CF sputum

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Background

Cystic fibrosis (CF) airway disease is associated with airway obstruction by secretions that are thought to be dehydrated. We hypothesized that CF sputum might become better hydrated and more easily cleared by cilia or cough after exposure to heated, fully humidified air.

Objectives

The objective of these experiments was to evaluate the effect of time and absolute humidity on CF sputum hydration, rheology, and transport properties.

Methods

Climate controlled chamber model

Humidifiers were modified to deliver inspiratory and expiratory humidity to CF sputa in a closed exposure chamber. Temperature and humidity were controlled as shown below.

	Time	Inspiratory Humidity	Expiratory Humidity
Air flow: 20 L/min	10 minutes	32 mgH$_2$O/L	44 mgH$_2$O/L
		44 mgH$_2$O/L	
	60 minutes	32 mgH$_2$O/L	
		44 mgH$_2$O/L	

Sputum

CF sputa were collected during pulmonary function testing from clinically stable patients.

Analysis of sputum properties

- **Interfacial tension**

Interfacial tension was measured at the sputum-air interface using the deNouy platinum-iridium ring technique.

- **Sputum hydration (% solids)**

Sputum hydration was determined by measuring the weight of sputa before and after lyophilisation to dryness for 24 hours.

- **Cough Transportability**

A simulated cough machine was used to measure the airflow-dependent clearability of sputa.

- **Dynamic rheology**

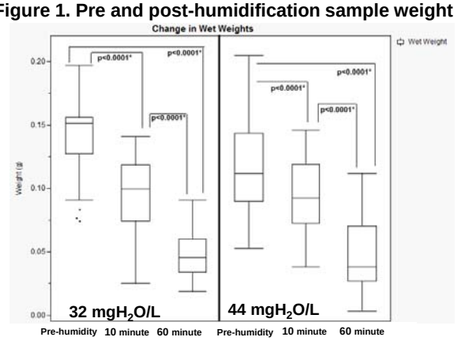
Dynamic viscoelasticity was measured using the AR1500ex rheometer with a custom made cone and parallel plate.

- **Mucociliary transportability**

A droplet of sputum was timed as the trailing edge moved across the extirpated ciliated palate of a leopard frog.

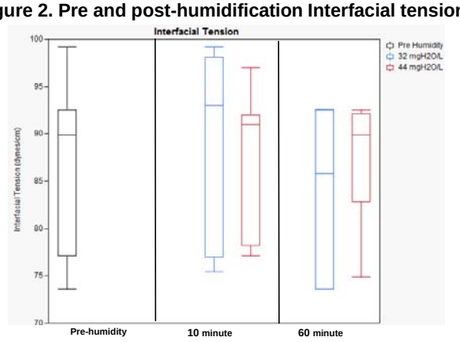
Results

Figure 1. Pre and post-humidification sample weight



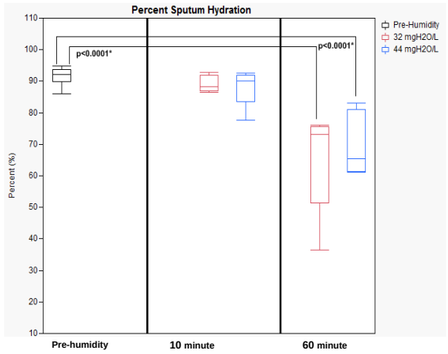
There was a *significant (p<0.0001) time-dependent decrease in sputum weight that was independent of absolute humidity

Figure 2. Pre and post-humidification Interfacial tension



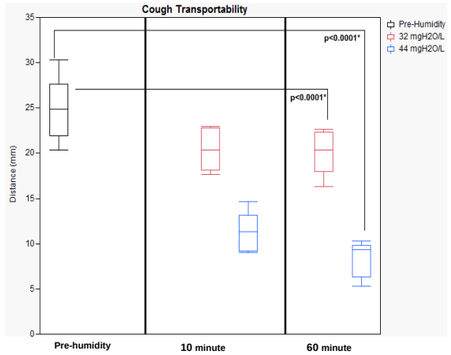
There was no significant change in interfacial tension after humidification exposure suggesting that the sample surface hydration remained stable for the full 60 minutes.

Figure 3. Pre and post-humidification sputum hydration



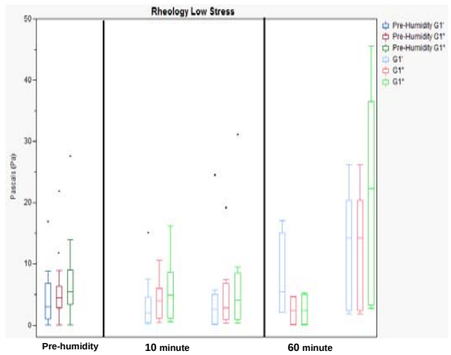
Exposure in the chamber for 60 minutes significantly decreased sputum hydration but this was independent of absolute humidity.

Figure 4. Pre and post-humidification cough transportability



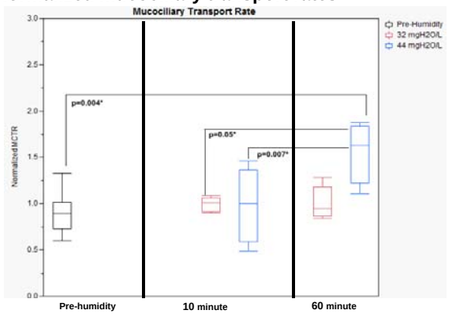
There was a time-dependent decrease in cough transportability that was independent of absolute humidity.

Figure5. Pre and post-humidification rheology, low stress (1 rad/sec)



There were no significant changes in dynamic viscosity, elasticity, or mechanical impedance.

Figure 6. Pre and post-humidification normalized mucociliary transport rates



After 60 minutes, sputum exposed to an absolute humidity of 44 mgH2O/L was transported about 70% faster than baseline MCTR but there was no observable difference after 10 minutes

Discussion

Although the lower respiratory airways are believed to be fully humidified in health, inhalation of dry air may exceed the natural airway humidification capacity and this may be more problematic in persons with CF where the airway secretions are believed to be intrinsically dehydrated. We simulated the bi-directional flow of normal ventilation across a flat exposure chamber with "inhalation" of fully humidified air at either 31° or 37° C and exhalation of humidified air at body temperature, 37° C at a rate of 12 breaths/minute.

Despite the attempt at humidification, the secretions dried out over 60 minutes with about 20% of the water loss in the first 10 minutes. This was independent of absolute humidity and this decreased cough transportability. The lack of changes in rheology and interfacial tension are interesting and the increase in MCTR at 60 minutes is unexplained. The drying may be due to lack of humidification and warming at the base (airway) side but, is probably unrelated to flow.

CONCLUSION

Despite attempting to model normal respiratory flow and humidification, CF sputum appeared to dehydrate in the exposure chamber over time and this was independent of absolute humidity in the airstream. Despite this, there were no significant changes in sputum rheology or interfacial (surface) tension. The decrease in cough transportability and the increase in mucociliary transportability at the higher humidity after 60 minutes is inexplicable given these other results.

References

1. Rubin BK, et al. Mucus, phlegm, and sputum in cystic fibrosis. *Respiratory Care* 54:726-32, 2009

2.Matsui, H. et al. Evidence for periciliary liquid layer depletion, not abnormal ion composition, in the pathogenesis of cystic fibrosis airways disease Cell 95: 1005-1015, 1998

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