Assessment of subjective sleep quality in iron deficiency anaemia

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Abstract

Objectives: We aimed to assess the effect of anemia on subjective sleep quality in patients with iron deficiency anemia (IDA).

Methods: One hundred and four patients diagnosed with IDA and 80 healthy individuals, who are gender and age matched, were included in the study. All participants were requested to fill 3 forms: a socio-demographic form (age, gender, marital status, income level and educational status), hospital anxiety and depression (HAD) scale and pittsburgh sleep quality index (PSQI).

Results: According to the HAD scale, the average anxiety score was found 9.24±4.37 in patients and 7.58± 4.07 in controls. And, the average depression score was 7.53±4.10 in patients and 6.41±2.74 in controls. The total sleep quality score was 6.71±3.02 in patients and 4.11±1.64 in controls. There was a statistically significant difference in terms of anxiety, depression and sleep quality scores. Linear regression analysis showed no association between anxiety and depression with poor sleeping.

Conclusion: IDA affects sleep quality irrespective of psychological symptoms such as depression and anxiety.

Keywords: Iron deficiency anemia, sleep quality, anxiety

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Introduction

After a negative iron balance in the body due to reasons such as chronic blood loss, increased iron demand, and absorption disorder, hemoglobin synthesis is compensated by mobilization of iron from stores and when the stores of iron fail to release adequate iron, iron deficiency anemia (IDA) develops[1]. Just like in our country, iron deficiency is the most common cause of anemia in the world and is more prevalent in women than men[2,3]. It has been known that more than 30% of those attending to hospitals in developed countries are anemic and the said ratio is much higher in developing countries.

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In developed countries, 3% of adult males, 20% of adult females and 50% of pregnant women have iron deficiency anemia[4,5]. Loss of appetite, tiredness, pale skin, lethargy, headache, tinnitus and impairments in cognitive and intellectual functions can be observed in IDA[6]. Iron plays a key role in the metabolism of monoamines in the brain thus iron deficiency leads to symptoms such as apathy, drowsiness, irritability and lack of attention occur due to impaired monoamine oxidase activity[7]. Patients affected from iron deficiency display many behavioral and emotional signs and have symptoms similar to the ones in depressive individuals[8].

Sleep is the period of physiological, periodic and reversible changes in consciousness and behaviour[9]. It is defined as a reversible state where interaction of the organism with the environment is lost temporarily, partially and periodically[10]. Nearly 30-33% of the society has a significant sleep problem. The said ratio is higher in older adults, those having a psychiatric disorder and specific groups with learning difficulties[11-14]. In various

studies, advanced age, female gender, stress, depression, anxiety, alcohol, substance abuse and physical diseases are the important factors causing sleep disorders[15,16].

Due to the key role of iron in the metabolism of monoamines in the brain and the role of the same monoamines in sleep physiology, we stipulated that sleep quality might deteriorate in IDA. In this context, studies usually have been performed in pediatric populations. To the best of our knowledge, there exist no studies examining subjective sleep quality in adult patients with IDA. Therefore, we aimed evaluating sleep quality in adult patients diagnosed with IDA.

Materials and methods

Our study is a prospective and cross-sectional study which has been carried out at Cumhuriyet University, medical faculty, hematology clinic between January 2013 and June 2013. Ethical committee approval was obtained from the ethics commitee of the medical faculty of Cumhuriyet University, and the study was in accordance with the declaration of Helsinki. One hundred and four patients diagnosed with IDA and gender and age matched 80 healthy individuals were included in the study. Loss of appetite and tiredness were the most common presentations. It was confirmed that there were no accompanying neurological or endocrinological diseases in patients with IDA.

The diagnosis of IDA was made by evaluating the levels of hemoglobin, transferrin saturation -calculated by the ratio of serum iron to serum iron binding capacity- and ferritin. Hemoglobin level below 13 mg/dL in men and 12 mg/dL in women, transferrin saturation ratio below 15%, and ferritin level below 15 ng/mL indicated IDA. The control group was composed of healthy volunteers who were regular blood donors in our hospital. Those having systemic diseases such as diabetes mellitus, hypertension, congestive heart failure, chronic obstructive pulmonary disease, coronary artery disease, rheumatoid arthritis, systemic lupus erythematosus and ankylosing spondylitis and any medication use were excluded from the study. The participants were asked to complete a socio-demographic form (age, gender, marital status, income level and educational status), hospital anxiety and depression scale and Pittsburgh sleep quality index.

Anxiety and depression parameters were tested by the hospital anxiety and depression scale (HAD). As the scores increase, depression and anxiety increase[16-17]. The Turkish version was developed by Aydemir[18] et al. The Pittsburgh sleep quality index (PSQI) was used to measure sleep disturbance. It is consisted of 19 items and over 7 domains that include subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications and daytime dysfunction. Greater PSQI scores show worse sleep quality. A global sum of 6 or greater indicates a "poor" sleeper[17-19]. The Turkish version was developed by Agargun[20] et al.

Statistical analysis

SPSS 15.0 statistical program (SPSS, version 15.0 for Windows; SPSS, Chicago, IL, USA) was used for statistical analysis. Continuous variables are presented as means ± SDs, and categorical variables are presented as percentages. Independent-sample t- test were used to compare patients and healthy individuals with regard to the study variables. Chi-square tests were used to compare data presented as percentages. Correlation analysis was performed using Pearson's coefficient of correlation. Linear regression analysis was utilized to assess the contributions of age, anxiety, and depression to poor sleeping.

Results

The patient population (average age: 32.57 ±10.19 years) were composed of 104 patients [81 (77.9%) female and 23 (22.1%) male]. The control group (average age: 30.44 ± 9.98 years) had similar socio-demographic characteristics and were composed of 80 healthy individuals [61 (76.2%) female and 19 (23.8%) male]. In terms of age and gender distribution, there was no statistically significant difference between the groups (t=1.42 p=0.16 ve x^2=0.069 p=0.793). The socio-demographic characteristics of the study groups are given in Table 1.

In terms of haemoglobin, hematocrit and MCV values, there was a statistically significant difference between the groups (t=16.95, p=0.001; t=6.77, p=0.001; t=15.78, p=0.001, respectively). The other hemogram parameters did not show any differences between the groups. The detailed hemogram values of the groups are shown in Table 2. In the patient group, the average serum ferritin level and total iron binding capacity were measured as 7.15±5.28 and 412.10±60.4, respectively.

In HAD scale, the average anxiety score was found

Table 1. Socio-demographic characteristics of the study groups

	Patients n (%)	Controls n (%)	Statistics (x^2)	p value
Gender				
Female	81 (77.9)	61 (76.2)	0.069	0.793
Male	23 (22.1)	19 (23.8)		
Educational status				
Primary school	33 (31.7)	27 (33.8)		
Secondary school	19 (18.3)	16 (20.0)	0.699	0.874
High school	36 (34.6)	28 (35.0)		
University	16 (15.4)	9 (11.2)		
Marital status				
Married	66 (63.5)	55 (68.8)	0.562	0.454
Single	38 (36.5)	25 (31.2)		
Income status				
Low-income	26 (25.0)	21 (26.2)	0.038	0.981
Middle-income	66 (63.5)	50 (62.5)		
High-income	12 (11.5)	9 (11.2)		

Table 2. Hemogram values

	Patients mean ± SD	Controls mean ± SD	T	p
Haemoglobin	10.05 ± 1.47	13.12 ± 0.76	16.96	**0.001***
Hematocrit	32.62 ± 3.64	36.11 ± 3.21	6.77	**0.001***
MCV	70.28 ± 7.84	85.24 ± 3.67	15.78	**0.001***
White Blood Cell	6.31 ± 1.37	6.16 ± 1.48	0.67	0.504
MCH	21.93 ± 3.43	21.81 ± 3.31	0.04	0.958
MCHC	30.90 ± 3.28	31.07 ± 3.60	0.33	0.741

*p<0.05, significant
MCV: mean corpuscular volume
MCH: mean corpuscular hemoglobin
MCHC: mean corpuscular hemoglobin concentration

9.24±4.37 in patients and 7.58±4.07 in controls (t=2.64, p=0.009). The average depression score was 7.53±4.10 in patients and 6.41±2.74 in controls (t=2.10, p=0.037). There was a statistically significant difference in terms of anxiety and depression scores. The number of patients who had an anxiety level above the cut-off score was 45 (43.3%) and it was 22 (27.5%) in the control group (x^2= 4.856 p=0.028). The number of patients who had a depression score above the cut-off score was 49 (47.1%) and it was 26 (32.5%) in the control group (x^2=4.00, p=0.045).

In PSQI, 70 (67.3%) patients and 32 (40.5%) controls reported a bad sleep quality. The number of patients who reported a bad sleep quality were statistically significantly higher than the controls (x^2=13.072; p<0.001). The total sleep quality score was 6.71±3.02 in patients and 4.11±1.64 in controls. In terms of total PSQI score, there was a statistically significant difference between the groups (t= 6.94, p<0.001).

With respect to the subscales of PSQI, subjective sleep score was found 1.33±0.81 in patients and 0.85±0.58 in controls, so, we have found a statistically significant difference between groups (t= 4.48, p<0.001). Sleep disorder score was 1.63±0.75 in patients and 0.93±0.57 in controls, so, we have found a statistically significant difference between groups (t=7.04, p<0.001). PSQI sucbscale scores of the groups are given in Table 3. In the regression analysis, we evaluated whether the presence of "sleep disorder" is associated with depression and anxiety. Linear regression analysis showed no association of anxiety (partial correlation coefficient: -0.176; p = 0.101) and depression (partial correlation coefficient: -0.086; p = 0.430) with poor sleeping.

Table 3. PSQI subscales

	Patients	Controls	Statistics	
	(mean ± SD)	(mean ± SD)	(t)	(p)
Subjective sleep quality	1.33 ± 0.81	0.85 ± 0.58	4.48	**0.001***
Sleep latency	1.33 ± 0.81	0.73 ± 0.64	5.49	**0.001***
Sleep duration	0.62 ± 0.84	0.56 ± 0.59	0.48	0.632
Habitual sleep efficiency	0.60 ± 0.77	0.38 ± 0.51	2.22	**0.028***
Sleep disturbances	1.63 ± 0.75	0.93 ± 0.57	7.04	**0.001***
Use of sleep medication	0.02 ± 0.20	0.00 ± 0.00	0.88	0.382
General dysfunction	1.19 ± 0.89	0.68 ± 0.63	4.40	**0.001***
Total sleep disorder	6.71 ± 3.02	4.11 ± 1.64	6.94	**0.001***

*p<0.05, significant

Discussion

Iron deficiency has been reported to cause behavioral and developmental symptoms by affecting transmitters such as serotonin, noradrenaline and dopamine, myelination, and the metabolic activity in the neurons[21,22]. It has been also reported that brain functions such as cognition and learning are affected in patients with IDA[23]. Peirano et al.[24] reported that relative to controls, children with IDA showed: a) longer duration of REM sleep episodes in the first third and shorter in the last third; b) more REM sleep episodes in the first third and fewer in the second third; and c) shorter latency to the first REM sleep episode and shorter NREM stage 2. So, their results show that IDA is associated with long-lasting alterations in the temporal organization of sleep patterns[24.] Peirano et al.[24] suggested that the changes in the neurotransmitter metabolism due to iron deficiency, pscyhological status or a possible restless leg syndrome (RLS) affected sleep negatively. These results could be explained by some mechanisms. One possible explanation for the differences that long-lasting effects of iron deficiency on the developing dopamine (DA) system are a promising example[25,26].

Iron has a complex effect on dopaminergic function. It is a cofactor for tyrosine hydroxylase and is integral to D2 receptor function[27]. Neuromodulation by the DA system plays an important role in sleep regulation, including the modulation of REM sleep quality, quantity, and timing[28,29]. Holst et al.[30], studied sleep–wake regulation in humans and combined pharmacogenetic and neurophysiologic methods to analyze the effects of the 3'-UTR variable-number-tandem-repeat polymorphism of the gene (DAT1, SLC6A3) encoding dopamine transporter. Their findings suggested that the dopamine transporter contributes to homeostatic sleep–wake regulation in humans. Fifel et al.[31], investigated alterations of circadian rhythms in non-human primate models following lesion of the dopaminergic nigro-striatal system.

Their results are of clinical importance and stress that sleep/wake disturbances associated with DA loss may be more severely affected than previously thought, in particular in sub-optimal lighting conditions. The dynamic balance between neurotransmitter systems is another important consideration. The ultradian alternation of NREM sleep/REM sleep appears to be controlled by a permanent interacting balance between brainstem aminergic and cholinergic neuronal discharges[32.] An additional explanation could be differing amounts of sleep alterations. In particular, RLS and periodic limb movements during sleep have been associated with conditions characterized by compromised iron status[33]. It has been known that iron deficiency plays an important role in the physiopathology of the RLS characterized by an irresistible urge to move legs as well as motor restlessness.

Iron treatment has been thought to increase sleep quality of the patients by decreasing RLS complaints. In a study of Allen et al.[34], prevalence of clinically significant RLS (RLS sufferers) was 23.9% in 251 patients with IDA, nine times higher than the general population. In another study, the said ratio was reported as 40%[35]. Patients with RLS were excluded from this study. In the present study, nearly 68% of the patients with IDA were shown to have an impaired sleep quality. Our findings support the idea that sleep quality is impaired in a significant portion of patients with IDA.

Depression and anxiety disorders are among the psychological disorders that affect sleep quality negatively. In a study conducted by Onder et al., depressive disorder was found to be a common disorder in patients with anemia[36]. In our study, similar to the literature, a major portion (nearly 45%) of the patients had high anxiety and depression scores. Son et al. reported that cognitive functions were worse in anemia patients when compared to healthy controls, which was shown to be associated with depressive disorder[37]. In the present study, logistic regression analysis showed that anemia affected sleep quality irrespective of the psychological symptoms.

To the best of our knowledge, there is no study in the literature that evaluated the association between laboratory values and sleep quality in adult population having IDA. Yehuda and collageus[38], examined hemoglobin levels and showed that sleep-deprived attention deficit hyperactivity disorder (ADHD) patients also suffer also from iron deficiency. However, Yehuda et al.[38], were not clear if iron deficiency was one of the core symptoms of this pediatric group or it was a consequence of poor food intake habits. Another study of the Yehuda[39], showed that iron deficiency might be associated with sleep disturbances and lower intelligence quality at pediatric population.

We have found no significant relation between the sleep quality and laboratory values of the patients. In our study, lack of significant correlation between lab-

oratory values and sleep quality scores was not an expected result. Shariatpanaahi et al.[40] reported that there was a weak correlation between serum ferritin level and depression. In another study, it was shown that serum ferritin and hemoglobin levels had no significant relation with depression level. Similar to the results of the previous studies, the results of our study showed that the sleep quality level could not be evaluated through hemogram, serum iron and ferritin levels in patients with IDA.

Limitations

Our study had some limitations. The first limitation was evaluating depression anxiety and sleep quality through self-report scales. The second limitation was not performing polysomnographic measurements. There is a possible discrepancy between objective sleep evaluation (by EEG or by Actigraph) and subjective evaluation (PSQI). Conducting a cross-sectional study could have affected the results, too.

Conclusion

Subjective sleep quality was evaluated in patients with IDA in the present study. The results showed that IDA affects sleep quality irrespective of psychological symptoms such as depression and anxiety. And also, it was shown that subjective sleep quality was worse in patients with IDA when compared to the healthy controls. The effects of anemia treatment on sleep quality were not assessed due to the cross-sectional nature of the study. Further studies, where anemia patients should be followed-up for an extended period of time and evaluated by polysomnography, are required.

Conflict of interest statement:

There is no conflict of interest.

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