Interplay between thermal transfers and degradation of the bronchial epithelium during exercise

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1. Introduction

Physiologists interested in the body's behaviour at exercise now recognize that the respiratory tract is not a limiting factor of endurance performance in healthy athletes. However, after several years of intense training, a majority of them develop various exercise-induced pathologies. The importance of the repetition of bronchial epithelium loss of integrity, consequent to a sustained high level of exercise ventilation, has been recently incriminated [1]. One physiological biomarker of the loss of epithelium integrity is the measurement of the concentration of club cells proteins 16kD (CC16) in urine or blood. An increase of this biomarker after exercise has been observed to be dependent on the intensity of exercise ventilation, leading to airway dehydration [1].

Interestingly, experimental [2] and modelling [3] works have shown that the bronchial epithelium and its mucus layer are a site of non-negligible evaporation during respiration. This evaporation (or condensation, especially during expiration [3]) is driven by a heat transfer between the air and the mucus layer, due to a temperature and humidity gradient at the air-tissue interface.

In previous works [3], we calculated that the influence of evaporation on the mucus water balance is non-negligible, especially in the first bronchial generations. We hypothesized that a water replenishment mechanism could act as a control process of this balance. Indeed, experimental works on epithelial cell cultures evaluated the magnitude of this mechanism of replenishment as about $0.3 \times 10^3 \,\mu l \, s^4 \, mm^2$ [4]. Interestingly, we calculated that, at rest, the average evaporation rate in the trachea is about $0.1 \times 10^3 \,\mu l \, s^4 \, mm^2$. By comparison of the orders of magnitude, we hypothesized that a large bronchial evaporation, namely during intense exercise, could perturbate the mucus water balance, possibly leading to a degradation of the bronchial epithelium.

2. Methods

Physiological data were obtained during a continuous 30-min exercise on a cycle ergometer in 16 healthy young subjects [5]. Heart rate ventilation, breathing frequency (FR) and tidal volume (TV) were measured continuously during the exercise, performed at an intensity of 70% of each subject maximum power output. Serum CC16 were measured at rest and 30 min post-exercise.

Numerical simulations are based on the model of Karamaoun et al. [2]. Transport equations of heat and water vapor are solved in an axisymmetric bronchial geometry, while taking the energy transfer at the air-mucus interface into account. Input parameters are the temperature (T_{in}) and relative humidity (RH_{in}) of the inspired air, as well as TV and FR, derived from correlations

established from the physiological data (see Table 1). Temperature profiles are calibrated on the data from McFadden et al. [2]. Tracheal RH values are predetermined based on literature data.

3. Results

Figure 1 presents the calculated values of the evaporation flux J_{exp} in the trachea at inspiration, depending on the simulation inspiration conditions summarized in Table 1.



Figure 1 Calculated average values of J_{exap} in the trachea for different values of the inspiration flow Q (in l/min). Blue dots are J_{exap} values computed for a constant RH=0.8 at the entrance of the trachea. Red dots are J_{exap} values computed for predetermined and variable RH values at the entrance of the trachea.

Q _{in} (l/min)	FR (s ⁻¹)	VT (l)	T _{in} (°C)	RH	$\mathbf{J}_{\mathrm{evap}}$	RH	$\mathbf{J}_{\mathrm{evap}}$
15	0.18	0.68	31.5	0.8	0.101	0.8	0.101
30	0.265	0.943	31	0.8	0.134	0.75	0.148
60	0.43	1.163	30	0.8	0.174	0.65	0.222
100	0.65	2.05	28.6	0.8	0.207	0.6	0.275

Horizontal grey line represents the theoretical replenishment threshold.

Table 1 Summarized inspiration conditions used for simulations.

4. Discussion and Perspectives

Results indicate that the evaporation is highly dependent on the ventilation rate and on the tracheal RH, which itself depends on the ventilation. Interestingly, the evaporation rate gets close to the replenishment rate at high ventilation, and could probably be superior at higher ventilation (and thus lower RH). This supports the hypothesis that bronchial evaporation could alter the mucus protective function, and thus the epithelium integrity, as measured by the serum CC16. Future works would have to focus on the automated determination of the RH value at the trachea entrance, depending on the inspiration conditions. This would allow to create a fully integrated computational tool to evaluate the evaporation in the bronchial tree, as a support of clinical data.

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6. References

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