In Critical Care Settings New Breath-Based Test for Lower Respiratory Tract Infections Shows 100% Sensitivity

A recent study published investigates how breath-based analytics could be used to accurately and early diagnose lower respiratory tract infections (LRTIs).

Study

In the current study, the researchers constructed a sensor based on an established substrate with high chemical affinity for human neutrophil elastase (HNE), which was incorporated into a breath-based in vitro assay.

Thereafter, exhaled breath samples were collected from intubated ICU patients and health volunteers at the Johns Hopkins Hospital. After breath collection, proteases within the sample were captured, incubated with the substrate sensor, and subjected to spectrometric characterization of the HNE cleavage product and sensor using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).

How are LRTIs Diagnosed?

LRTIs, which include bronchitis, pneumonia, and bronchiolitis, are the fifth leading cause of death worldwide, with over 2.74 million deaths reported in 2015. Notably, this statistic does not include deaths attributed to tuberculosis or the coronavirus disease 2019 (COVID-19), both of which are lung infections associated with significant mortality.

LRTI diagnosis is often based on microbiological methods like culture, which are often time-consuming and labor-intensive processes. Molecular techniques like nucleic acid amplification testing (NAAT), the most notable of which is the polymerase chain reaction (PCR) assay, are highly sensitive methods that can provide results more rapidly than microbiological assays. However, these methods require pathogen materials to be present within the samples, which prevents clinicians from distinguishing between infection and colonization.

In an effort to overcome the limitations associated with conventional diagnostic techniques, researchers have investigated the clinical feasibility of measuring host response factors. Proteases, for example, are often dysregulated during LRTIs and, as a result, have been investigated for their diagnostic accuracy.

Accuracy of Protease Activity Detection

A ten- and nine-fold increase in HNE activity was observed in LRTI patients due to protease overactivation compared to patients without LRTIs and healthy controls, respectively. No

significant difference in HNE concentrations was observed between non-LRTI patients and healthy controls.

The accuracy of diagnosis with this platform was evaluated with a receiver operating curve (ROC), with an area under the curve (AUC) value of 0.987. With the threshold for HNE detection set to 0.2 picomolar (pM), the in vitro assay was 100% sensitive and 86.7% specific.

Measured HNE activity was strongly associated with protein concentration in the breath samples. This corroborates earlier research reporting that high HNE activity arises due to the exaggerated production of HNE proteins.

Several other proteases were identified in exhaled breath samples, thus indicating that other protease-based assays could be developed for LRTI diagnosis.

Advantages of the HNE Approach

Immunoassays quantify total proteases without distinguishing between those that are active or inactive. Comparatively, the in vitro assay developed in the current study measures the functional state of HNE, thus emphasizing its importance in diagnosing LRTIs. This approach can also allow clinicians to determine the stage and severity of the infection, as protease activity shifts rapidly with progressing inflammation.

As compared to earlier NE-based tests, the current assay does not involve the use of potentially toxic volatile reporter molecules and is not dependent on the amount of substrate administered to and absorbed by the host. The use of MALDI-TOF, a widely used clinical assay tool known for its practicality and user-friendliness, could potentially allow this to become a point-of-care diagnostic test for LRTI.

Conclusion

Our results demonstrate that this breath-based in vitro assay provides high diagnostic performance for LRTIs, suggesting that the technology may be useful in the near term for the accurate diagnosis of LRTIs."

The current study was conducted in a critical care setting; therefore, larger studies should be conducted across multiple settings and geographical locations to establish its validity as a screening and detection tool when LRTI is clinically suspected.

The study findings can also help create a protease profile based on which multiplexed protease panels can be developed. Multiplexed systems that rely on dozens of proteases would improve the generalizability and accuracy of the assay. Overall, this technology could significantly advance medical diagnostic capability in LRTIs.

Source:

https://www.news-medical.net/news/20240929/New-breath-based-test-for-lower-respiratory-tract-infections-shows-10025-sensitivity-in-critical-care-settings.aspx