

A CLINICAL TRIAL OF MELATONIN IN ELDERLY PATIENTS WITH INSOMNIA

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ABSTRACT

BACKGROUND: The quality of life in the fast ageing population in the twentieth century is of great importance. Insomnia and melatonin levels in the geriatric population greatly affect sleep quality thereby also affecting blood pressure, mood changes and immune functions in this large segment of population.

AIM: To study the effect of melatonin in elderly persons with insomnia whether it restores sleep quality and sleep duration.

METHODS: Insomnia is defined as inadequate sleep. Thirty subjects participated in the study, 20 females and 10 males. The study was conducted on subjects attending the OPD at the Nepalgunj Medical College & Teaching Hospital at Kohalpur between December 2008 and March 2010. Age group of the subjects ranged from 36 years to 80 years. All subjects were administered melatonin 3 mgm tablets before going to bed for 10-20 days. All data obtained were subjective relying on patient's recall and compliance.

RESULTS: In 26 patients the quality of sleep was good and they felt relaxed and cheerful. In 15 patients melatonin was combined with alprazolam 0.25 mgm. Adverse effects were reported by a few subjects (like tachycardia, headache & depression). One case reported hypothermia.

CONCLUSION: Melatonin has a beneficial effect in elderly subjects with insomnia.

KEYWORDS: Aging, Circadian rhythm, Insomnia, Melatonin, Quality of sleep, Sleep disturbances.

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INTRODUCTION

Three centuries ago Rene Descartes described the pineal gland as “SEAT OF THE SOUL”. Melatonin was identified in the 1950s. In 1954 Kitay and Altschules' book “The pineal gland” was published. Aaron Lerner isolated melatonin in 1958.

Ageing of the population is one of the most important developments of the 20th century. By 2025 AD 65 year olds will outnumber teenagers by almost 2: 1. Thus there is a new emphasis on research and applications that prolong life (i.e. hormones, nutrition, antioxidants, vitamins, exercises and yoga programs).

Anti aging medicines will be the most profound social and economic issue of the 21st century. Of all the hormones melatonin appears to have the greatest anti aging potential.^{1,2,3,4} Melatonin keeps our bio clock ticking in rhythm. As age advances melatonin levels decline sharply and consequently our biorhythm gets disturbed. It is involved in the synchronization of circadian rhythmicity to the light dark cycle.^{3,5} It thus bio regulates the sleep wake cycle, blood pressure, mood changes and immune functions.

How might melatonin prolong life? ^{6,7}The possible mechanisms include reducing free radical damage, stimulating anti-aging immune system^{3,4}, protecting the cardiovascular system, stabilizing the body's biological rhythms⁵ and stimulating the production of growth hormone.

☛ Physiology of melatonin secretion

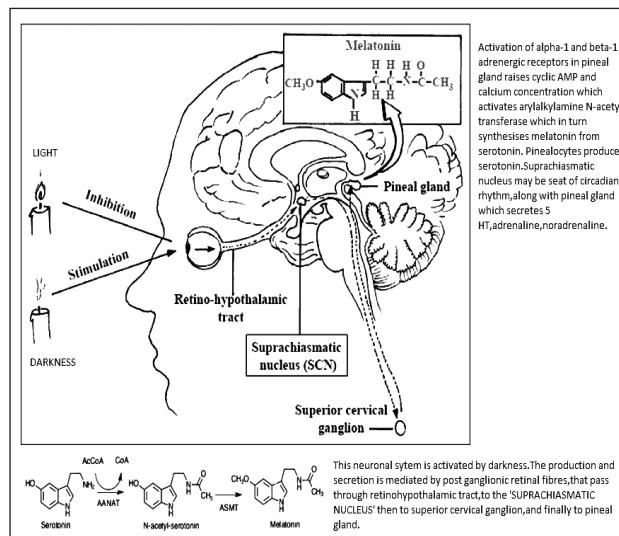
☛ The highest night time secretion of melatonin peaks between 2 to 4 AM.⁸

☛ The physiological blood levels of melatonin are as follows:-

- In children, from 1-3 years 250 pg / mL,
- In older children, from 8-15 years 120 pg / mL,
- In older adults, from 50-70 years 20 pg / mL,

The physiological concentration is below 100 pg / mL. Peak levels are reached 20 minutes after oral ingestion. It has a half-life of 30-60 minutes. Melatonin is metabolised in the liver to 6-sulfatoxy melatonin (6-SMT) and excreted in the urine. Melatonin levels decline as puberty occurs, it continues to decline in middle age whereas older people produce negligible amount of melatonin.

Figure 1: Physiology of Melatonin Secretion



METHODS

Thirty patients, attending medical and gynaecology OPD at Nepalgunj Medical College Teaching Hospital, Kohalpur, Banke, Nepal, from December 2008 to March 2010 with disturbed bio rhythms and sleep disorders were included in this study. Twenty subjects were female and ten were male subjects. The subjects were within the age group of 36 to 80 years. All were prescribed Meloset 3 mg tablets, 30 minutes prior to bed once at night time initially for 10 days with one week washout period. Four subjects were diabetic, 16 after undergoing hysterectomy, 12 with hypertension and 6 with depression.

The subjects in the study had at least one chronic disease and were currently taking at least one medication for sleep. After due approval from the hospital ethics committee, the results were subjectively assessed from the patients by asking questions about sleep induction, sleep quality, duration of sleep and if there were any adverse effects. The data obtained were subjective relying on patient's recall and compliance. All patients were administered melatonin for a total of 20 days. After a week of wash out period patients were crossed over to the opposite treatment. Objective methods like wrist actigraph, polysomnograph recorded sleep or 6 SMT concentration in urine were not used as outcome parameters.

OBSERVATIONS AND RESULTS

Thirty patients who were recruited for this study were in the age group from 35-80 years.

Table 1: Age wise distribution of subjects.

Subject age groups	No of subjects(<i>n</i> =30)
31 – 40 years	6%
41 – 50 years	27.5%
51 – 60 years	27.5%
61 – 70 years	33%
71 – 80years	6%

The subjects in the study had at least one pre-existing chronic disease and were currently taking at least one medication for sleep.

Table 2: Pre-existing medical conditions in study group

Medical condition	No of female subjects(<i>n</i> =20)	No of male subjects(<i>n</i> = 10)
Insomnia	35%	90%
Depression	20%	20%
Hypertension	20%	80%
Diabetes Mellitus	10%	20%
Post-menopausal syndrome	60%	

All patients showed change in time to sleep onset. All had good sleep quality and were feeling relaxed.⁹

Table 3: Melatonin efficacy -- Sleep induction time

Time to sleep onset	Improved	Delayed / No change
Female subjects	90%	10%
Male subjects	90%	10%

All had good sleep quality and were feeling relaxed.⁹Total day time sleep was unchanged, suggesting lack of hang over effect with melatonin.¹⁰ Blood pressure and heart rate were unchanged. One male subject who experienced nightmares as if somebody is standing nearby discontinued the medicine after initial treatment. Two female subjects undergoing psychiatric treatment for depression complained of delay in onset of sleep till the wee hours of morning also discontinued treatment. One subject is still continuing the drug for six months.

Table 4: Melatonin efficacy -- Sleep Quality

Sleep Quality	Improved	No change / Delayed
Female subjects (<i>n</i> =20)	80%	20%
Male subjects (<i>n</i> =10)	90%	10%

Table 5: Melatonin efficacy - Duration of sleep

Duration of sleep	Increased duration of sleep	No change
Female subjects (<i>n</i> =20)	90%	10%
Male subjects (<i>n</i> =10)	90%	10%

Ninety percent of our subjects reported increased and satisfying duration of sleep with melatonin while 2 patients of

severe depression did not show beneficial effect. Subjects had deep satisfying quality of sleep and woke up refreshed. Only one subject reported drowsiness and that too only in the early morning which quickly passed off and did not interfere with his daily routine.

DISCUSSION

Insomnia is defined as inadequate sleep.^{7,11} It is further divided into difficulty in falling asleep (sleep onset insomnia), difficulty in staying asleep (sleep maintenance insomnia) and sleepiness despite adequate duration of sleep (non restorative sleep). Our patients were assessed for efficiency of sleep induction and duration of sleep. We have relied on patient provided sleep information rather than objective data. In elderly people with sleep disorders melatonin deficiency may play a key role and replacement therapy may be beneficial.^{3,4} Melatonin improves both quality and duration of sleep.⁶ This suggests that the mechanism of action is not a sedative effect but a retraining of the endogenous circadian rhythm.^{10,12} Following a 2.5 mgm dose plasma melatonin concentration returned to baseline within 7 hours.¹³ Melatonin use should be discouraged in children less than 12 years of age.⁹ Adverse effects observed in clinical trials include tachycardia, headache, depression, sedation and pruritus.⁴ We have not come across such side effects. Given its short half-life it is unlikely that melatonin acts only through a direct hypnotic effect. It is hypothesized that it has a phase shifting effect on circadian rhythm effects. Melatonin may affect sleep behaviour through thermo regulatory mechanism. There is about 40 % decrease in nocturnal temperature due to increased melatonin concentration at night. Decreasing core body temperature can facilitate sleep.

CONCLUSION

The authors conclude that melatonin has a beneficial effect on elderly patients with insomnia. There was no drug dependence, no overdose complication whereas it may postpone ageing and age related complications. It may work as a mood elevator in case of erratic mood swings, stimulating an ageing immune system. It works as a highly efficient free radical scavenger, more effective than Vit. E. Thus melatonin is the wonder drug of the millennium.

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