管哮喘是一种呼吸系统慢性炎症性疾病,支气管细胞内存在氧化应激反应,导致脂质过氧化,从而产生 VOC,VOC 与呼吸道上皮和黏膜发生化学反应[22-23]。这种化学反应的结果是可以通过检测抗原物质的 IgE 抗体得到的,这是触发气道炎症反应的根本原因,同时还可以使呼吸道细胞脱水导致气道重塑[24-25]。BÖNISCH U 等[26]发现 VOC 可能通过干扰成熟树突状细胞功能和诱导氧化应激来增加过敏性反应,考虑将 VOC 作为过敏性疾病发展的危险因素。WANG F 等[27]研究表明 VOC 改变了微小 RNA 调节基因表达的模式,从而导致癌症和炎症性疾病的发生。KAWANO T 等[28]证实 VOC 之一的乙醛可导致部分支气管哮喘患者气管收缩,可增强支气管哮喘患者的气道炎症及气道高反应性。研究[29]发现在成人支气管哮喘中呼出的 VOC 与炎症有关,VOC 可以作为识别支气管哮喘的候选生物标志物。CALDEIRA M 等[30]发现十四烷、癸烷和壬醛可作为过敏性哮喘的潜在呼吸生物标记物。有研究[31]发现生活在吸烟家庭环境中的儿童,出现喘息发作的可能性是非吸烟家庭的 4 倍。SAIF N T 等[11]认为油漆是室内 VOC 来源之一,需要采取多种策略来管理油漆中 VOC 对健康的影响。酮类与支气管哮喘的急性发作有关,苯与重度的哮喘症状呈中度正相关[32-33]。乙烷是由氧化应激引起的脂质过氧化的产物,在 FEV_1 预测值 < 60% 的支气管哮喘患者中,乙烷的含量高于 FEV_1 预测值 > 60% 的支气管哮喘患者,但在经过类固醇治疗的支气管哮喘患者中减少,提示乙烷可能是支气管哮喘治疗效果的潜在生物学标志物[34]。

3 电子鼻在支气管哮喘诊断方面的应用

3.1 电子鼻对支气管哮喘的诊断能力

支气管哮喘目前常用肺功能进行诊断,但对于儿童和老人,往往无法正确配合肺功能检查,这就迫切需要替代的诊断工具[35]。FARRAIA M 等[36]通过电子鼻分析呼出的 VOC 曲线,可用作筛查支气管哮喘症状控制不佳患者的一种快速、无创的评估工具。BRINKMAN P 等[37]通过一项前瞻性研究比较气相色谱-质谱和电子鼻技术测量呼出的 VOC 区分临床稳定型支气管哮喘和未控制型支气管哮喘诊断率分别为 77%、86%。临床新开发了一种基于金属氧化物半导体与肺活量测定法的电子鼻,使用该电子鼻技术,支气管哮喘的诊断准确率为 87%[38]。电子鼻可以在年龄配对的情况下区分支气管哮喘患者与非吸烟健康者(准确率分别为 100% 和 90%),但是并不能区分轻度和重度支气管哮喘[39]。FENS N 等[40]研究证实,呼出 VOC 谱在区分支气管哮喘和慢性阻塞性肺疾病中诊断率可分别达到 88%、83%。DRAGONIERI S 等[41]发现电子鼻可以区分过敏

性鼻炎患者是否伴随支气管哮喘。一项多中心横断面研究[42]发现,电子鼻可以鉴别支气管哮喘临床表型(嗜酸性粒细胞型、中性粒细胞型)。MEYER N 等[43]证实 VOC 可以区分健康和支气管哮喘受试者(敏感性为 100.0%,特异性为 91.1%),并通过聚类分析发现支气管哮喘患者临床症状相似但 VOC 谱不同,VOC 谱相似但临床特征不同的支气管哮喘簇。TENERO L 等[44]在一项横断面研究中发现 VOC 能够区分儿童支气管支气管哮喘是否得到控制。

3.2　电子鼻预测与监测能力

电子鼻对支气管哮喘诊断率与呼出气一氧化氮、痰中嗜酸性粒细胞接近,但通过 VOC 分析比一氧化氮、痰中嗜酸性粒细胞更能准确地预测类固醇反应,并对支气管哮喘患者后续治疗方案的制订具有一定的指导意义[45]。SMOLINSKA A 等[23]发现呼出的 VOC 可以鉴别暂时性喘息、健康、支气管哮喘儿童,能预测支气管哮喘的后续发展,并指导支气管哮喘的早期治疗。相关研究[46]对呼出的 VOC 进行分析发现,VOC 可以筛选出需要使用类固醇治疗的儿童支气管哮喘患者。LAMMERS A 等[47]通过一项前瞻性试验发现鼻病毒感染成人健康组和支气管哮喘组后,支气管哮喘组电子鼻波动迅速增加,表明电子鼻技术还可以用于监测病毒感染后的支气管哮喘发作,从而指导后续治疗。

4　总　结

电子鼻是临床新检测技术,可通过检测 VOC 来了解支气管哮喘患者的病情以及鼻炎患者是否伴随支气管哮喘,对于早期快速筛查支气管哮喘、评估类固醇治疗效果以及预测类固醇反应,是一种经济、快速和诊断率高的诊断方法。

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