BRIEF REPORT

Sleep Problems and Risk of Fibromyalgia: Longitudinal Data on an Adult Female Population in Norway

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Objective. Sleep problems are common among patients with fibromyalgia (FM). However, it is not known whether poor sleep is a contributing factor in FM or a consequence of the illness. The aim of the current study was to prospectively investigate the association between self-reported sleep problems and risk of FM among adult women.

Methods. We longitudinally studied 12,350 women who did not have FM, musculoskeletal pain, or physical impairments at baseline (1984–1986). A generalized linear model was used to calculate the adjusted relative risk (RR) of FM at followup in 1995–1997.

Results. Incident FM was reported by 327 women at followup. A dose-dependent association was found between sleep problems and risk of FM (P for trend < 0.001), with an adjusted RR of 3.43 (95% confidence interval [95% CI] 2.26–5.19) among women who reported having sleep problems often or always, compared to women who never experienced sleep problems. Age-stratified analysis showed that women age ≥45 years who reported having sleep problems often or always had an adjusted RR of 5.41 (95% CI 2.65–11.05), whereas the corresponding RR for women ages 20–44 years who reported having sleep problems often or always was 2.98 (95% CI 1.76–5.05).

Conclusion. These prospective data indicate a strong dose-dependent association between sleep problems and risk of FM. The association is somewhat, although not significantly, stronger in middle-aged and older women than in younger women.

Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome with a complex etiology. The prevalence of FM in the general adult population is ~3–5%, with a predominance among women (1). Disturbed sleep (e.g., insomnia and nocturnal awakening) and undue fatigue due to nonrestorative sleep are common comorbid symptoms in patients with FM (2,3). Self-reported sleep problems in patients with FM have been substantiated by polysomnographic recordings, showing alterations in sleep architecture and electroencephalographic sleep pattern, in some but not all studies (4). Whether poor sleep is a contributing factor in the development of FM or, rather, develops as a consequence of the illness is currently not known. We prospectively studied a large and unselected population of women who did not have FM, musculoskeletal pain, or physical impairment at baseline, to investigate whether sleep problems increase the risk of FM development.

PATIENTS AND METHODS

Study population. The (Helseundersøkelsen i Nord-Trøndelag [Nord-Trøndelag Health Study] [HUNT study]) is a collaborative effort of the HUNT Research Centre at the Norwegian University of Science and Technology, the Nord-Trøndelag (Norway) County Council, and the Norwegian Institute of Public Health. All residents of Nord-Trøndelag County age ≥20 years were invited to participate in 2 separate phases of the HUNT study: first in 1984–1986 (HUNT 1) and then in 1995–1997 (HUNT 2). Among 42,568 women who were eligible, 38,274 (89.9%) accepted the invitation to participate in the HUNT 1 and completed a questionnaire that was sent with the invitation. A clinical examination was conducted, at which body mass and height were measured and the women were given a second questionnaire to complete at home and return in a prestamped envelope. For the HUNT 2, 46,709 women were invited to participate, and 34,518 (73.9%) accepted the invitation. The procedures were similar to those described for the HUNT 1, although both the questionnaires and the clinical examination were more comprehensive.

There were 24,357 women who participated in both the HUNT 1 and the HUNT 2, and these women were selected for the present study. Of these 24,357 women, we excluded 6,093...
who reported that their musculoskeletal pain had lasted 10 years or more (i.e., who had pain at baseline), as well as 4,719 women with missing information on duration of musculoskeletal pain (n = 206), FM (n = 1,914), sleep problems (n = 2,592), or body mass index (n = 7). We also excluded women who reported that they were physically impaired (n = 495) and women who used sedative and/or sleeping medicine on a daily or weekly basis (n = 700). As a result, this study is based on 12,350 women who were apparently free from musculoskeletal pain and movement disorders at baseline.

The study was approved by the Regional Committee for Ethics in Medical Research and carried out according to the requirements of the Declaration of Helsinki.

Study variables. Fibromyalgia. In the HUNT 2, participants were asked to report physician-diagnosed FM and duration of musculoskeletal pain. The diagnosis of FM (yes/no) was confirmed by the question “Has a doctor ever said that you have fibromyalgia (fibrositis/chronic pain syndrome)?” However, no information about the time of diagnosis was collected. Musculoskeletal pain (yes/no) was assessed with the question “During the last year, have you had pain and/or stiffness in your muscles and limbs that has lasted for at least 3 consecutive months?” If yes, the participants were asked to indicate the duration of symptoms (number of months if symptoms had lasted <1 year, and number of years if symptoms had lasted ≥1 year). The latter information was used to exclude women who reported musculoskeletal pain of ≥10 years’ duration.

Sleep problems. Sleep problems at baseline (i.e., HUNT 1) were assessed with the question “During the last month, have you had any problems falling asleep or sleep disorders?” Response options were “never,” “sometimes,” “often,” and “almost every night” (the last defined as “always”). In the statistical analysis, “often” and “always” were collapsed into one category.

Statistical analysis. A generalized linear model for the binomial family was used to estimate relative risk (RR) of FM at followup associated with sleep problems at baseline. Precision of the estimated RR was assessed by calculating the 95% confidence interval (95% CI), and trends across categories of sleep problems were calculated by treating the categories as an ordinal variable in the regression model. Our basic models were adjusted for age in 10-year categories (20–29 years, 30–39 years, up to 60–69 years, with ages older than 69 years combined into one category of ≥70 years). In additional multivariable models we also controlled for potential confounding by frequency of physical exercise sessions per week (none, <1, 1, 2–3, ≥4, or unknown), body mass index (kg/m²) (<18.5, 18.5–24.9, 25.0–29.9, or ≥30.0), psychological well-being (depressed, somewhat happy, happy, or unknown), smoking status (never, former, current, or unknown), and education (<10 years, 10–12 years, ≥13 years, or unknown).

Since sleep problems increase steadily with age (5), we conducted age-stratified analyses to examine risk of FM related to sleep problems in women ages 20–44 years at baseline and women age ≥45 years at baseline. Statistical interactions were examined using a likelihood ratio test after inclusion of the product term of sleep problems and age in the regression model.

RESULTS

Baseline characteristics of the study population categorized by frequency of sleep problems are shown in Table 1. At followup, 327 women reported incident FM, corresponding to an overall incidence of 2.6%. The incidence proportion was 3.2% among women ages 20–44 years and 1.7% among women age ≥45 years.

Table 2 shows the age- and multivariable-adjusted RRs for FM associated with frequency of sleep problems in the overall study population and for the age strata 20–44 years and ≥45 years. Sleep problems were positively associated with risk of FM in a dose-dependent manner in the overall study population and within both age strata (P for trend < 0.001 for all associations). In the overall study population, the adjusted RR for FM development was 3.43 (95% CI 2.26–5.19) among women who reported experiencing sleep problems often or always, compared to women without sleep problems. Correspondingly, women who reported experiencing sleep problems sometimes had a 2-fold increase in risk of FM (adjusted RR 1.98 [95% CI 1.58–2.49]).

Although there was no statistical interaction between age and sleep problems (P = 0.41 by likelihood ratio test), we observed that women age ≥45 years who often or always had sleep problems had an adjusted RR for FM development of 5.41 (95% CI 2.65–11.05) compared to those without sleep problems, whereas the corresponding association among women age 20–44 years was 2.98 (95% CI 1.76–5.05).

In a supplementary analysis comparing the 3,949 women who reported any sleep problem (sometimes, often, or always) with the 8,401 women who reported no sleep problem, we found an adjusted RR of 2.10 (95%
If this reflects a true causal association, the attributable fraction is 65%, i.e., among women with sleep problems, approximately two-thirds of the incident cases of FM are caused by sleep problems.

DISCUSSION

The results of this study indicate that, among adult women, sleep problems are closely associated with risk of FM development. The risk increases in a dose-dependent manner according to the frequency of the sleep problems, with the association being somewhat stronger among middle-aged and older women compared to younger women.

The exact mechanism by which poor sleep can cause chronic widespread musculoskeletal pain is uncertain. Experimental studies have shown that sleep deprivation as well as interruption of slow-wave sleep (i.e., stage 4 sleep) in healthy subjects may induce mechanical hyperalgesia at multiple body sites (6,7)—i.e., symptoms similar to those observed in patients with FM. Sleep deprivation has also been associated with elevated plasma levels of markers of inflammation (8,9) and reduced endogenous pain-inhibitory capacity (10). In patients with FM, sleep problems have been shown to predict exacerbation of pain during a 1-year followup period (2). It is therefore possible that long-lasting sleep problems render the individual more susceptible to development of chronic widespread pain, as well as exacerbation of such pain. A recent prospective population-based study showed that sleep problems at baseline increased the risk of chronic widespread pain at 15-month followup (11), supporting the idea that poor sleep is an important predictor of future development of chronic widespread pain. However, unlike our study, subjects with localized musculoskeletal pain at baseline were not excluded from the study population (11), and this may hamper the conclusions that can be drawn from the data.

Although the current study had obvious strengths, such as the prospective design and the large, population-based sample size, there were also some limitations. First, sleep problems were assessed by a single question that did not permit diagnosis of sleep disorders (e.g., insomnia) according to established standards (12). Misclassification of sleep problems is possible, although it is not likely that such misclassification would have been differential between women who developed FM and those who did not. Second, incidence of FM was based on self-reports of physician-diagnosed FM. Some cases may therefore not have fulfilled recommended criteria for FM diagnosis (13) at followup. Third, although we adjusted for several potential confounders known to affect sleep, the difference between age-adjusted and multivariable-adjusted risk estimates was small. Residual confounding due to unknown and unmeasured factors cannot be ruled out. In particular, anxiety is strongly associated with sleep problems (14) as well as with FM (15).

In conclusion, this study provides evidence of a

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<table>
<thead>
<tr>
<th>Sleep problems</th>
<th>No. developing FM/total</th>
<th>Age-adjusted RR</th>
<th>Multivariable-adjusted RR (95% CI)†</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women studied</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>171/8,401</td>
<td>1.00</td>
<td>1.00 (referent)</td>
<td></td>
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<tr>
<td>Sometimes</td>
<td>131/3,571</td>
<td>2.05</td>
<td>1.98 (1.58–2.49)</td>
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<tr>
<td>Often/always</td>
<td>25/378</td>
<td>3.95</td>
<td>3.43 (2.26–5.19)</td>
<td>&lt;0.001</td>
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<td>Women ages 20–44 years</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>142/5,735</td>
<td>1.00</td>
<td>1.00 (referent)</td>
<td></td>
</tr>
<tr>
<td>Sometimes</td>
<td>92/1,906</td>
<td>1.93</td>
<td>1.85 (1.43–2.40)</td>
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<td>Often/always</td>
<td>15/184</td>
<td>3.36</td>
<td>2.98 (1.76–5.05)</td>
<td>&lt;0.001</td>
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<tr>
<td>Women age ≥45 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>29/2,666</td>
<td>1.00</td>
<td>1.00 (referent)</td>
<td></td>
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<tr>
<td>Sometimes</td>
<td>39/1,665</td>
<td>2.59</td>
<td>2.53 (1.55–4.12)</td>
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<tr>
<td>Often/always</td>
<td>10/194</td>
<td>6.02</td>
<td>5.41 (2.65–11.05)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* FM = fibromyalgia; RR = relative risk; 95% CI = 95% confidence interval.
† Adjusted for age (20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, or ≥70 years), frequency of physical exercise sessions per week (none, 1, 2–3, 4, or unknown), body mass index (<18.5 kg/m², 18.5–24.9 kg/m², 25.0–29.9 kg/m², ≥30.0 kg/m²), psychological well-being (depressed, somewhat happy, happy, or unknown), smoking status (never, former, current, or unknown), and education (<10 years, 10–12 years, ≥13 years, or unknown).
strong dose-dependent association between frequency of sleep problems and risk of FM in adult women. Future studies should investigate whether early detection and treatment of sleep problems can reduce the risk of developing chronic widespread pain.

**AUTHOR CONTRIBUTIONS**

Both authors were involved in drafting the article or revising it critically for important intellectual content, and both authors approved the final version to be published. Dr. Mork had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** Mork, Nilsen.

**Acquisition of data.** Mork, Nilsen.

**Analysis and interpretation of data.** Mork, Nilsen.

**REFERENCES**