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Journal search and commentary

Article reviewed: Mortality associated with sleep duration and insomnia ☆

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Objectives

Evaluate a large population survey (Cancer Prevention Study II) to determine if sleep duration, report of insomnia and sleeping pill use were associated with increased risk of mortality.

Study design

Retrospective statistical review of an existing data base for factors predicting mortality over a 6-year period (1982–1988).

Study population

About 1.1 million, mostly friends and relatives of American Cancer Society volunteers, completed health questionnaires in the fall of 1982 and 6-year mortality/survival data were available on 98% of this sample in 1988. This provided a sample for mortality assessment of 636,095 women and 480,841 men. Ages ranged from 30 to 102 years with mean (SD) ages of 57 (11) for women and 58 (10) for men.

Methods

All analyses were done separately for men and women. The major sleep-related variables analyzed were the participants report in 1982 of: (1) average hours of sleep each night coded into hour categories from 2 to 9 h. Responses of sleep length of 9.5–16.5 h were coded as a final category ($\geq$10 h). (2) Average times a month with insomnia coded into categories of 0, 1, 2, 3, 4–9 and 10 or more. No definition of insomnia was provided for the subject. (3) Average number of days using 'prescription sleeping pills' in the past month coded as none, 1–29/month and $\geq$30/month. Prescription sleeping pills were not further defined, nor were examples provided. The questionnaire given the participants did ask separately about the use of diazepam (Valium) and chlordiazepoxide (Librium).

Cox proportional hazards survival models were used with 32 covariates entered into the primary model, 29 for other risk factors considered to be significantly associated with mortality, plus the three sleep factors. The 29 risk factors covered standard demography, personal habits, BMI, health status including history of significant health-related items, and medication use considered a possible affect to mortality. Factors with probability of mortality association of $>$0.10 had been eliminated. Data for a given factor are presented as hazard ratios indicating the added risk relative to the selected reference value for the variable. For the sleep-related factors the reference values were 7 h for sleep duration (estimated to have the best survival value) and none for both insomnia and sleeping pill use.

Results

Reported sleep durations mode of 8.0 exceeded the median of about 7.5 h for both males and females with missing data of about 1.5% for this variable. Insomnia was reported for females and males respectively as: none, 49 and 70%; some, 41 and 24%; and missing data, 10 and 6%. Prescription sleeping pill use was reported for females and males respectively as: none, 47 and 46%; 1–29/month, 3.4 and 2.3%; $\geq$30/month, 0.5 and 0.4%; and missing data, 49.2 and 48.7%. The paper indicates that this sample, compared to the USA population of the same age, showed a 20% lower mortality rate, but the distribution of causes of mortality was similar.

Sleep duration of 7 h had the lowest mortality rates, and for both male and females the co-variate adjusted mortality risk increased for longer sleep duration by about 12% for 8,

☆ Kripke DF, Garfinkel L, Wingard DI, Klauber MR, Marler MR. Arch Gen Psychiatry 2002;59:131–136.

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20% for 9 and 37% for 10 or more hours For sleep duration shorter than 7 h, the co-variate adjusted risk increased by about 7% for 6, 9% for 5, 14% for 4 and 25% for 3 h sleep duration. Gender differences were small. The report of any nights with insomnia, compared to no nights of insomnia, was associated with a *decreased* co-variate adjusted mortality risk of 13–19% for women and 4–13% for men, with no clear relation to number of nights with insomnia except that the lowest number (1/month) had the highest relative decrease in mortality, differing significantly from most other insomnia rates. Reported use of prescription sleeping pills for both females and males alike showed increased mortality rates, compared to no use, of about 13% for use 1–29/month and about 24% for use ≥30/month. Number of nights with insomnia increased with shorter duration of sleep times. Number of nights using sleeping pills increased mostly with shorter duration of sleep times, but also increased with sleep duration of 9 or more hours. These patterns were the same for both males and females. BMI for men increased with sleep durations shorter than 7 h, but showed no increase for longer sleep durations. BMI for women increased both with sleep durations shorter than 7 and longer than 8 h.

Conclusions

The authors conclude that increasing sleep duration longer than 7.5 h is associated with proportionally significant increasing mortality risk, while decreasing duration shorter than 7 h produces only a small increase in mortality risk, except for those reporting only 3 h of sleep. Thus, longer duration of sleep is a more significant risk factor than shorter sleep. The report of insomnia appears to indicate a *reduced* co-variate adjusted mortality risk, particularly for occasional insomnia. The use of prescription sleeping pills is associated with increased mortality risk, greater for regular nightly use than for occasional use. The authors conclude that 'patients with insomnia without underlying comorbidities can be reassured that there appears to be no survival risk, as long as the patients refrain from long-term use of sleeping pills'.

Comment

Will our patients who sleep less, have insomnia and avoid using prescription sleeping pills live longer? These data certainly support this view, and if taken in this way would at least argue that sleeping pills should be prescribed with great caution. But there are some technical problems, a logical error and an inherent contradiction in these conclusions.

First, from a technical standpoint this is, overall, an excellent set of analyses. The statistical analysis used represents one of the best current approaches to these types of data and the sample size is sufficiently large to justify using the large number of co-variates. This provides a reasonable control to remove effects from factors that might create an artifact effect for the sleep variables. The problem with the data lies not in the statistics but in the original questions asked and the nature of the population analyzed. The questions on sleep duration seemed well drafted, but the 'insomnia' and 'sleeping pills' questions seem a bit vague. It is not clear how the respondents interpreted these questions. The frequency of insomnia analyzed did not include any categories that might have related to the more severe insomnia patients, but instead lumped these into one category of occurrence ≥10/month, limiting analyzes of the more severe insomnia. The frequency division for sleeping medication use into 'occasional' and 'daily' use seems appropriate for detecting the extreme effects. The major technical problem limiting the value of these data is the nature of the population studied. This study is from a convenience population — friends and associates of volunteers who certainly do not reflect the population of the USA. Indeed, this population has a lower mortality rate than the general population, and may have other unknown differences. In this regard it is noteworthy that while, as noted in the paper, the increased mortality with longer sleep times has been previously reported in population-based studies, this is only half the picture. It is also the case that, in contrast to the results published here, population-based studies, such as those reported for the recent Japanese population-based survey [1], have reported an almost equal increase in mortality risk with shorter sleep times.

Second, despite the quality of data analyses, the conclusions make the serious error of assuming that these types of data establish a causal relationship. This type of study, at its best, is meant to provide indications of possible causal relationships that need to be verified by further studies. Thus, the studies are not ends in themselves but a guide for future research, and the conclusions need to be very carefully stated to emphasize that the results do not indicate a causal relationship. It should be noted that this particularly applies to sleep issues, which are not known to have any direct effect on mortality except for aspects of certain sleep disorders such as sleep apnea. Sleep is more a quality of life issue than a survival issue, and any statistical relationship to mortality therefore requires developing some concept of mechanism.

The third, and most disturbing, aspect of this study is the inherent contradiction in the conclusion. The increased mortality with sleeping pill use has to be seen as indicating some relation to the problems or conditions that lead to the use of sleeping medications. Presumably, the patients were given these medications to improve sleep and the use of these medications therefore represents a proxy measure of more severe insomnia. Since we have no mechanism suggesting that the medications themselves decrease life expectance, it seems more prudent to attribute this effect to consequences associated with severe insomnia. That is, the data indicate that relative mortality risk is greater for

patients whose insomnia is severe enough to justify prescribing sleeping medications, pointing to a very different message than the one suggested by the author. It may also explain the increase in the use of the sleeping medication among those whose sleep durations are longer than 7 h. The sleeping medication use may also lead the subject to deny any current insomnia problem, even though there may be a persistent insomnia disorder. Thus, the insomnia question in this survey may have little relation to sleep disorders involving insomnia. Avoiding prescription of sleep medication is not likely to alter survival, but those patients who reach the point of needing daily sleeping medications might be considered to have a higher mortality risk than those not needing such treatment. This may be an indication that, as sleep medicine clinicians, we need to pay more attention to these patients, but not to deny them treatment which may be providing significant relief.

References

[1] Kojima W, Wakai K, Kawamura T, Tamakoshi A, et al. Sleep patterns and total mortality: a 12-year follow-up study in Japan. J Epidemiol 2000;10(2):87–93.