The association of sleep quality with dry eye disease: the Osaka study

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Introduction

Dry eye disease (DED) is widely recognized as a multifactorial chronic disease that is highly prevalent in many countries, including Japan. DED has recently gained recognition as a public health problem.¹² DED presents with various symptoms that significantly affect the quality of life and work ability, as well as the physical, social, and psychological well-being of an individual, by causing impaired visual function, psychological problems, or both.³⁻⁹

Ocular symptoms such as dryness, eyestrains, and blurry vision are commonly reported symptoms related to visual display terminal (VDT) users.¹⁰ VDT exposure has been increasing among office workers because of the rapid advancement of information technology. A recent large-scale epidemiologic study of office workers in Japan concluded that VDT work is considered one of the key risk factors for DED.¹¹⁻¹³ These studies illustrate how significantly DED can impact a patient’s functioning in the modern technological society.

On the other hand, sleep is essential to our physical and mental well-being, and the number of people with a sleep deficiency seems likely to increase. Sleep deficiencies significantly affect the quality of life and work ability, as well as the physical, social, and psychological well-being of an individual, by causing impaired visual function, psychological problems, or both.¹⁰⁻¹⁴ Furthermore, mental health maintenance...
has been increasingly recognized as critical with respect to the management of office workers, and several studies have shown that sleep quality is associated with the mental health of office workers. Recent studies also suggest that a sleep disturbance is associated with circadian rhythm disruption and even hypertension (HT) and metabolic syndrome. It has been reported that tear secretion and tear stability have a circadian rhythm. A study also suggested that the tear secretion system might be associated with the renin–angiotensin system, as metabolic syndrome patients have lower tear secretion.

Accordingly, we speculate that sleep quality is associated with DED. We conducted the present study to clarify the relation between poor sleep quality and DED. Thus, the aim of this study was to investigate the relationship between sleep quality and DED among VDT workers.

Materials and methods
In 2011, we conducted a cross-sectional survey of all the employees, mainly consisting of young and middle-aged Japanese office workers, who used VDT at a company in Osaka, Japan (N=672; age range =26–64 years). The detailed study protocols have been shown in previous reports, and the methods and grading scale used in this study have been previously published. All ophthalmic examinations were performed by seven ophthalmologists who were DED specialists. In order to unify assessment of objective evaluation, the DED specialists reconfirmed the DED scoring system before examination. We investigated the association of DED parameters (the Schirmer test-I values, tear film break-up time [BUT] test values, corneal and conjunctival staining scores, and symptoms) with physical activity level and sleep quality. Written informed consent was obtained from all participants. Candidates with a history of refractive surgery were excluded from the study. Contact lens wearers and those with meibomian gland dysfunction were included in this study. We defined the duration of VDT use (stratified, none to over 10 hours in 1-hour categories) including both office and beyond office hours and contact lens use (yes or no). Past/current history of certain common systemic diseases such as HT, diabetes mellitus, depression, and use of systemic medications was determined by asking the participants whether they had ever been told by their physicians that they had these conditions, or they had used any systemic medications, including antidepressants. The research followed the tenets of the Declaration of Helsinki, and this study design was approved by the Institutional Review Board of Ryogoku Eye Clinic in Tokyo, Japan.

Diagnosis of DED
On the basis of the dry eye examination results including the Schirmer test, fluorescein and lissamine green staining, BUT, and the symptom questionnaire, the participants were classified into the following three groups: definite DED, probable DED, and non-DED. A dry eye diagnosis was made according to the latest Japanese dry eye diagnostic criteria (2006) as follows: 1) presence of dry eye symptomatology; 2) presence of qualitative or quantitative disturbance of the tear film (Schirmer test ≤5 mm or BUT ≤5 seconds); and 3) presence of keratoconjunctival epithelial damage (total score of fluorescein and lissamine green staining ≥3 points). A diagnosis of definite DED required adherence to all the three criteria. Subjects fulfilling two of the three criteria were diagnosed with probable DED, and those fulfilling one or none of the three criteria were given the diagnosis of non-DED.

Ocular surface symptom questionnaire
We used a 29-item questionnaire to evaluate the symptoms associated with dry eyes (Table S1). The questionnaire consisted of three categories: 12 questions on dry eye symptoms, nine on visual symptoms, and eight on environmental factors. Each question was answered with a frequency graded on a 5-point severity scale: 0, always; 1, often; 2, sometimes; 3, rarely; and 4, never. The total symptom score was calculated using the following formula: questionnaire score = (sum of the scores from all the answered questions ×100)/(total number of questions answered ×4). The validity and reliability of this questionnaire had been confirmed.

Sleep quality
A Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) was used to measure the patients’ recent sleep quality and sleep quantity. PSQI is an effective and useful instrument for measuring subjective sleep quality and sleep disturbances. The PSQI consists of 17 items, generated from seven components, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, sleep medication usage, and daytime dysfunction. The score for each component ranged from 0 to 3. The sum of the scores of these seven components provided a global PSQI score that ranged from 0 to 21. Generally, higher scores indicate poorer sleep. In PSQI-J, a cutoff score of >5.5 has a sensitivity of 80.0%–85.7% for various patient groups and a specificity of 86.6% for control subjects.

Statistical analysis
Categorical variables were analyzed using the $\chi^2$ test, and continuous variables using Student’s $t$-test. After adjusting
for any possible confounders (sex, age, and VDT hours), analysis of variance was used to estimate the impact of DED on the PSQI score. Additional adjustment for HT and diabetes mellitus (which was not associated with PSQI score, data not shown) did not affect the findings and was not included in the final models. P-values <0.05 were considered significant. All statistical analyses were performed using Statistical Analysis Software, Version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

The survey response rate for completing the PSQI, the dry eye questionnaires, and the dry eye examinations was 57.0% (383/672). We did not observe any subjects who had been diagnosed with depression and anxiety in the present study. The respondents’ characteristics are summarized in Table 1. In comparison with the non-DED group, there were more females in the DED group. Subjects in the DED group showed longer VDT use than those in non-DED group.

A comparison of the sleep quality between DED and non-DED groups is shown in Table 2. The total mean PSQI global score was 5.1±2.3. In the DED group, 45% of the participants reported poor sleep quality, while 34% of those in the non-DED group reported the same, with a significant difference found in the global score between the DED group (5.4±2.2) and the non-DED groups (4.6±2.3; Student’s t-test, P=0.002) (Table 2).

Next, we investigated the association between the DED parameters and the PSQI score. The abnormal Schirmer value group had a significantly higher rate of abnormal sleep quality than that of normal Schirmer value group (P=0.021) (Table 3). No significant differences were observed between the groups in PSQI scores, BUT, and ocular surface staining score. The dry eye symptom score was significantly higher in the abnormal sleep quality group (28.2±15.3) than that in the normal sleep quality group (22.1±12.2, P<0.001) (Figure 1).

Furthermore, a significant association between the DED and the PSQI score (P=0.005) (Table 4) was found while analyzing models to evaluate the association between the PSQI score and the DED, after considering the possible influence of other factors known to be associated with DED (age, sex, and VDT hours).

Discussion

In this cross-sectional study, we found that sleep quality was associated with DED among the office workers, and 45% of the participants in the DED group reported poor sleep quality. The results of our study suggested that sleep disturbances seem to be an influencing factor of DED, especially with dry eye symptoms (Figure 1). PSQI-J score was significantly associated with DED (P=0.005). This study revealed that all patients with definitive DED had chronic discomfort present in eyes during wake and sleep.

Previous studies reported that a sleep disturbance because of sleep apnea syndrome, which is characterized by recurrent complete or partial upper airway obstructions during sleep, was associated with DED.31-33 Sjögren’s syndrome is often

Table 1 Characteristics of the study respondents who completed the dry eye disease examination and the Japanese version of the Pittsburgh Sleep Quality Index questionnaire

<table>
<thead>
<tr>
<th></th>
<th>DED (definite + probable) group</th>
<th>Non-DED</th>
<th>Total</th>
<th>P-value (DED vs non-DED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Definite</td>
<td>Probable</td>
<td>Subtotal</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>206</td>
<td>249</td>
<td>134</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>21 (48.8)</td>
<td>128 (62.1)</td>
<td>149 (59.8)</td>
<td>103 (76.9)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>22 (51.2)</td>
<td>78 (37.9)</td>
<td>100 (40.2)</td>
<td>31 (23.1)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>40.8±7.1</td>
<td>42.7±8.3</td>
<td>42.4±8.1</td>
<td>42.7±9.0</td>
</tr>
<tr>
<td>Age (category)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20s, n (%)</td>
<td>3 (7.0)</td>
<td>9 (4.4)</td>
<td>12 (4.8)</td>
<td>13 (9.7)</td>
</tr>
<tr>
<td>30s, n (%)</td>
<td>16 (37.2)</td>
<td>65 (31.6)</td>
<td>81 (32.5)</td>
<td>31 (23.1)</td>
</tr>
<tr>
<td>40s, n (%)</td>
<td>18 (41.9)</td>
<td>90 (43.7)</td>
<td>108 (43.4)</td>
<td>55 (41.0)</td>
</tr>
<tr>
<td>50s, n (%)</td>
<td>6 (14.0)</td>
<td>42 (20.4)</td>
<td>48 (19.3)</td>
<td>35 (26.1)</td>
</tr>
<tr>
<td>VDT time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>8.4±2.1</td>
<td>8.1±2.3</td>
<td>8.1±2.3</td>
<td>7.6±2.1</td>
</tr>
<tr>
<td>VDT time (two categories)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;8 h, n (%)</td>
<td>31 (72.1)</td>
<td>146 (70.9)</td>
<td>177 (71.1)</td>
<td>113 (84.3)</td>
</tr>
<tr>
<td>≥8 h, n (%)</td>
<td>12 (27.9)</td>
<td>60 (29.1)</td>
<td>72 (28.9)</td>
<td>21 (15.7)</td>
</tr>
</tbody>
</table>

Notes: *χ² test; **Student’s t-test.
Abbreviations: DED, dry eye disease; SD, standard deviation; VDT, visual display terminal; h, hours.
Table 2  Sleep quality and dry eye disease

<table>
<thead>
<tr>
<th>Category</th>
<th>DED (definite + probable)</th>
<th>Non-DED</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean ± SD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal, n (%)</td>
<td>137 (55.0)</td>
<td>89 (66.4)</td>
<td>226</td>
<td>0.002*</td>
</tr>
<tr>
<td>Abnormal, n (%)</td>
<td>112 (45.0)</td>
<td>45 (33.6)</td>
<td>157</td>
<td></td>
</tr>
</tbody>
</table>

Notes: *Student’s t-test. **χ² test.
Abbreviations: DED, dry eye disease; PSQI-J, Japanese version of the Pittsburgh Sleep Quality Index; SD, standard deviation.

Table 3  The Japanese version of the Pittsburgh Sleep Quality Index questionnaire score and dry eye objective parameters

<table>
<thead>
<tr>
<th>n</th>
<th>PSQI-J score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;5.5 (normal)</td>
</tr>
<tr>
<td>Schirmer value</td>
<td>226</td>
</tr>
<tr>
<td>=5 mm (abnormal), n (%)</td>
<td>29 (45.3)</td>
</tr>
<tr>
<td>&gt;5 mm (normal), n (%)</td>
<td>173 (58.2)</td>
</tr>
<tr>
<td>BUT</td>
<td>11,12</td>
</tr>
<tr>
<td>=5 s (abnormal), n (%)</td>
<td>53 (61.6)</td>
</tr>
<tr>
<td>&gt;5 s (normal), n (%)</td>
<td>187 (58.6)</td>
</tr>
<tr>
<td>Ocular surface</td>
<td>226</td>
</tr>
<tr>
<td>staining score</td>
<td>39 (60.9)</td>
</tr>
</tbody>
</table>

Abbreviations: BUT, tear film break-up time; PSQI-J, Japanese version of the Pittsburgh Sleep Quality Index; s, seconds.
be conducted implementing objective tools to evaluate sleep quality. Also, we would like to investigate subtypes of sleep disturbance and DED. In this study, we had no participants with sleep apnea, but such connection among DED, sleep disturbance, and sleep apnea should be investigated. Furthermore, as with all cross-sectional studies, a causal relationship remains unclear. In the future, given the results of this study, we should consider the impact of nighttime and daytime exposures to VDT separately on DEDs and examine those persons who have the same VDT exposure time. Also, the VDT work-related complaints such as headache and shoulder pain, in addition to DED, should be investigated about their effects on sleep as a prospective study.

**Conclusion**

In conclusion, although larger longitudinal or interventional trials are necessary, we found that sleep quality is associated with DED. A sleep disturbance seems to be an influencing factor on DED, especially on dry eye symptoms.

**Table 4** Dry eye disease associated with the Japanese version of the Pittsburgh Sleep Quality Index questionnaire score and adjusted for other factors

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry eye</td>
<td>1</td>
<td>40.027</td>
<td>40.027</td>
<td>7.96</td>
<td>0.005</td>
</tr>
<tr>
<td>Sex</td>
<td>1</td>
<td>2.700</td>
<td>2.700</td>
<td>0.54</td>
<td>0.464</td>
</tr>
<tr>
<td>Age (four categories)</td>
<td>3</td>
<td>29.549</td>
<td>9.850</td>
<td>1.96</td>
<td>0.120</td>
</tr>
<tr>
<td>VDT working hours</td>
<td>1</td>
<td>3.651</td>
<td>3.651</td>
<td>0.73</td>
<td>0.395</td>
</tr>
<tr>
<td>(two categories)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Error</td>
<td>376</td>
<td>1,891.247</td>
<td>5.030</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>382</td>
<td>1,975.473</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note:* Adjusted for sex, age, and VDT working hours for each group.

*Abbreviations:* df, degrees of freedom; F, F-value; MS, mean square; SS, sum of squares; VDT, visual display terminal.

**Acknowledgments**

We thank Dr Yuji Nishiwaki for his valuable advice.

This study was supported by a grant-in-aid from the Ministry of Education, Science, Sports, and Culture and Grant-in-Aid for Young Scientists (B), 2279192, 2010. Part of this study was sponsored by Santen Pharmaceutical Co., Ltd., Osaka. Provision of facilities and transport of equipment were supported by Santen Pharmaceutical Co., Ltd. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

We have the following interests. During the 36 months prior to submission, Dr Yokoi was a consultant for Kissei Co., Ltd. and Rohto Co., Ltd. Dr Kinoshita was a consultant for Santen Pharmaceutical Co., Ltd and Otsuka Pharmaceutical Co., Ltd. Dr Tsubota was a consultant for Santen Pharmaceutical Co., Ltd., AcuFocus, Inc, Bausch Lomb Surgical, Pfizer, and Thea. Dr Uchino Y, Dr Uchino M, Dr Komuro, Dr Kato, Dr Yokoi, Dr Sonomura, and Dr Kawashima received funding from a commercial source (Santen Pharmaceutical Co., Ltd). This does not alter our adherence to all the Clinical Ophthalmology policies on sharing data and materials.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**

10. Kawashima M, Uchino M, Kawazoe T, Kamiyashiki M, Sano K, Tsubota K. A field test of a web-based screening for dry eye disease to enhance awareness of eye problems among general internet users: a latent decision to publish, or preparation of the manuscript.
### Table S1 Newly designed Dry Eye Symptom Questionnaire

#### Three-part questionnaire

**A Symptom frequency and severity scores for dryness**

1. Do you feel dryness in your eyes?
2. Are your eyes uncomfortable?
3. Do you experience a foreign body sensation in your eyes?
4. Do you have any pain in your eyes?
5. Do you feel any eyestrain?
6. Do you have any discomfort in your eyes?
7. Are your eyes bloodshot?
8. Do you have any itching in your eyes?
9. Do you have any difficulty opening your eyes?
10. Do you have any irritation in your eyes?
11. Do your eyes feel heavy?
12. If you have any other symptoms, please write it in the parentheses beneath and circle the frequency

Total (1–12): ( ) – A

**B Symptom frequency severity scores for visual disturbance**

13. Do you have hazy vision?
14. Do you have any glare?
15. While reading, do your dry eye symptoms worsen, and it becomes hard to continue reading?
16. While driving, do your dry eye symptoms worsen, and it becomes difficult to drive?
17. While operating the computer, do your dry eye symptoms worsen, and it becomes difficult to continue?
18. While watching TV or movies, do your dry eye symptoms worsen, and it becomes difficult to watch?
19. Do you have any after-images?
20. Do you think that blinking affects your sight?
21. Can you keep your eyes open without blinking for 10 seconds or more?

Total (13–21): ( ) – B

**C Symptom frequency severity scores for environmental and lifestyle factors: Do your dry eye symptoms worsen?**

22. When the wind is strong?
23. When it is dry in winter or summer?
24. When the air conditioning is on?
25. While flying?
26. When you feel stressed in daily life?
27. After alcohol consumption?
28. When you smoke or are exposed to someone smoking next to you?
29. When you are wearing contact lenses?

Total (22–29): ( ) – C

**Notes:** Of the 29 questions, 1 through 29, except for 21, were classified into the following five stages: 4, always; 3, often; 2, occasionally; 1, rarely; and 0, never. Question 21 was classified into the following five stages: 4, not possible; 3, with difficulty; 2, moderately possible; 1, probable; and 0, not a problem.