CORRESPONDENCE

Does theophylline really improve acute mountain sickness?

To the Editor:

Fischer *et al.* [1] report that theophylline improves acute mountain sickness (AMS). This is of high interest, as there may be an adenosine-sensitive mechanism of hypoxic respiratory control and therapy, with a specific adenosine antagonist like theophylline, which may potentially influence respiratory adaptation to hypoxia. However, recent studies in human and animal experiments, which sought to evaluate the influence of theophylline on hypoxic ventilatory response (HVR) to normobaric hypoxia in laboratory conditions, gave no evidence for an influence of theophylline on chemoreceptor responsiveness [2]. To verify the authors' conclusions, we evaluated the effect of 300 mg theophylline on respiration in hypobaric hypoxia at moderate altitude.

We performed a randomized, double-blind, placebo-controlled, crossover trial in eight healthy nonacclimatized men aged 24–42. Participants were randomized to 300 mg oral nonretarded theophylline or placebo immediately after transport to 2,600 m altitude by cable car. P_{a,O_2} and P_{a,CO_2} were analysed before and after 2 h rest after medication [3]. The procedure was repeated after 1 week in the other test condition. Differences in blood gas concentrations before and after medication were analysed by paired t-tests.

Results are shown in table 1. Mean (95% confidence interval) difference in P_{a,O_2} between test conditions was 0.88 mmHg (0.57–2.32 mmHg, $p=0.195$), and 0.55 mmHg (0.91–1.91 mmHg, $p=0.430$) for P_{a,CO_2} .

P_{a,O_2} did not change in either test condition during the observation period and P_{a,CO_2} decreased due to HVR, but theophylline did not enhance this decrease. Although we did not measure respiration directly, our data indicate that theophylline does not influence acute ventilatory adaptation at moderate altitude.

We cannot comment on a further potential beneficial effect of theophylline on AMS from our own data, because we, like the authors, did not evaluate the effect of theophylline in AMS-patients, but in a small group

of healthy volunteers. AMS incidence at 3,500 m altitude is about 30% (and only 8% at our investigation altitude), so we can reckon on very few AMS patients in this trial [4, 5]. The subjects in the reported field experiment had only low AMS scores and therefore suffered very mild to moderate signs and symptoms of AMS.

Although these scores may be improved by theophylline, we do not think that the authors conclusions are based on very convincing evidence.

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Table 1. – P_{a,O_2} and P_{a,CO_2} in mmHg (mean $\pm$ SD) in eight subjects at 2,600 m altitude before and 2 h after intake of 300 mg theophylline or placebo

	P_{a,O_2} 0 min	P_{a,CO_2} 0 min	P_{a,O_2} 120 min	P_{a,CO_2} 120 min
Theophylline	68.63 $\pm$ 4.78	35.25 $\pm$ 1.28	68.88 $\pm$ 4.58	33.13 $\pm$ 1.46
Placebo	68.75 $\pm$ 3.77	35.63 $\pm$ 1.19	69.75 $\pm$ 3.28	34.00 $\pm$ 0.53