Introduction

Muscle is the largest tissue in the human body and the size of muscle is significantly regulated by the protein myostatin. Chronic hypoxemia in vivo induces muscle atrophy in both healthy mountaineers and patients with COPD (figure 1). However, both COPD patients and mountaineers are difficult models to study due to several confounding factors. Chronic hypoxia in mice and COPD patients co-presents with elevated myostatin, suggestive of a causative role. We previously showed that 2 hours hypoxia (12 % O\textsubscript{2}) induced a decrease in muscle myostatin and a trend towards increased plasma myostatin concentration in healthy individuals. We therefore aimed to determine the effect of time in hypoxia, hypothesizing that an increase in hypoxic exposure time would result in a greater myostatin protein decrease in muscle and corresponding increase in plasma concentration.

Methods

Healthy males (N = 8, 30.3 years of age) visited the laboratory twice. Visit one consisted of screening and consent. In visit two, participants attended in a fasted state, immediately gave a muscle biopsy and venous plasma sample, then were placed in a normobaric hypoxic chamber (12 % O\textsubscript{2}) for 10 hours, with a second plasma sample taken after 2 hours. Immediately post hypoxic exposure a second biopsy and third plasma sample was taken (figure 2).

Results

| Table 1: Subject characteristics (N = 8). Expressed as mean (SD). |
|---------------------------------|----------------|----------------|----------------|----------------|
| Height (cm) | Weight (kg) | BMI (kg.m\textsuperscript{-2}) | FFM (%) | SaO\textsubscript{2} (%) |
| 180 | 78.99 | 24.22 | 85.1 | 97.9 |
| (0.70) | (9.83) | (1.79) | (7.19) | (1.1) |

Figure 3: SaO\textsubscript{2} is decreased during 10 hours 12 % O\textsubscript{2}. * indicates significance from baseline (p < 0.05).

Expression of the bioactive peptide in muscle tissue showed trends towards an increase after 10 hours hypoxia, with a 44 % increase over control values (p = 0.06, figure 4A). Conversely, the inhibitory propeptide did not increase (figure 4B).

Discussion

Here we show increased muscle myostatin peptide in response to 10 hours hypoxia in healthy males. Calculation of plasma myostatin responses is ongoing; we hypothesize an increase will be seen, representing muscle secreting myostatin in an endocrine manner. While here we show an increase in muscle myostatin after 10 hours hypoxia, our previous 2 hour experiment showed a decrease in muscle expression, suggesting a time-dependent effect. We propose a temporal response of muscle myostatin modelled below (figure 6). Lack of alteration in Akt signaling suggests hypoxic atrophy may occur via increases in degradation, not decreases in synthesis of muscle protein. This trend is similar in vivo in muscle from COPD patients. Our next study will examine the effect of dose (12 % vs 10 % O\textsubscript{2}) upon myostatin signalling. Increased myostatin expression in muscle may explain the witnessed atrophy seen in various hypoxic conditions such as COPD and mountaineering.

Figure 5: A) 10 hours of 12 % O\textsubscript{2} does not alter expression levels of phosphorylation of Akt (S473) or B) total Akt. Representative images shown.

Expression of pAkt (S473) / total Akt ratio did not change, nor did either individual component (Figure 5 A & B).

Figure 6: Proposed temporal changes in myostatin peptide in muscle in response to a hypoxic stimulus.