Effects of acetazolamide and temazepam on sleep at high altitude (Abstract)

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During an expedition to the Himalayas the sleep of six trekkers was recorded electroencephalographically between 1000 and 1800 m, 2700 and 3600 m and 4100 and 4846 m. Three of the subjects ingested acetazolamide 500 mg/day during the ascent and the other three ingested placebo.

There was some evidence that the subjects adapted to the relatively uncomfortable sleeping conditions during the initial part of the ascent. However at 4100 to 4846 m, compared with 2700 to 3600 m, there was difficulty in falling asleep, (mean sleep onset latencies 11.9 and 38.8 minutes respectively), marked reduction in sleep duration in the first 6 hours of the night (314.5 and 263.8 minutes respectively) and reduced sleep efficiency index (0.87 and 0.70 respectively). When the sleep of the subjects who ingested acetazolamide was compared with the sleep of placebo subjects over the three altitudes, wakefulness and drowsy sleep were reduced (91.7 and 56.6 minutes respectively), sleep

duration in the first 6 hours was increased (230.6 and 309.0 minutes respectively) and sleep efficiency was improved (0.75 and 0.83 respectively). All comparisons were significant at the 5% level.

Temazepam was also used between 4100 and 4846 m and led to less wakefulness and drowsy sleep (136.1 and 53.8 minutes respectively) and increased sleep duration in the first 6 hours (230.9 and 290.0 minutes respectively). There were no prolonged sleep latencies in subjects who used temazepam, and in subjects who used both acetazolamide and temazepam sleep efficiency was at sea level values. There was improved sleep with acetazolamide and difficulties in falling asleep were avoided with temazepam, while acetazolamide and temazepam together appeared to sustain sleep. These studies would suggest that both acetazolamide and temazepam have a useful role in the management of altitude insomnia.

Effects of almitrine and acetazolamide on ventilation (Abstract)

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Periodic breathing and hypoxaemia occur frequently during sleep at high altitude and are diminished by acetazolamide. Almitrine is a ventilatory stimulant which may prevent sleep disturbance at high altitude. In a double blind and randomized fashion the effect of almitrine, acetazolamide and placebo on the control of ventilation and sleep was studied in five healthy climbers in a heated laboratory on Mount McKinley (4400 m). Poikilocapnic hypoxic ventilatory response (HVR) and the ventilatory response to oxygen breath-

ing was measured during the waking state. Arterial oxygen saturation and pattern of breathing were measured during 3 hour sleep studies. HVR ($-VE/-SaO_2$) was augmented with almitrine (-0.9 ± 1.0) compared with placebo and acetazolamide (both -0.6 ± 0.5). Oxygen breathing decreased ventilation more with almitrine ($-19.0 \pm 27.0\%$) and placebo ($-21.1 \pm 18.0\%$) than with acetazolamide ($-2.5 \pm 10.0\%$) ($P < 0.05$). Almitrine and acetazolamide both increased arterial oxygen saturation during sleep although

almitrine caused increased periodic breathing. This might be expected if it augments peripheral chemoreceptor response. Acetazolamide decreases periodic breathing which is consistent with its action at the central chemoreceptors. Acetazolamide is a superior drug for elimination of periodic breathing and severe hypoxaemia during sleep at high altitude.

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Changes in body weight, fat and muscle mass at high altitude and the effect of acetazolamide (Abstract)

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Body weight changes were studied during walking ascent and descent to 4846 m in 19 subjects, ten of whom were taking acetazolamide. Body fat was assessed using fat fold calipers at three skin locations. Muscle thickness was measured in both arms and legs using a portable linear array ultrasound unit. At high altitude weight was maintained in subjects on acetazolamide but tended to fall in subjects on placebo. During descent there was marked weight loss in both groups; mean loss 3.2 kg in subjects on acetazolamide and 4.1 kg in those on placebo. Body fat tended to fall but only by 0.12 kg and 0.4 kg in the two groups respectively. Muscle thickness in the thigh

was significantly reduced at high altitude by 3.4 mm (8.5%) in the acetazolamide group and 4.9 mm (12.9%) in the placebo group. Loss of muscle in the upper arm was less, but the difference between the groups was greater. This muscle wasting could account for the greater part of the overall weight loss. At high altitude calorie intake was surprisingly low at approximately 2000 K cal daily but with adequate protein (73 g/day). It remains to be shown whether muscle loss can be prevented by dietary manipulation but a significant beneficial effect of acetazolamide has been demonstrated.

Reference

Bradwell, A.R., Dykes, P.W., Coote, J.H. *et al.* Effect of acetazolamide on exercise performance and muscle mass at high altitude. *Lancet* 1986, *ii*; 1001–1005.