Introduction

Breathlessness and reduced exercise tolerance are well known symptoms of COPD. Both lead to less physical activity and worsen the disease, as physical inactivity is related to systemic inflammation in COPD. Its known from healthy sedentary subjects, that they respond with increased levels of plasma IL6, TNF-α and markers for oxidative stress following maximal cycling exercise. The basic idea for using the exercise challenge model was primarily the hypothesis, that an exercise challenge amplifies biomarker signals that are related to specific pathophysiological processes in COPD.

Methods

Twenty-three smokers with moderate COPD mean age 55 (46 to 68) y, FEV1 %pred. 66.1 ± 7.2) and 23 gender- and age-matched healthy smokers (54 (42 to 65) y, FEV1 %pred. 112.5 ± 14.1) underwent up to 30 min constant load exercise (75 % of max. work load maintainable for at least 30 sec) on 2 occasions separated by 4 weeks (second challenge n=20/19). Serum samples were obtained before, 5 min after the start, at the end of exercise (due to exhaustion), and after 20 min of rest.

Results

Smokers with COPD showed significantly higher concentrations of serum IL6, CRP, soluble (s)VCAM1, sICAM1, and VWF before exercise compared to smoking controls, while no difference in MPO was observed between groups. The median exercise time until exhaustion was 10.5 and 9.5 min in COPD and 19.0 and 24.0 min in healthy smokers. Healthy smokers showed a significantly greater increase (% end compared to pre-exercise) in serum IL6 (p=0.01) and CRP (p=0.05) and a larger decline (p=0.03) in serum MPO. A similar result was obtained when the % change per minute was compared between groups. We observed a significant correlation between serum concentrations of IL6 and CRP before, during, and at the end of exercise (all subjects, r = 0.49, 0.53, 0.45, at least p<0.003). We found a very good reproducibility for the exercise capacity (ICC=0.86, r=0.87), moderate values for the change in IL6 concentration relative to baseline (0.53, 0.54), and a fairly good repeatability for the absolute serum concentration of MPO (0.72, 0.72) and VWF (0.61, 0.60) at the end of exercise.

Fig 1: Study design

Fig 2: Individual time points until the exercise challenge was terminated. Left: smokers with COPD, right: healthy smokers. The y-axis displays the absolute time point from the start of exercise.

Fig 3: Time course for the serum concentrations of IL6, MPO, CRP, sVCAM1, sICAM1, VWF and LTB4 separately for smokers with (open symbols) and smokers without COPD (closed symbols). The results of visit 1 is displayed on the left (n=23/23), the results of the repeated visit (28±6 days later, n=20/19) on the right. The blood was drawn before (displayed at 0 min), after 5 min of exercise (displayed at 5 min), at the time of exhaustion or a maximum duration of 30 min exercise, and following a period of 20 min of rest (both displayed at the median duration for each group).

Conclusion

A constant load exercise changes the serum concentration of inflammatory and endothelial function markers. Differences between groups were observed for IL6 and MPO. The response to exercise was repeatable for most markers, which is required for the use of this model in pharmacological intervention studies.

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