Jet Lag

ABSTRACTS

Arendt J., 1997. Treatment of circadian rhythm disorders - Melatonin.
Benoit O., 1996. Circadian sleep-wake disorders.
Bjorvatn B., 1997. [Phototherapy of jet lag, night work and sleep disorders]
Christiansen AL., 2001. [Jet leg].
Comperatore CA., 1996. Melatonin efficacy in aviation missions requiring rapid deployment and night operations.
Croughs RJM.., 1996. Melatonin and jet lag
Herxheimer A., 2002. Melatonin for the prevention and treatment of jet lag.
Juneja LR., 1999. L-theanine-a unique amino acid of green tea and its relaxation effect in humans.
Kakuda T, 2000. Inhibiting effects of theanine on caffeine stimulation evaluated by EEG in the rat.
Lagarde D., 1997. [Role of the pharmacopoeia in the prevention of jet-lag].
Skene D.J., 1996. Use of melatonin in circadian rhythm disorders and following phase shifts.
Waterhouse J., 1997. Travel and body clock disturbances.
Wright JE., 1983. Effects of travel across time zones (jet-lag) on exercise capacity and performance.

Treatment of circadian rhythm disorders - Melatonin

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Chronobiology International (USA), 1997, 14/2 (185-204)

Melatonin has clear acute and delayed effects on sleep and circadian rhythms. Decrements in core temperature and alertness have been found at different times of day following low pharmacological and physiological doses of melatonin. When correctly timed, melatonin induces both phase advances and phase delays of the circadian system in humans. When timed to advance, the decrement in temperature and alertness and the degree of shift are closely related to dose. In both stimulation and field studies, correctly timed melatonin can alleviate some of the problems of shiftwork and jet lag, notably enhancing sleep and alertness and hastening adaptation of rhythms to the imposed schedule. Performance effects and changes in sleep architecture need to be fully evaluated. The optimization of
dose and formulation is also an area that requires furter work. Whether or not recently developed melatonin analogs will prove more or less useful than melatonin in adapting to phase shift remains to be seen. If incorrectly timed, melatonin has the potential to induce deleterious effects. While short-term studies indicate that it has very low toxicity, there are no long-term safety data. All of the studies reported here concern healthy adult volunteers and the use of a preparation licensed for human experimental use and available on a named
patient basis on prescription. There are not data on uncontrolled preparations available over the counter in some countries. Its effects in pregnancy, interaction with other medications, and many other considerations remain to be addressed. Thus, while melatonin is useful in well-controlled conditions, the indiscriminate use of unlicensed preparations is not advisable.

Circadian sleep-wake disorders

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Revue du Praticien (France), 1996, 46/20 (2442-2447)

The circadian system is synchronized on 24-hour by the light-dark synchronizer and by the social time cue. The circadian rhythm sleep disorders share a common underlying chronobiological basis. These disorders may be due to either jet-lag, shift-work or to lesions of the peripheral visual pathway. The delayed sleep phase syndrome, the advanced sleep phase syndrome, the non 24-hour syndrome as well as the irregular sleep-wake patterns are described. Therapeutic approaches, in particular with melatonin and (or) bright light, are presented.

[Phototherapy of jet lag, night work and sleep disorders].

[Article in Norwegian]
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Tidsskr Nor Laegeforen 1997 Jun 30;117(17):2489-92

Jet lag, complaints associated with night work, and certain sleep disorders may be caused by misalignment between the endogenous circadian rhythm and the sleep/wake cycle. The authors discuss how light influences and regulates the circadian rhythm. The endogenous circadian rhythm is generated by the suprachiasmatic nucleus, and the effect of light is mediated to this nucleus directly via the retinohypothalamic tract. The effect is dependent on the timing of the light exposure relative to the nadir of the endogenous rhythm, which
usually is located at about 5:00 AM. Exposure to bright light before nadir induces a phase delay, whereas a phase advance is obtained with exposure to light after nadir. The paper describes how bright light treatment can be used to reduce the effects of jet lag and of night work, sleep phase disturbances and early morning awakenings. Melatonin administration is an alternative treatment for the same type of disorders, and is also discussed in the article.

[Jet leg]. [Article in Danish]

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Ugeskr Laeger 2001 Jan 8;163(2):149-55

The aim of the paper is to give a review of jet-lag (Time Zone Change Syndrome) with regard to aetiology, symptomatology and pathophysiology. Furthermore we give recommendations on treatment of jet-lag. The literature has focused intensely on the potential benefit of phototherapy and/or use of melatonin as treatment modalities for jet-lag. Both phototherapy and melatonin have the capability to accelerate reentrainment of the circadian rhythm after flights across multiple time zones, thereby reducing jet-lag. We stress the importance of correct timing of phototherapy and use of melatonin and suggest that the traveller adapts to the "social" rhythm at the flight destination as well.

Melatonin efficacy in aviation missions requiring rapid deployment and night operations

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Aviation Space and Environmental Medicine (USA), 1996, 67/6 (520-524)

Background: The rapid deployment of Army aviation personnel across time zones, combined with missions beginning immediately upon arrival, results in desynchronization of physiological and cognitive performance rhythms. Implementation of effective countermeasures enhances safely, health, well- being, and mission completion. The naturally occurring hormone melatonin has been suggested as an effective countermeasure for jet lag and shift lag because of its influence on the human circadian timing system and its hypnotic properties.

Melatonin and jet lag

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Netherlands Journal of Medicine (Netherlands), 1996, 49/4 (164-166)

Jet lag is an ill-defined phenomenon resulting from rapid transmeridional flight and is considered to be due to desynchronization of circadian rhythms. The role of the pineal gland hormone, melatonin, in the synchronization of biological rhythms has raised interest in its use to alleviate jet lag. Indeed, recent studies support the use of this well-tolerated drug as a remedy for jet lag on long-haul flights.

Melatonin for the prevention and treatment of jet lag.

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Cochrane Database Syst Rev. 2002;(2):CD001520.

BACKGROUND: : Jet-lag commonly affects air travellers who cross several time zones. It results from the body's internal rhythms being out of step with the day-night cycle at the destination. Melatonin is a pineal hormone that plays a central part in regulating bodily rhythms and has been used as a drug to re-align them with the outside world.

OBJECTIVES: : To assess the effectiveness of oral melatonin taken in different dosage regimens for alleviating jet-lag after air travel across several time zones.

SEARCH STRATEGY: : We searched the Cochrane Controlled Trials Register, MEDLINE, EMBASE, PsychLit and Science Citation Index electronically, and the journals 'Aviation, Space and Environmental Medicine' and 'Sleep' by hand. We searched citation lists of relevant studies for other relevant trials. We asked principal authors of relevant studies to tell us about unpublished trials. Reports of adverse events linked to melatonin use outside randomised trials were searched for systematically in 'Side Effects of Drugs' (SED) and SED Annuals, 'Reactions Weekly', MEDLINE, and the adverse drug reactions databases of the WHO Uppsala Monitoring Centre (UMC) and the US Food & Drug Administration.

SELECTION CRITERIA: : Randomised trials in airline passengers, airline staff or military personnel given oral melatonin, compared with placebo or other medication. Outcome measures should consist of subjective rating of jet-lag or related components, such as subjective wellbeing, daytime tiredness, onset and quality of sleep, psychological functioning, duration of return to normal, or indicators of circadian rhythms.

DATA COLLECTION AND ANALYSIS: : Ten trials met the inclusion criteria. All compared melatonin with placebo; one in addition compared it with a hypnotic, zolpidem. Nine of the trials were of adequate quality to contribute to the assessment, one had a design fault and could not be used in the assessment. Reports of adverse events outside trials were found through MEDLINE, 'Reactions Weekly', and in the WHO UMC database.

MAIN RESULTS: : Nine of the ten trials found that melatonin, taken close to the target bedtime at the destination (10pm to midnight), decreased jet-lag from flights crossing five or more time zones. Daily doses of melatonin between 0.5 and 5mg are similarly effective, except that people fall asleep faster and sleep better after 5mg than 0.5mg. Doses above 5mg appear to be no more effective. The relative ineffectiveness of 2mg slow-release melatonin suggests that a short-lived higher peak concentration of melatonin works better. Based on the review, the number needed to treat (NNT) is 2. The benefit is likely to be greater the more time zones are crossed, and less for westward flights. The timing of the melatonin dose is important: if it is taken at the wrong time, early in the day, it is liable to cause sleepiness and delay adaptation to local time. The incidence of other side effects is low. Case reports suggest that people with epilepsy, and patients taking warfarin may come to harm from melatonin.

REVIEWER'S CONCLUSIONS: : Melatonin is remarkably effective in preventing or reducing jet-lag, and occasional short-term use appears to be safe. It should be recommended to adult travellers flying across five or more time zones, particularly in an easterly direction, and especially if they have experienced jet-lag on previous journeys. Travellers crossing 2-4 time zones can also use it if need be. The pharmacology and toxicology of melatonin needs systematic study, and routine pharmaceutical quality control of melatonin products must be established. The effects of melatonin in people with epilepsy, and a possible interaction with warfarin, need investigation.

L-theanine?a unique amino acid of green tea and its relaxation effect in humans.

Juneja, L.R. et al.

Trends Food Sci. Technol. 1999; 10: 199-204.

No abstract available.

Inhibiting effects of theanine on caffeine stimulation evaluated by EEG in the rat.

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Biosci Biotechnol Biochem. 2000 Feb;64(2):287-93.

In this study, the inhibiting action of theanine on the excitation by caffeine at the concentration regularly associated with drinking tea was investigated using electroencephalography (EEG) in rats. First, the stimulatory action by caffeine i.v. administration at a level higher than 5 micromol/kg (0.970 mg/kg) b.w. was shown by means of brain wave analysis, and this level was suggested as

the minimum dose of caffeine as a stimulant. Next, the stimulatory effects of caffeine were inhibited by an i.v. administration of theanine at a level higher than 5 micromol/kg (0.781 mg/kg) b.w., and the results suggested that theanine has an antagonistic effect on caffeine's stimulatory action at an almost equivalent molar concentration. On the other hand, the excitatory effects were shown in the rat i.v. administered 1 and 2 micromol/kg (0.174 and 0.348 mg/kg) b.w. of theanine alone. These results suggested two effects of theanine, depending on its concentration.

[Role of the pharmacopoeia in the prevention of jet-lag]. [Article in French]

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Bull Soc Pathol Exot 1997;90(4):291-2

Long-haul flights allow rapid crossing of times zones. When four time zones are crossed, the transmeridian flight induce jet-lag syndrome. Jet-lag is essentially composed of digestive and behavioural disturbances (insomnia and/or drowsiness). It is due to an immediate conflict between external time cues, which have been phase-advanced or phase-delayed by eastward or westward flight, respectively, and the endogenous clock. This conflict induces a desynchronization of the biological rhythms. Different counter-measures could be advised, but the most used is the pharmacological one. Hypnotics like benzodiazepines, cyclopyrones or imidazopyridines induce a recovery sleep but could also induce secondary effects in case of chronic use. Melatonin secreted by pineal gland needs more studies before a safety use for jet-lag treatment. Psychostimulants are able to induce a prolonged wakefulness. But amphetamine-like substances have to be forbidden because of the importance of side effects. New researches are studying a new galenic form of caffeine: the time release caffeine, which permits to induce a long and good quality wakefulness.

Use of melatonin in circadian rhythm disorders and following phase shifts

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Acta Neurobiologiae Experimentalis (Poland), 1996, 56/1 (359-362)

Following abrupt phase shifts (real or simulated time zone changes, night shift work) there is desynchronisation between the internal circadian rhythms (including melatonin) and the external environment with consequent disturbances in sleep, mood and performance. In humans the pineal hormone melatonin has phase-shifting and resynchronising properties with regard to a number of circadian rhythms. Suitably timed melatonin administration hastened adaptation to phase shift and significantly improved self-rated jet lag in large numbers of time zone travellers. Preliminary results in night shift workers showed improved daytime sleep and night-time alertness. In simulated experiments, appropriately timed melatonin improved subjective sleep, alertness and performance and facilitated the readaptation of the melatonin rhythm following a rapid 9 h advance phase shift. Melatonin has also been assessed in circadian rhythm disorders with disturbed sleep (blindness and delayed sleep phase insomnia). Compared with placebo, melatonin significantly improved sleep and synchronised the sleep wake cycle in some blind subjects. Melatonin treatment significantly advanced the sleep onset time in delayed sleep phase insomnia. Taken together these findings suggest that melatonin is of benefit in facilitating adaptation to forced phase shifts and in conditions of circadian rhythm disturbance.

Travel and body clock disturbances.

Waterhouse, J. et al.

Sports Exer. Injury 1997; 3(1): 9-14.

No abstract available.

Effects of travel across time zones (jet-lag) on exercise capacity and performance.

Wright JE, Vogel JA, Sampson JB, Knapik JJ, Patton JF, Daniels WL.

Aviat Space Environ Med. 1983 Feb;54(2):132-7.

Eighty-one healthy male soldiers, aged 18-34, were studied for 5 d before and 5 d after an eastward deployment across six time zones to determine the effects of translocation on exercise capacity and performance. Fatigue, weakness, headache, sleepiness, irritability, and other commonly reported symptoms occurred in the majority of subjects. Most, but not all, of the symptoms were

diminished or absent by the fifth day following the translocation. Cardiorespiratory function and perception of effort during both submaximal and maximal treadmill exercise were unaffected. Isometric strength of the upper torso, legs, and trunk extensor muscles also was not changed. Dynamic strength and endurance of elbow flexors declined significantly. Dynamic knee extensor strength and endurance scores exhibited a progressive decrement prior to translocation and were inconsistent suggesting that the stress of repetitive testing outweighed any jet-lag effects on performance capacity. Performance times for a 270 m sprint were increased for the first 4 d following translocation as were times for a 2.8 km run on the second and third days and for a 110 m lift and carry on the third day after deployment. Times for a 6.5 m rope climb did not change. These findings indicate that certain symptoms and physiological capacities are affected as a result of multiple time zone translocation. However, the specific mechanisms involved, the factors influencing the magnitude of any physiological alterations, and the ultimate impact of these capacity changes on actual physical performance remain to be clarified.