Evaluation of Sleep Quality and Fatigue in Hospitalized Patients

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Abstract

Background: Hospitalization can significantly disrupt sleeping patterns. Insomnia in the hospitalized patient leads to increased fatigue.

Aims and Objectives: The aim of this study was to evaluate and compare sleep quality and fatigue of the hospitalized patients and match healthy controls.

Methodology: This is a descriptive cross-sectional study. A total of 150 hospitalized patients (internal clinics=75, surgical clinics=75) and 50 healthy controls constituted the sample. As the data gathering tools, a questionnaire form, Pittsburgh Sleep Quality Index, and Visual Analogue Scale for Fatigue were used. The data was evaluated after transferring to SPSS 11.0 database in percentage, mean, independent group’s t-test, one way-ANOVA, LSD post hoc, chi-square, cronbach’s alpha coefficient, pearson product-moment correlation.

Results: We found worse sleep quality and more fatigue in patients compared to controls. Female patients reported greater sleep disturbances and more severe fatigue than did male patients. It was found that the severity of fatigue was significantly correlated to sleep quality score.

Conclusions: These results suggest that sleep quality and fatigue of inpatients is worse than healthy persons; there are significant relationships between sleep quality and fatigue, indicating the need for more individualized supportive nursing care. Patients with hospitalized need professional support from nurse. It is expected that nurses should have the basic knowledge about sleeping problems and fatigue in hospitalized patients when providing care to patients because of possible interactions with other treatments.

Keywords: Sleep, Sleeps Quality, Fatigue, Hospitalized Patients, Nursing.

Introduction

Sleep is one of the physical needs for all humans. Sleep affects quality of life and well-being and is seen as an important variable of health (Potter & Perry 2009). Sleep quality has a restorative function and promotes health and a feeling of well-being, in the presence of a balance between rest and sleep on the one hand and activity on the other (Edéll-Gustafsson et al. 2003). Sleep quality is important for two reasons. First of all, complaints related to sleep quality are common. Bedtime and sleeping difficulties are the major factors affecting sleep quality and account for 15-35% of these difficulties. Second of all, low sleep quality is an indicator of many illnesses (Doğan et al. 2005). Fatigue affects a person’s health, reduces performance and is a subjective feeling of low vitality that disrupts daily functioning; with lifetime prevalence in the community of roughly 20% (Addington et al. 2001). Fatigue should prompt evaluation for possible anemia, nutritional deficits, sleep disturbance,
muscular reconditioning, and neurology impairment. Other common problems include poor appetite with possible weight loss, falls, and sexual dysfunction (Volk & Grassi 2009). The relationships between sleep problems and fatigue have been described previously (McCann & Boore 2000, Edéll-Gustafsson et al. 2003, Strober & Arnett 2005, Uhlin & Edéll-Gustafsson 2006, Lee et al. 2007, DE Lange et al. 2009).

Hospitalization can significantly disrupt sleeping patterns. These may be caused by a variety of exogenous factors such as ward environmental noise, bright lighting and repetitive staff interventions, medication or endogenous factors such as delirium, depression, anxiety, stress, inability to lie down comfortably and pain (Erser et al. 1999, Raymond et al. 2001, Frighetto et al. 2004, Hocaoglu 2009). Researchers have shown that insomnia in the hospitalized patient leads to increased fatigue, irritability, and aggressiveness as well as decreased pain tolerance (Raymond et al. 2001, Lenhart & Buysse 2001, Frighetto et al. 2004). Henderson has stated that the function of nurses in relation to needs for sleep is to help patients with their sleeping problems and resting. Need for sleep is a part of basic human needs and their daily activities. It is expected that nurses should have the basic knowledge about sleeping problems and fatigue in hospitalized patients when providing care to patients because of possible interactions with other treatments (Potter & Perry 2009).

The aim of this study was to evaluate sleep quality and fatigue in inpatients in different clinics, and find out if there was any difference of sleep quality and fatigues between inpatients and healthy people.

**Methodology**

**Patients**

The sample comprised of 150 patients, living in Kırşehir in the midst of Turkey, who had been having treatment in internal medicine, chest diseases, neurology, cardiology, physical therapy and rehabilitation, infection disease, general surgery, brain surgery, eye and ear, nose and throat, orthopedics, urology clinics for at least a week constituted the study population at a state hospital. The inclusion criteria were: being conscious, alert, able to communicate verbally, capable of answering questionnaires, and agreeing verbally to participate in the study. Informed consent to the study design was obtained from all patients. The personnel such as teachers, employees and civil servants working at the Health School and at hospital who do not have sleep and fatigue problems, and any health problems constituted the control group. The number of patients was determined by using the stratified sampling method. The samples were divided into two groups according to the following reasons: sleeping problems are seen in internal medicine sleeping and fatigue problems were mostly related to their various illnesses (75 patients) (McCann & Boore 2000, Bourguignon et al. 2003, Doğan et al. 2005, Strober & Arnett 2005, Pollard et al. 2006, Uhlin & Edéll-Gustafsson 2006, Lee et al. 2007); in surgical clinics, patients sleeping and fatigue problems were related to pain, limitation of movements and worries related to operations (75 patients) (Raymond et al. 2001, Doğan et al. 2005, Privette et al. 2009). The description of the patient and control groups were similar (p>0.05), and are shown in Table 1.

**Questionnaires**

As the data gathering tools, a questionnaire form, Pittsburgh Sleep Quality Index (PSQI) and Visual Analogue Scale for Fatigue (VAS-F) were used. The questionnaire included four sociodemographic questions such as age, gender, education level, and marital status and one question related to have been having a treatment in clinics.

The questionnaire was developed by the researchers. The time needed to answer the questionnaire was a few minutes. Buysse et al. (1989) developed the PSQI that is a self-rated questionnaire to measure sleep quality in clinical population. Ağargün (1996) conducted its validity and reliability work in Turkey. PSQI is self-rated questionnaire that provides an index of sleep quality for a 1-month interval. The PSQI contains 24 questions. Nineteen questions were self-rating questions. First 18 questions include seven subcomponents such as quality of sleep, sleep
latency, length of sleep, sleeping habits, sleep disorders, usage of sleeping pills and daytime activity disorder. The roommate or partner of the inpatient answered five questions. Question 19 is not taken into consideration at scoring. Each component scores between 0 and 3 points. The total index score is between 0 and 21. The PSQI total score of 5 and above indicates bad sleep quality. The time needed to answer the PSQI was approximately 8-10 minutes. In this study, it was found that Cronbach’s alpha internal consistency coefficient was .66.

VAS-F, which measures patients’ perceived fatigue and energy, was developed in 1991 by Lee et al. The scale consists of 18 items related to fatigue and energy, has simple instructions, and is completed with minimal time and effort. For each question, the individuals are asked to choose a number from 0 to 10. A zero (0) would mean “no fatigue” and ten (10) would mean “exceeding fatigue” (Lee et al. 1991). The validity and the reliability of the Turkish version of VAS-F were established by Yurtsever and Bedük (Yurtsever & Bedük 2003). The time needed to answer the VAS-F was approximately 5-7 minutes. In this study, Cronbach’s alpha of fatigue subscale was .89 and energy subscale was .85.

Procedures
Since the hospital director’s approval is enough to carry out the descriptive studies in the hospital, the study was approved by the director of the hospital. The participants were informed about the aim and method of the study; they were told that their participation was voluntary, and that they have the right to withdraw at any point. Participants were told that all information would be kept strictly confidential. We applied the questionnaire, PSQI and VAS-F to patient and control groups in different places.

Statistical analysis
All data management and statistical analysis were performed using SPSS, Version 11.0 for Windows software (SPSS 1999). The frequencies, percentage, mean and standard deviations were calculated to give a general description of the data collected. Groups were compared at the bivariate level using t-tests for continuous variables and chi-square tests for categorical variables. Cronbach’s alpha coefficient was used for reliability analysis. Pearson product-moment correlation was performed for relationship of scales. One way-ANOVA analysis, independent group’s t test, and LSD post hoc test were used to determine which of the socio-demographic variables were related to the PSQI and VAS-F. For all the analyses, a P value less than .05 was considered to be statistically significant.

Results
Participants
A general description of the patients and control groups is given in Table 1. Of the total sample, 52% were male, 28.5% were of age 65 and over, 64.5% were married, and 27% had at most primary school education. Patient groups were less educated than were healthy control groups, but a statistically significant difference between their education levels were not found. Patients had higher scores than did healthy individuals on the PSQI and VAS-F Fatigue subscale. Control group had higher scores than did patients on the VAS-F Energy subscale.

Predictors of sleep quality
A statistically significant difference was found between PSQI and gender (p<0.05) in patients. In this respect, the patient’s age, marital status, and education levels were not considered to influence the patient’s sleep quality (p>0.05). In control group, gender (p<0.01) and marital status (p<0.05) were found to be significant predictors of sleep quality. In both groups, female individuals had worse sleep quality than males. Single + widowed + divorce individuals had worse sleep quality than married individuals in the control group (Table 2).
### Table 1. Description of sample by group (n=200)

<table>
<thead>
<tr>
<th></th>
<th>Total sample (n=200)</th>
<th>Patient group (n=150)</th>
<th>Control group (n=50)</th>
<th>Significance test $\dagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (% male)</td>
<td>52.0</td>
<td>51.3</td>
<td>54.0</td>
<td>$X^2=0.107$; df 1</td>
</tr>
<tr>
<td>Age (% 65 and over)</td>
<td>28.5</td>
<td>30.0</td>
<td>24.0</td>
<td>$X^2=5.087$; df 3</td>
</tr>
<tr>
<td>Marital status (% married)</td>
<td>64.5</td>
<td>68.0</td>
<td>54.0</td>
<td>$X^2=3.210$; df 1</td>
</tr>
<tr>
<td>Education level (%)</td>
<td>27.0</td>
<td>31.3</td>
<td>16.0</td>
<td>$X^2=9.725$; df 5</td>
</tr>
<tr>
<td>PSQI Score: mean (SD)</td>
<td>6.37 (3.38)</td>
<td>6.63 (3.34)</td>
<td>5.60 (3.41)</td>
<td>$t=1.881$; df 198</td>
</tr>
<tr>
<td>VAS-F Score: mean (SD)</td>
<td>83.66 (23.37)</td>
<td>83.52 (22.94)</td>
<td>84.08 (24.84)</td>
<td>$t=-0.145$; df 198</td>
</tr>
<tr>
<td>VAS-F Fatigue Score:</td>
<td>56.34 (25.57)</td>
<td>57.60 (24.04)</td>
<td>52.56 (29.64)</td>
<td>$t=1.210$; df 198</td>
</tr>
<tr>
<td>VAS-F Energy Score:</td>
<td>27.32 (10.62)</td>
<td>25.92 (10.06)</td>
<td>31.52 (11.23)</td>
<td>$t=-3.309$; df 198</td>
</tr>
</tbody>
</table>

$\dagger$Patients and control groups, p>0.05

$p<0.001$
### Table 2. Socio-demographic variables to the Visual Analogue Scale for Fatigue (VAS-F) in patient and control group’s individuals

<table>
<thead>
<tr>
<th>Socio-demographic variables</th>
<th>Patient group n (%)</th>
<th>PSQI Scores X± SD</th>
<th>VAS-F Scores X± SD</th>
<th>Energy X± SD</th>
<th>Control group n (%)</th>
<th>PSQI Scores X± SD</th>
<th>VAS-F Scores X± SD</th>
<th>Energy X± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>-Female</td>
<td>73 (48.7)</td>
<td>7.28±3.45</td>
<td>62.10±21.01</td>
<td>24.90±9.30</td>
<td>23 (46.0)</td>
<td>7.00±3.89</td>
<td>67.08±30.22</td>
<td>28.17±12.71</td>
</tr>
<tr>
<td>-Male</td>
<td>77 (51.3)</td>
<td>6.01±3.13</td>
<td>53.33±26.02</td>
<td>26.88±10.69</td>
<td>27 (54.0)</td>
<td>4.40±2.43</td>
<td>40.18±23.17</td>
<td>34.37±9.09</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>-20-34</td>
<td>36 (24.0)</td>
<td>6.11±3.24</td>
<td>56.36±27.01</td>
<td>27.77±11.57</td>
<td>20 (40.0)</td>
<td>5.60±3.25</td>
<td>50.15±30.72</td>
<td>33.55±12.17</td>
</tr>
<tr>
<td>-35-49</td>
<td>29 (19.3)</td>
<td>6.82±3.47</td>
<td>54.68±26.72</td>
<td>26.34±10.27</td>
<td>9 (18.0)</td>
<td>5.22±2.94</td>
<td>48.44±27.15</td>
<td>30.77±7.88</td>
</tr>
<tr>
<td>-50-64</td>
<td>40 (26.7)</td>
<td>6.52±2.77</td>
<td>60.40±25.13</td>
<td>26.15±5.94</td>
<td>9 (18.0)</td>
<td>4.33±1.87</td>
<td>56.66±30.55</td>
<td>30.00±11.86</td>
</tr>
<tr>
<td>-65 +</td>
<td>45 (30.0)</td>
<td>7.02±3.82</td>
<td>58.00±18.67</td>
<td>23.95±6.01</td>
<td>12 (6.0)</td>
<td>6.83±4.66</td>
<td>56.58±31.81</td>
<td>29.83±12.08</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>-Married</td>
<td>102 (68.0)</td>
<td>6.88±3.41</td>
<td>57.39±23.61</td>
<td>25.77±9.82</td>
<td>27 (54.0)</td>
<td>4.66±2.67</td>
<td>49.51±26.22</td>
<td>29.70±10.39</td>
</tr>
<tr>
<td>-Single + Widowed + Divorce</td>
<td>48 (32.0)</td>
<td>6.10±3.17</td>
<td>58.06±25.18</td>
<td>26.22±10.65</td>
<td>23 (46.0)</td>
<td>6.69±3.90</td>
<td>56.13±33.46</td>
<td>33.65±12.03</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Illiterate</td>
<td>38 (25.3)</td>
<td>7.44±3.35</td>
<td>62.34±15.75</td>
<td>22.97±8.37</td>
<td>9 (18.0)</td>
<td>5.66±3.27</td>
<td>60.33±27.09</td>
<td>28.33±12.54</td>
</tr>
<tr>
<td>-Literate</td>
<td>14 (9.3)</td>
<td>6.57±4.53</td>
<td>54.21±23.06</td>
<td>24.14±11.34</td>
<td>9 (18.0)</td>
<td>4.88±2.52</td>
<td>51.44±27.67</td>
<td>35.66±5.52</td>
</tr>
<tr>
<td>-Primary school</td>
<td>47 (31.3)</td>
<td>6.25±2.90</td>
<td>54.19±22.18</td>
<td>26.65±8.00</td>
<td>8 (16.0)</td>
<td>7.12±3.97</td>
<td>58.87±28.86</td>
<td>22.00±12.40</td>
</tr>
<tr>
<td>-Secondary school</td>
<td>18 (12.0)</td>
<td>6.50±3.46</td>
<td>70.55±20.91</td>
<td>23.27±8.68</td>
<td>6 (12.0)</td>
<td>4.83±2.99</td>
<td>39.50±19.36</td>
<td>36.33±7.94</td>
</tr>
<tr>
<td>-High school</td>
<td>14 (9.3)</td>
<td>6.78±3.04</td>
<td>46.71±35.71</td>
<td>33.64±12.35</td>
<td>9 (18.0)</td>
<td>7.00±4.52</td>
<td>68.77±35.09</td>
<td>32.22±14.60</td>
</tr>
<tr>
<td>-University</td>
<td>19 (12.7)</td>
<td>6.00±3.59</td>
<td>54.84±32.14</td>
<td>28.10±12.40</td>
<td>9 (18.0)</td>
<td>4.00±2.44</td>
<td>32.77±26.71</td>
<td>35.11±6.66</td>
</tr>
</tbody>
</table>

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Table 3. The distribution of the mean PSQI in patient and control groups

<table>
<thead>
<tr>
<th>Mean PSQI Scores</th>
<th>Patient Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>(X \pm SD)</td>
</tr>
<tr>
<td>5 and over</td>
<td>104 (69.3)</td>
<td>6.63±3.34</td>
</tr>
<tr>
<td>4 and under</td>
<td>46 (30.7)</td>
<td>(Max:17, Min:0)</td>
</tr>
</tbody>
</table>

Table 4. The distribution of the mean PSQI and VAS-F scores of patients according to the clinics they were in

<table>
<thead>
<tr>
<th>Groups</th>
<th>n (%)</th>
<th>PSQI Scores</th>
<th>VAS-F Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(X \pm SD)</td>
<td>t p</td>
<td>(X \pm SD)</td>
</tr>
<tr>
<td>Internal clinics</td>
<td>75 (50.0)</td>
<td>6.69±3.35</td>
<td>57.14±23.75</td>
</tr>
<tr>
<td>Surgical clinics</td>
<td>75 (50.0)</td>
<td>6.57±3.35</td>
<td>58.06±24.48</td>
</tr>
</tbody>
</table>

Table 3 presents the distribution of the mean PSQI in patient and control group. As seen in Table 3, the mean PSQI scores of the patients are found higher than that of control group, but a statistically significant difference between their sleep qualities were not found (p>0.05).
The mean PSQI scores of the patients in Table 4 were compared according to the clinics they were in, the difference was not found to be significant (p>0.05). The sleep quality of patient’s surgical clinics was worse than that of internal clinic patients.

**Fatigue**

In patients, there was a significant difference between fatigue subscale and gender (p<0.01), education level (p<0.05), energy subscale and education level (p<0.05). There was a significant difference between the patient groups of education level compared by using LSD post hoc test. In control group, gender was found to be the only significant factor of fatigue (p<0.01). In both groups, female individuals were more fatigued and less energetic than male individuals. Secondary school graduate and illiterate individuals were more fatigued than the others; illiterate subjects had less energy than the others in patient group (Table 2).
The mean VAS-F scores of the patients were compared according to the clinics they were in, the difference was not found to be significant (p>0.05) and shown in Table 4. The surgical clinic patients were more fatigued and less energetic than internal clinic patients.
The sleep quality was significantly correlated to VAS-F score (r= .273, p= 0.001).

**Discussion**

This study was designed to provide objective measures of the quality of sleep and severity of fatigue. When the literature was examined, it was seen that sleep quality scale results pointed out high scores for hospitalized patients in the original studies of Lenhart and Buysse (2001), Frighetto et al. (2004), Doğan et al. (2005), Young et al. (2008), Humphries (2008), Lane and East (2008), and Young et al. (2009). Our findings are in line with the Uhlin and Edell-Gustafsson (2006), Brown et al. (2007), and Jones et al. (2009) studies in which there was fatigue in hospitalized patients.
Doğan et al. (2005) and Trible et al. (2002) found that gender was related to sleep quality. These studies show that sleep quality of female individuals were worse than male individuals. Similarly in this study, it was found that sleep quality was associated with gender, females in both in patient and control groups had worse sleep quality than males. The reason for this difference could be due to sexual discrimination by society, heavier duties of females at home and in society, and males having more often rest periods than females during the day. However, Edéll-Gustafsson et al. (2003) has found that men consider their quality of sleep to be significantly better than women. Vitiello et al. (2004) found that a considerable correspondence between subjective and objective sleep quality was observed for men, but not for women.

Similarly, our findings are in line with another study that shows the difference between sleep quality and patient’s age, marital status, and education levels had no statistical difference (Doğan et al. 2005). In this study, increasing age of individuals worsened sleep quality. Increasing age was associated with less sleep quality. There are many studies, which indicate sleep quality gets worse and time of staying awake during the night increases as age increases (Buysse et al. 1991, Tribl et al. 2002, Doğan et al. 2005, Potter & Perry 2009). This may be caused by lesser sleep requirements of older people. For sleep effectiveness, length of hospitalization resulted in lower scores. Thus, for patients with prolonged duration of hospital stay, special attention should be paid to their sleep patterns (Frighetto et al. 2004). Vitiello et al. (2004) found that indicating that while aging results in significant changes in sleep. Another similarity in our study as compared to the previous report is that we found the highest mean PSQI score in the single + widowed + divorced group than married group. We found that the highest mean sleep quality was found for the illiterate group (7.44), a result that is consistent with the previous study (Doğan et al. 2005).

In this study, the mean PSQI scores of patients are found higher than that of control group. Previous investigations have revealed that the most common factors affecting sleep in hospitalized patients include the effects of illness, environmental sleep disruption, additional medication, anxiety, and depression. Besides, sleep quality effects factors such as pain, breathing problems, pre or post operational problems, fear, worry, patients staying in a different environment that normal, temperature, noise produced by machines, footsteps, voices of staff, radio or television sounds, creaking doors, thoughts of not carrying out their responsibilities at home. Unit environmental and personal factors, factors that are amenable to therapeutic interventions, strongly influence the sleep experience (Buyssse et al. 1989, Buyssse et al. 1991, Lenhart & Buysses 2001, Tranmer et al. 2003, Frighetto et al. 2004, Doğan et al. 2005, Young et al. 2008, Humphries 2008, Lane & East 2008, Young et al. 2009).

Past surveys have implied that internal clinic patient’s sleep quality was worse (Young et al. 2008, Young et al. 2009). Different studies have showed that sleep quality of patients in surgical clinics were worse than that of internal clinic patients (Tranmer et al. 2003, Doğan et al. 2005, Lane & East 2008). Lane and East (2008) study found that environmental noise, pain and tension were most likely to disrupt the sleep of surgical patients. It has also suggested four recommendations to improve the sleep of hospital patients. Thus, result reported in this study is in line with the results of the previous studies. The reason for low quality of sleep in patients hospitalized in surgical clinic might be preoperative worries, fears and postoperative pains experienced in preoperative period. It was found that along with worse sleep quality, also the fatigue levels were higher in surgical clinic patients compared to internal clinic patients. The relation between sleep quality and fatigue supports this finding. In other words, low sleep quality may cause fatigue or fatigue may cause low sleep quality.

Fatigue is a common and generally overlooked symptom in chronic disease population (Belza 1995, Swain 2000, Barnes 2002, Wolfe 2004, Uhlin & Edell-Gustafsson 2006, Theander et al. 2008, Hägglund et al. 2008). Belza et al. (1995) and Huyser et al. (1998) found that gender was related to fatigue. However, patients reported a
moderate level of fatigue (mean of 44 on the SF-36); with no difference in the reports of men and women in Gift and Shepard study (Gift & Shepard 1999). These studies show that women reported more fatigue than men. In this study, it was found that there was a strong association between fatigue subscale and gender, and the average fatigue level of female participants was higher than male participants. Secondary school graduate and illiterate individuals were more fatigued than the others. The reason for this might be the fact that the literate individuals are less capable of coping with fatigue. This study showed that sleep quality was related to fatigue. Low sleep quality may cause fatigue, and fatigue may lower sleep quality. In other words, there is a parallel relation between them and they may trigger each other. It is significantly associated with individual factors such as sleep problems, poor physical health. Insomnia in the hospitalized patient leads to increased fatigue, irritability and aggressiveness, decreased pain tolerance (Frighetto et al. 2004). The score for cognitive behavioral fatigue, dysphoria and somatic effects of sleep loss were also higher in our study than have been reported among men and women in the general Swedish population aged 50-64 years (Broman et al. 1996).

This study has two limitations. First, our sample size is relatively small to generalize. Second, uses of drugs with sedating, lengths of stay, previous inpatient experience, disease type of patients were not investigated in this study. If these variables have been investigated, different results may be discovered. Despite these limitations, these study findings of sleep quality and fatigue patients may have implications for researchers and health care providers.

Conclusion

These results suggest that sleep quality and fatigue of inpatients is worse than healthy individuals. Poor sleep can lead to increased fatigue, negative mood and disorientation. Findings indicate the need for the clinical nurse to assess patient sleep patterns during hospitalization and then evaluate the need for sleep promotion strategies. Consequently, nurses should be more sensitive to patients’ sleeping problems. Nurses should also determine the factors that cause sleep problem and fatigue in patients. They should give better service in regard to determined etiologies.

Acknowledgments

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