Ministry of Higher Education
& Scientific Research
University of Diyala

Volatile Organic Compounds in Exhaled Breath is Related to Diseases

(Literature Review)

Submitted to the Council of the College of Medicine, Diyala University, In Partial Fulfillment of Requirements for the Bachelor Degree in medicine

By

Abdullah Hussein Naeem

Supervised by :

Prof. Dr. amer dawood

Apr 2022

Page number

Abstract :

Exhaled breath analysis is a promising non-invasive method for rapid diagnosis of diseases and contains volatile organic compounds (VOCs) that can differentiate diseased from healthy individuals. The aim of this study was to determine whether analysis of VOCs in exhaled breath can be used as a non-invasive monitoring tool for VAP.

Diagnostic methods are not only costly but are also invasive, thereby adding to people's stress. It has been appreciated for many decades that the analysis of trace volatile organic compounds (VOCs) in exhaled breath could potentially provide cheaper, rapid, and non-invasive screening procedures to diagnose and monitor the diseases of the lung. However, after decades of research associated with breath biomarker discovery, no breath VOC tests are clinically available.

It is therefore of interest to find a new method that allows fast, reliable, non-invasive VAP diagnosis. Using exhaled breath for disease diagnosis is a promising technique that may be able to fulfil these criteria.

Exhaled breath contains a multitude of volatile organic compounds (VOCs) originating from both exogenous and endogenous sources. Endogenous VOCs are produced by biological processes including oxidative stress and inflammation in the human body [7] [8] as well as by invading microorganisms [9] . Upon their production, VOCs are excreted into the blood after which they diffuse into the lungs where they are exhaled. Oxidative stress and inflammation induce alterations in the composition of VOCs excreted by the affected organ and thus the exhaled breath. Additionally, microorganisms themselves may produce specific compounds leading to different VOC profiles in exhaled breath.

2 - Diagnosis and Investigation of Diseases:

2-1 Ventilator-associated Pneumonia:

In reviewing the most recent studies to investigate the relationships between Volatile Organic Compounds in exhaled breath (VOCs) and Ventilator-associated Pneumonia. We found a significant and strong association between VOCs and ventilator-associated pneumonia (VAP)

In a modern study, VOC profiles were determined in exhaled breath of patients clinically suspected of VAP to discriminate patients with VAP from other critically ill ventilated patients. Of 100 patients, 32 were diagnosed with VAP by quantitative BAL analysis. This ratio was in line with earlier publications [10] [11]

The identified VOCs include 2-methylbutane, heptane, dodecane and tetradecane (alkanes), carane (hydrocarbon ring structure), ethanol and isopropyl alcohol (alcohols), acrolein and tetradecanal (aldehydes).

The remaining compounds were identified as acetone (ketone), ethylbenzene (aromatic hydrocarbon) and tetrahydrofuran (oxygen-containing heterocyclic compound)

2-3: Asthma:

In two recent studies [15][16], asthma diagnosis was tested using Gas Chromatography Mass Spectrometry (GC-MS) analysis. For example, Dallinga et al. [17] analyzed the breath samples of 63 asthmatic children and compared them to breath samples from 57 healthy controls (5 to 16 years old). Only eight VOCs were found to be needed to discriminate diseased from healthy children (with a sensitivity of 89% and a specificity of 95%) [17]. A set of eight compounds was used in another study to discriminate between healthy and asthmatic children; however just one of them, 2-octenal, was proposed as a certain marker of asthma, because the authors concluded that *the others may have other possible origins* [18]

This leads as to know that asthma also can be diagnosed using VOCs in exhaled breath.

2-4 Lung Cancer:

Different statistical approaches and machine learning algorithms have been used in order to classify the samples analyzed by GC-MS, coming from patients with lung cancer and from healthy controls [19,20,21,22,23]. In an attempt to get closer to a standardization of lung cancer diagnosis, Kischkel et al. applied five different algorithms to process their GC-MS data [48]. Their results concluded that exhaled VOCs are dependent on a multitude of factors, other than the investigated diseases (i.e., patients' medical history, environmental conditions) [24].

GC-MS profiles of potential markers of lung cancer were investigated in four different studies by a Polish group [25,26] . They carried out qualitative and quantitative measurements by sampling human breath using solid phase SPME and gas chromatography—time-of-flight mass spectrometry (GC–TOF/MS), obtaining possible biomarkers (19 to 32 VOCs) at the level of parts per billion, when more subtypes of lung cancer were investigated (SCLC, NSCLC, adenocarcinoma, planoepitheliale, squamous cell carcinoma). Sons et al [27] used GC-MS to investigate two types of lung cancer: adenocarcinoma and squamous cell carcinoma, covering all four stages of the disease, and proposed just two key volatile biomarkers that were found at significantly higher concentrations in the breath of the lung cancer patients compared to the controls:

1-butanol and 3-hydroxy-2-butanone (acetoin)

In the summary of the author's research he found that there is relationship between VOCs and lung cancer, but it is too early to depend on VOCs as a definitive diagnosis tool for this disease [28].

3- Conclusion:

In summary, the current epidemiological data, has demonstrated that it is possible to distinguish diseases according to a certain volatile organic compounds in exhaled breath

However, the current diagnostic tools in using exhaled VOCs are promising, it is simple, safe and non invasive but are far away of being used in private clinic and even in hospitals.

We still need to know more about types of VOCs and which type is caused by which disease.

4 – Key message:

Exhaled breath enables non-invasive diagnosis of different diseases. And thus, violet organic compounds are related to disease.

5- References:

1 - Garwood, P. World No Tobacco Day 2019: Don't Let Tobacco Take Your Breath Away; News Release; World Health Organization:Geneva, Switzerland, 2019.

2 - Wang, H.; Naghavi, M.; Allen, C.; Barber, R.M.; Carter, A.; Casey, D.C.; Charlson, F.J.; Chen, A.Z.; Coates, M.M.; Coggeshall, M.; et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: A systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016, 388, 1459–1544

3- Vos, T.; Allen, C.; Arora, M.; Barber, R.M.; Brown, A.; Carter, A.; Casey, D.C.; Charlson, F.J.; Chen, A.Z.; Coggeshall, M.; et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: A systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016, 388, 1545–1602

4 - Ego, A., Preiser, J. C. & Vincent, J. L. Impact of diagnostic criteria on the incidence of ventilator-associated pneumonia. Chest. 147(2), 347–355 (2015).

5 - Melsen et al. Attributable mortality of ventilator-associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies. Lancet Infect Dis. 13, 665–671 (2013).

6 - Fagon et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. Ann Internal Med. 132, 621–630 (2000).

7 - Miekisch, W., Schubert, J. K. & Noeldge-Schomburg, G. F. Diagnostic potential of breath analysis–focus on volatile organic compounds. Clin Chim Acta. 347, 25–39 (2004).