Sleep disorders and melatonin rhythms in elderly people

I Haimov, M Laudon, N Zisapel, M Souroujon, D Nof, A Shlitner, P Herer, O Tzischinsky, P Lavie

Sleep Laboratory, Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel
I Haimov, *doctoral student*
A Shlitner, *senior research assistant*
P Herer, *statistician*
O Tzischinsky, *doctoral student*
P Lavie, *professor of behavioural biology*

Neurim Pharmaceuticals Ltd, Tel Aviv, Israel
M Laudon, *director of research and development*

Department of Biochemistry, George S Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv
N Zisapel, *professor of biochemistry*

Maccabi Pharmaceuticals Ltd, Tel Aviv
M Souroujon, *director, main laboratory*
D Nof, *general director, Maccabi laboratories*

Correspondence to:
Dr Lavie.

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Biological aging is often associated with problems with sleep and daytime napping.¹ There is considerable evidence linking melatonin, produced by the pineal gland, with the sleep-wake cycle. When administered orally to humans or animals it enhances sleep² and has a synchronising effect on circadian rhythms. Circulating melatonin concentrations decrease in old age, and its time of secretion is delayed.³ We examined whether sleep disorders in old age were associated with changes in concentration of 6-sulphatoxymelatonin, the major urinary measure of melatonin.

Patients, methods, and results

The study population comprised four groups: (a) eight independently living patients with insomnia (four men, four women, mean age 73.1 (SD 3.9)); (b) 15 patients with insomnia (five men, 10 women, mean age 82.1 (8.8)) who had lived a minimum of six months in a nursing home; (c) 25 elderly patients without sleep disorders (19 men, six women, mean age 71.4 (5.2)) who were living independently in the community; and (d) 12 young men (mean age 24.0 (1.6)) without sleep disorders. None suffered from sleep apnoea, dementia, or depression or were taking any soporific drugs.

Subjects' sleep was continuously monitored for one week by miniature actigraphs worn on the wrist. This device translates wrist movements into an electrical signal. Recordings were analysed to determine duration of sleep (total number of minutes defined as sleep), sleep efficiency index (sleep duration as a percentage of total time in bed), and mean activity level (the mean level of actigraphic recording throughout sleep).⁴ These measures were averaged across all available nights for each subject. Urine was collected approximately every two hours for 24 or 38 hours on the days following the week of actigraphic recording, and 6-sulphatoxymelatonin was assayed in duplicate.⁵ The interassays and intra-assay coefficients of variation were 7% and 5% respectively. We determined the time of onset of the nocturnal rise in 6-sulphatoxymelatonin excretion, the peak value, and the time of the peak.

Two tailed *t* test analysis showed a significant difference in sleep efficiency and activity level between elderly patients without sleep disorders and those with insomnia ($t=4.32$, $P<0.0001$, $t=4.40$, $P<0.0001$, respectively). Analysis of variance of peak amplitude of the four groups showed significant differences ($F=15.47$, $P<0.0001$) (figure). Mann-Whitney *U* tests showed significantly lower peaks of secretion in the patients with insomnia who lived independently (1.8 (0.7) $\mu\text{g/h}$) and in those who lived in nursing homes (0.7 (0.7) $\mu\text{g/h}$) compared with the elderly patients without sleep disorders (3.3 (2.0) $\mu\text{g/h}$) ($Z=-1.71$, $P<0.04$; $Z=-4.34$, $P<0.0001$, respectively) and the young men (4.2 (2.5) $\mu\text{g/h}$) ($Z=-2.53$, $P<0.006$; $Z=3.97$, $P<0.0001$, respectively). There was no significant difference in secretion between the elderly patients without sleep disorders and the young men ($Z=1.18$, $P>0.24$).

Spearman correlations (one tailed) showed that the onset of nocturnal 6-sulphatoxymelatonin secretion

and its peak concentration correlated with measures of the quality of sleep determined actigraphically. A lower peak correlated with lower sleep quality, as indicated by lower sleep efficiency ($r=0.43$, $P<0.002$). Likewise, the time of onset of secretion was negatively correlated with sleep efficiency ($r=-0.34$, $P<0.03$).

Mean 6-sulphatoxymelatonin concentrations over 24 hours in elderly people without sleep disorders ($\square$), independently living patients with insomnia ($\bullet$), patients with insomnia living in nursing home ($\circ$), and young men without sleep disorders ($\blacksquare$)

Comment

We found a correlation between disturbances of rhythm of 6-sulphatoxymelatonin excretion and poor sleep quality in elderly subjects. All patients with insomnia had a significantly lower sleep efficiency and a higher activity level during sleep; their 6-sulphatoxymelatonin excretion was characterised by a lower peak, with delayed onset and peak times. Peak excretion in the elderly subjects was 49% lower than that in young subjects, although the peak in elderly subjects without sleep disorders did not differ significantly from that in the young subjects. Our data suggests a relation between deficiency of melatonin or disruption of its rhythms and an increased prevalence of sleep disorders with advancing age. In addition, we hypothesise that a lack of exposure to bright light in institutions may lead to diminution of 6-sulphatoxymelatonin excretion in old age.

In conclusion, melatonin deficiency seems to be a key variable in the incidence of sleep disorders in elderly people, and melatonin replacement therapy may prove beneficial.

- 1 Dement W, Richardson G, Prinz P, Carskadon M, Kripke D, Czeisler C. Changes of sleep and wakefulness with age. In: Finch C, ed. *Handbook on the biology of aging*. New York: van Nostrand, 1985:692-717.
- 2 Gwinner E, Benzinger J. Synchronization of a circadian rhythm in pinealectomized European starlings by daily injections of melatonin. *J Comp Physiol [A]* 1978;127:209-13.
- 3 Sharma M, Palacios-Bois J, Schwartz G, Iskandar H, Thakur M, Quirion R, Nair NPV. Circadian rhythms of melatonin and cortisol in aging. *Biol Psychiatry* 1989;25:305-19.
- 4 Sadeh A, Alster J, Aurbach D, Lavie P. Actigraphically based automatic bedtime sleep-wake scoring: validity and clinical applications. *Journal of Ambulatory Monitoring* 1989;2:209-16.
- 5 Wisberg J, Hauri P, Harris C. The scoring of wrist actigraphy in insomnia. *Sleep Research* 1990;19:384.

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