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POSTER ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Analysis of Volatile Organic Compounds in Exhaled Air in Patients with Sickle Cell Disease during Vaso-Occlusive Episodes

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Background: Sickle cell disease (SCD) is an inherited red blood cell disorder characterized by hemolytic anemia, inflammation and vaso-occlusion. Due to the process of vaso-occlusion patients with SCD experience unpredictable and painful vaso-occlusive episodes (VOE), causing stress and disruption of daily life. To date, we lack adequate markers to predict the development of a VOE before it occurs. In other conditions such as asthma, exhaled air analyses have shown to be of diagnostic value and may predict exacerbations. In the human body, metabolic processes generate volatile organic compounds, that are first released into the blood, and then exhaled by the lungs. As a result, exhaled air consists of several volatile, organic compounds that may reflect pathophysiological disease processes. As we presently lack urgently needed biomarkers to predict VOEs, the aim of this study was to identify distinctive volatile organic compounds in exhaled air (eVOC) during VOE in patients with SCD, that may serve as predictors of VOE when detected in low quantities as a VOE is evolving.
Methods: In this longitudinal, observational single center cohort study, patients with SCD aged 6 years or older were eligible if they were hospitalized for a VOE at Amsterdam University Medical Centers between October 2021 and March 2023. Following informed consent, an exhaled air sample was taken during hospitalization, and one at least 4 weeks after discharge from the hospital (steady state). Clinical data were collected from medical files including demographics, medical history, medication use and laboratory values during steady state, and during hospitalization for VOE. Patients were instructed not to eat, drink or take medication orally 2 hours prior to the measurements. Exhaled air samples were collected in Nalophan bags, and the eVOCs were transferred to stainless steel thermal desorption tubes filled with Tenax GR for analysis by gas chromatography-mass spectrometry. The Wilcoxon signed-rank test was used to test for differences in eVOCs between VOE and steady state. Significantly different eVOCs were tentatively identified by linking raw chromatograms to corresponding metabolites based on NIST-library matching. The significance level was set to 0.05. All analyses were performed using R Studio (version 1.3.1093) software.
Results: In total, 25 patients with SCD were included in this study, providing 71 exhaled air samples. The mean age at inclusion was 25.7 years (SD ±10.2). The majority of the participants had SCD genotype HbSS (60%). At time of exhaled air measurement during hospitalization, participants had symptoms for the median number of 1 day (IQR 0.5-3), and the median pain score was 6 out of 10 (IQR 3-7). A total of 58 different fragments could be identified between VOE and steady state (Wilcoxon rank $p < 0.05$), representing 26 unique eVOCs. The majority of these eVOCs were alkanes, alkenes, and esters. A representing compound for each chemical group is shown in Figure 1. In the majority of the patients, cyclohexane,1,2,4-trimethyl and propanoic acid, ethyl ester were upregulated during VOE, while 1-propene, 2-methyl- was downregulated.
Conclusion: This pilot study identified 26 compounds in exhaled air that differentiated VOE from steady state in patients with SCD. Thus, analysis of exhaled air could serve as a promising, non-invasive and patient-friendly biomarker to predict VOE in SCD. Further identification of the discriminative compounds in exhaled air could provide valuable insights into the metabolic processes during VOE.

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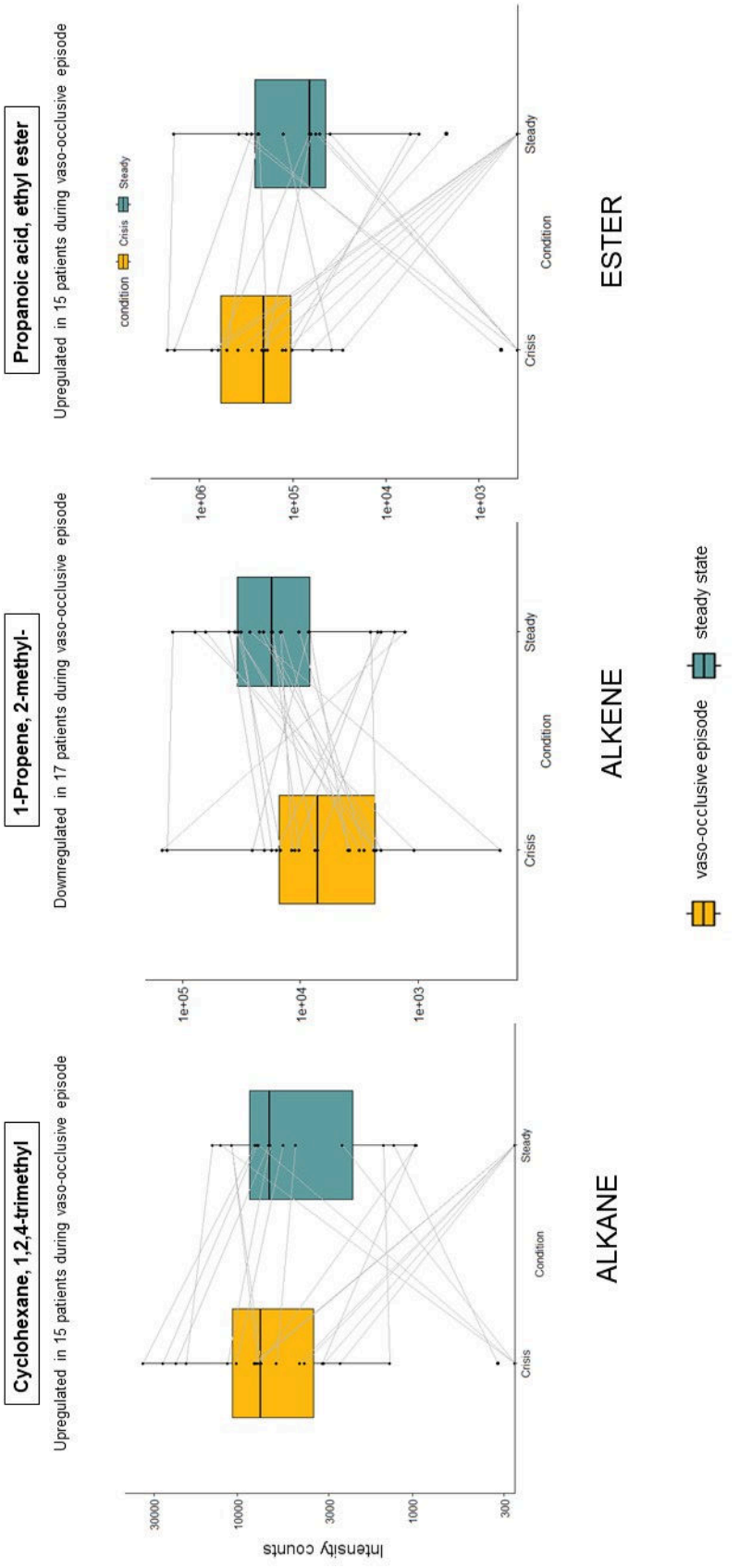

Figure 1