ANALYSIS OF CHANGES IN SPUTUM RHEOLOGY AND COMPOSITION IN MECHANICALLY VENTILATED PATIENTS - AN OBSERVATIONAL STUDY

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Introduction

Invasive mechanical ventilation is one of the fundamental life sustaining treatments provided in critical care. Patients receiving invasive ventilation are at risk of increased sputum retention in the lower airways[1]. Sputum retention can result in complications such as infection, atelectasis, large airway obstruction and ventilatory failure. Despite the importance of sputum burden on patient progress and outcomes, there is a paucity of research in this area.

Multiple strategies are employed to reduce sputum burden, including humidified ventilator circuits, regular chest physiotherapy and suctioning. Mucoactive drugs such as carbocysteine are frequently used although there is little evidence of benefit. One reason for this is the lack of a surrogate marker for their efficacy. This study explored the feasibility of using the rheological properties of sputum, determined via oscillatory rheological experiments as a method of quantifying biophysical changes of sputum from ventilated patients. As an initial proof of concept, this observational study explored changes of sputum over time in ventilated patients. Additionally using infrared absorption studies, the molecular changes of sputum were also investigated.

Aims
This was an observational study in patients who required prolonged invasive ventilation. Our primary objectives were to:

1. Measure serial biophysical changes to sputum in patients who are mechanically ventilated
2. Identify changes to sputum molecular composition using Fourier Transform Infrared Spectroscopy (FTIR)
3. Attribute changes in biophysical properties of sputum to any molecular compositional changes by comparing rheological measures with FTIR findings

Method

A favourable ethical opinion was received from the Wales Research Ethics Committee in November 2023. Patients were enrolled if they were ventilated within an Intensive Care Unit within Cwm Taf Morgannwg University Health Board and an emergency deferred consent model was used. Sputum samples were collected daily for up to seven days of ventilation. Data was collected from participants' medical notes to inform factors that may alter sputum composition.
Samples were stored at -80°C until sent for measurement. Rheological analysis and Fourier transform infrared spectroscopy were performed on all samples. 21 patients were recruited into the study initially. 7 participants were then excluded for a number of reasons including transfer to another hospital, inability to confirm consent and failure to collect sputum.

Rheological Measurement

There are numerous contributors to the changes in properties of sputum in health and disease. However, the main points of interest in ventilated patients are the biophysical properties of sputum[2]. The study of rheology is the best fit for these biophysical properties. Rheology is concerned with viscosity, elasticity and flow points of materials. Overall, from rheological measurement we can provide a measure for the energy required to make sputum flow, helping us address the clinical question of how to more easily aspirate viscous sputum from ventilated patient's lungs.

Fourier Transform Infrared Spectroscopy (FTIR)

By measuring the absorption of infrared light within the sample across different infrared wavelengths, a molecular 'fingerprint' is produced of the sample. Using this fingerprint changes in sputum composition can be identified[3].
FTIR can potentially identify changes in the molecular structure of sputum resulting in biophysical changes. This will provide additional supporting evidence for the mechanistic influences of changes in sputum.

Results and Progress – So Far!

Analysis of results is ongoing. So far in the study, there have been several challenges. Firstly, a number of confounding variables have affected sputum samples. For example, the decision to start mucolytic therapy was at the discretion of the clinician, resulting in different use in different patients. Secondly, sputum sampling was inconsistent. For many of the patients in the study we were unable to collect enough sputum to reliably run the required testing. This has resulted in fewer data points per patient than intended.

Of the data collected and analysed so far, there are two findings discussed below:

1. FTIR fingerprint is different for patients intubated for a respiratory condition versus non-respiratory indication

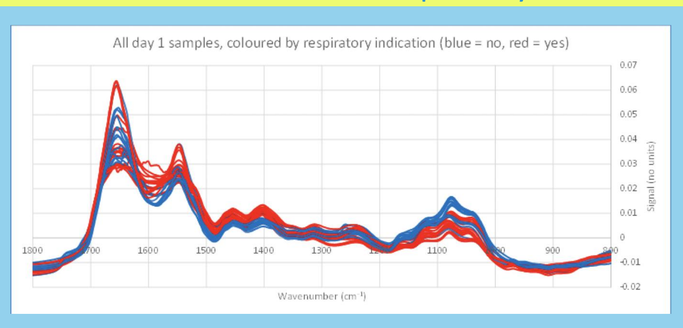

Figure 1: Different peaks in absorbance of infrared (y axis) between day 1 sputum samples (x axis) from patients intubated for a respiratory condition (red) and patients intubated for a non-respiratory condition (blue).

Figure 1 shows a difference in the molecular make-up of the sputum between the two groups. This suggests in future research, when exploring the use of empirical mucoactive drugs, the two groups of patients should be treated differently. The main difference in infrared absorption suggested a reduction in glycosylation for the respiratory patients. This, for example would suggest the need for further investigation of carbocysteine.

2. Rheological testing on sputum samples did not suggest a benefit to mucoactive drugs used within this patient cohort.

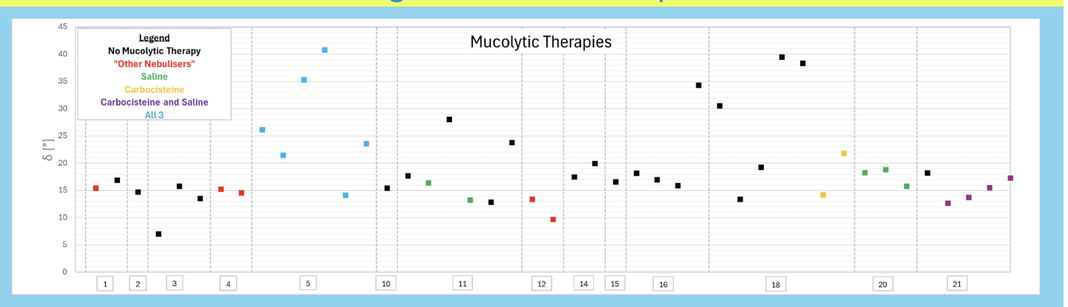

Figure 2: Phase angle δ (y axis) from rheological testing. Values nearing 90^0 suggest a more viscous-liquid substance and values near 0^0 suggest a more solid substance. The samples are colour coded as per the key on the top left. The x-axis shows individual patients who were in the study and each data point corresponds to a different day in the study.

From these preliminary rheological experiments, it could not be determined whether the administration of mucoactive drugs had any appreciable impact on the rheological properties of sputum. That is not to say that the drugs have no impact, only that defined trends could not be found from the small scope of this study.

Future prospects

As results have not been fully analysed, we have a number of questions remaining. These include:
•Is there a difference in infrared absorbance between samples with a high phase angle versus a low phase angle?
•Is there any change in infrared absorption between samples before and after starting carbocysteine?
•What do the peak infrared absorption changes represent as molecular changes within sputum?

References

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