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## ABSTRACTS

### Melatonin Sleep Studies

#### TREATMENT OF DELAYED SLEEP PHASE SYNDROME

Delayed sleep phase syndrome (DSPS) is a common but little reported cause of severe insomnia. Affected individuals complain of difficulty falling asleep and difficulty awaking at socially acceptable hours. It results from a dysregulation of the circadian sleep-wake cycle. DSPS presents in clinically heterogeneous ways as modulated by motivation, psychopathology, drug status, and treatment compliance factors. Patients respond variably to the range of possible treatments. Bright light treatment potentially corrects the circadian abnormality of DSPS. Other treatments reported to relieve some DSPS patients include schedule shifts, drugs, and vitamin and hormone treatments. The safety and efficacy of light treatment have not been conventionally defined, but available information suggests that it is ophthalmologically safe. At present, DSPS must be managed empirically by various methods. (69 Refs.)

*Gen Hosp Psychiatry (U S.) Sep 1995, 17 (5) p335-45*

## MELATONIN REPLACEMENT THERAPY OF ELDERLY INSOMNIACS

Changes in sleep-wake patterns are among the hallmarks of biological aging. Previously, we reported that impaired melatonin secretion is associated with sleep disorders in old age. In this study we investigated the effects of melatonin replacement therapy on melatonin-deficient elderly insomniacs. The study comprised a running-in, no-treatment period and four experimental periods. During the second, third and fourth periods, subjects were administered tablets for 7 consecutive days, 2 hours before desired bedtime. The tablets were either 2 mg melatonin administered as sustained-release or fast-release formulations, or an identical-looking placebo. The fifth period, which concluded the study, was a 2-month period of daily administration of 1 mg sustained-release melatonin 2 hours before desired bedtime. During each of these five experimental periods, sleep-wake patterns were monitored by wrist-worn actigraphs. Analysis of the first three 1-week periods revealed that a 1-week treatment with 2 mg sustained-release melatonin was effective for sleep maintenance (i.e. sleep efficiency and activity level) of elderly insomniacs, while sleep initiation was improved by the fast-release melatonin treatment. Sleep maintenance and initiation were further improved following the 2-month 1-mg sustained-release melatonin treatment, indicating that tolerance had not developed. After cessation of treatment sleep quality deteriorated. Our findings suggest that for melatonin-deficient elderly insomniacs, melatonin replacement therapy may be beneficial in the initiation and maintenance of sleep.

*Sleep (UNITED STATES) Sep 1995, 18 (7) p598-603,*

## IMPROVEMENT OF SLEEP QUALITY IN ELDERLY PEOPLE BY CONTROLLED-RELEASE MELATONIN

Melatonin, produced by the pineal gland at night, has a role in regulation of the sleep-wake cycle. Among elderly people, even those who are healthy, the frequency of sleep disorders is high and there is an association with impairment of melatonin production. We investigated the effect of a controlled-release formulation of melatonin on sleep quality in 12 elderly subjects (aged 76 [SD 8] years) who were receiving various medications for chronic illnesses and who complained of insomnia. In all 12 subjects the peak excretion of the main melatonin metabolite 6-sulphatoxymelatonin during the night was lower than normal and/or delayed in comparison with non-insomniac elderly people. In a randomised, double-blind, crossover study the subjects were treated for 3 weeks with 2 mg per night of controlled-release melatonin and for 3 weeks with placebo, with a week's washout period. Sleep quality was objectively monitored by wrist actigraphy. Sleep efficiency was significantly greater after melatonin than after placebo (83[SE 4] vs 75[3]%,  $p < 0.001$ ) and wake time after sleep onset was significantly shorter (49 [14] vs 73 [13] mm,  $p < 0.001$ ). Sleep latency decreased, but not significantly (19 [5] vs 33 [7] mm,  $p = 0.088$ ). Total sleep time was not affected. The only adverse effects reported were two cases of pruritus, one during melatonin and one during placebo treatment: both resolved spontaneously. Melatonin deficiency may have an important role in the high frequency of insomnia among elderly people. Controlled-release melatonin replacement therapy effectively improves sleep quality in this population.

*Lancet (ENGLAND) Aug 26 1995, 346 (8974) p541-4,*

## MELATONIN IMPROVES EVENING NAPPING

Twelve young adults were treated with either melatonin, 3 mg or 6 mg, or placebo, at two different times before an early evening nap (18.00-20.00 h) according to a balanced double-blind Latin square design. Polysomnographic monitoring revealed that both dosages of melatonin significantly shortened sleep latency and increased total sleep time in comparison to placebo, irrespective of the time of administration. Subjects also tended to assess their sleep as 'deeper' after melatonin treatment. Based on previous data and the present results, it was concluded that exogenous melatonin exerts hypnotic effects only when circulating levels of endogenous melatonin are low.

*Eur J Pharmacol (NETHERLANDS) Mar 6 1995, 275 (2) p213-6,*

## SLEEP-INDUCING EFFECTS OF LOW DOSES OF MELATONIN INGESTED IN THE EVENING

We previously observed that low oral doses of melatonin given at noon increase blood melatonin concentrations to those normally occurring nocturnally and facilitate sleep onset, as assessed using an involuntary muscle relaxation test. In this study we examined the induction of polysomnographically recorded sleep by similar doses given later in the evening, close to the times of endogenous melatonin release and habitual sleep onset. Volunteers received the hormone (oral doses of 0.3 or 1.0 mg) or placebo at 6, 8, or 9 PM. Latencies to sleep onset, to stage 2 sleep, and to rapid eye movement (REM) sleep were measured polysomnographically. Either dose given at any of the three time points decreased sleep onset latency and latency to stage 2 sleep. Melatonin did not suppress REM sleep or delay its onset. Most volunteers could clearly distinguish between the effects of melatonin and those of placebo when the hormone was tested at 6 or 8 PM. Neither melatonin dose induced "hangover" effects, as assessed with mood and performance tests administered on the morning after treatment. These data provide new evidence that nocturnal melatonin secretion may be involved in physiologic sleep onset and that exogenous melatonin may be useful in treating insomnia.

*Clin Pharmacol Ther (U.S.) May 1995, 57 (5) p552-8,*

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