RESEARCH ARTICLE

The relationship between serum bicarbonate, pH level and sleep quality in haemodialysis patients: A cross-sectional study from Turkey

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Abstract

Objective: To investigate the relationship of blood pH and bicarbonate levels with sleep disorders in patients with end-stage renal disease.

Methods: The cross-sectional study was conducted at Kocaeli Derince Health Practice and Research Center, Kocaeli, Turkey, in July 2015, and comprised stable haemodialysis patients aged over 18 years who had undergone at least 3 months of treatment. The Pittsburgh sleep quality index was used to assess sleep quality, and the Epworth sleepiness scale was used to assess sleepiness. Blood urea nitrogen levels were measured to determine dialysis success. SPSS 17 was used for data analysis.

Results: Of the 62 patients, 22(35.4%) were good sleepers, while 40(65.6%) were bad sleepers, and 11(17.7%) had excessive daytime sleepiness. There was no significant difference between poor and good sleepers with respect to venous pH (p=0.197) and bicarbonate (p=0.305) levels. Also, the two levels did not differ significantly between patients with routine or excessive daytime sleepiness (p>0.05). Patients with excessive daytime sleepiness had significantly lower calcium (p=0.046) and higher creatinine (p-0.014) levels and were older (p=0.01). Age was the only independent predictor of both the index and the scale scores (p<0.05 each).

Conclusions: Sleep disorders and sleepiness were found to be high in haemodialysis patients and there was a strong correlation between sleep disturbance and age. There was no correlation of either state with patients' bicarbonate or venous pH values.

Keywords: Acidosis, Bicarbonate, Haemodialysis, Insomnia, Sleep. (JPMA 70: 42; 2020).
https://doi.org/10.5455/JPMA.298730

Introduction

Chronic kidney disease (CKD) is an important public health issue. Hospitalisation, rehospitalisation and presentations to emergency department (ED) in these patients are higher than the general population, which is associated with increased healthcare expenditure.[1-3] Sleep disorders are an important issue in haemodialysis patients.[4] It has been shown that patients with end-stage renal disease (ESRD) are more likely to have sleep disorders than the normal population. Sleep structure is altered in these patients, and they frequently suffer from a variety of sleep disorders.[5-7] Furthermore, these problems contribute to an increased morbidity and mortality in these patients.[8,9] Another factor that plays an important role in the lives of haemodialysis patients is metabolic acidosis. Metabolic acidosis has been shown to be associated with nutritional problems, fatigue, renal osteodystrophy, and conditions that may be associated with sleep disorders, such as inflammation, but only few studies have evaluated the relationship between sleep disturbances and metabolic acidosis.[10,11] Among them, no study has evaluated the relationship of excessive daytime sleepiness (EDS) with either blood potential of hydrogen (pH) or bicarbonate levels. The current study was planned to investigate the relationship of blood pH and bicarbonate levels with sleep disturbances in ESRD patients.

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Patients and Methods

The cross-sectional study was conducted at Kocaeli Derince Health Practice and Research Center, Kocaeli, Turkey, in July 2015. After approval was obtained from the institutional ethics committee, the sample size was calculated using G power software assuming alpha to be 0.05, beta 0.80, and the effect size of 0.3.[12] The sample was raised with consecutive stable haemodialysis patients aged over 18 years who had undergone at least 3 months of treatment at the hospital's Haemodialysis Unit. Informed consent was obtained from all the subjects.

Those excluded were patients with haemolytic disease or a recent blood transfusion history, chronic obstructive pulmonary disease (COPD), obstructive sleep apnoea, active liver disease, malignancy, peripheral revascularisation within the preceding 6 months, lower extremity ischaemic ulcer, acute coronary syndrome, cerebrovascular disease, alcohol usage, and anti-depressant or anti-psychotic drug treatment.

The subjects filled out questionnaires during dialysis sessions or while waiting for a dialysis session. Before the forms were filled out, detailed information on the illness was provided on the forms, and help in filling out the forms was provided if necessary.

The Epworth sleepiness scale (ESS) score was used to assess daytime sleepiness. The scale is a simple measure with 8 different everyday activities (watching television, reading a book in a sitting position, sitting in a public area quietly, riding in a car, lying down in the afternoon, talking to someone else, sitting quietly after lunch without alcohol, sitting in a car for a few minutes in the traffic) that are used to evaluate sleepiness or the potential to fall asleep. Each question has a 0-3 score range; 0 = no sleepiness, and 3 = excessive sleepiness. The total score range is 0-24, with scores >9 indicating EDS.[13] The ESS's test-retest reliability and acceptable validity have been reported,[14] and it has already been adapted to Turkish language.[15] For ESS assessment, patients were divided into two groups; score <9 and >9.

The Pittsburgh sleep quality index (PSQI) was used to assess overall sleep quality.[16] It has also been adapted to Turkish language.[17] It is a 19-item measure of sleep quality and impairment in the preceding month. It consists of 24 questions; 19 self-assessment questions, and 5 to be answered by a spouse or roommate. Eighteen questions are scored and divided into 7 components: sleep latency, subjective sleep quality, usual sleep activity, sleep duration, sleep medication use, sleep disturbance and daytime dysfunction. Each component is scored 0-3. The total score of the 7 components yields the total score. A total score >5 points indicates poor sleep quality. For PQSI assessment, patients were divided into 2 groups; score <5 and >5.

Demographic characteristics were recorded from the patients' hospital records. Samples for blood analysis were obtained during fasting just before the haemodialysis session. Blood for pH analysis was taken during the mid-dialysis days. Whole blood counts of blood urea nitrogen (BUN), creatinine, albumin, sodium, potassium, calcium, phosphorus, chloride, lipid profile, intact parathyroid hormone (PTH), serum C-reactive protein (CRP), and uric acid were obtained. BUN levels were measured to determine dialysis success. Venous blood samples were obtained immediately before the dialysis session to calculate blood pH, bicarbonate and anion gap values. The formula used for the anion gap calculation was: $(Na^+ + K^+) - (Cl^- + HCO_3^-)$.[18]

Data was analysed using SPSS 17. The results were expressed as mean and standard deviation (SD) or as frequencies and percentage as appropriate. Comparisons between groups were performed with Student's t test, and the Mann-Whitney U test was used for variables that were not normally distributed. Pearson's correlation test was used for normally distributed variables, and Spearman's rank correlation test was used for non-normally distributed variables. Fisher's exact test was used for comparisons of categorical variables between the groups. Factors reaching statistical significance and the traditional risk factors were then entered into a backward stepwise multiple linear regression analysis. $P<0.05$ was considered statistically significant.

Results

Of the 62 patients, 38(61.3%) were males and 24(38.7%) were females. The overall mean age was 58.37±11.42 years. The aetiology of renal insufficiency was diabetes mellitus 15(24.2%), hypertension (HTN) 20(32.3%), cancer 2(3.2%), glomerulonephritis 4(6.4%), vesico-ureteral reflux and pyelonephritis 5(8.1%), nephrolithiasis 5(8.1%) amyloidosis 1(1.6%), and unknown 10(16.1%). The mean duration of haemodialysis was 59.76±46.62 months (Table 1). The mean ESS score was 5.21±3.82, while the

Table-1: Baseline demographic characteristics.

Parameter	Value n,(%)
Male/female (n)	38(61.3) / 24(38.7)
Mean age (y)	58.37±11.42
Duration of haemodialysis, (months)	59.76±46.62
Presence of coronary artery disease (n) (Yes/No)	13(21) / 49(79)
Presence of hypertension (n) (Yes/No)	20(32.3) / 42(67.7)
Presence of diabetes mellitus (n) (Yes/No)	23(37.1) / 39(62.9)
Smoker/nonsmoker (n)	13(21) / 49(79)
Haemodialysis access (fistula/graft/catheter) (n)	56(90.3) / 2(3.2) / 4(6.5)
Married/unmarried (n)	49(79) / 13(21)
Self-reported economic status (satisfactory/unsatisfactory) (n)	26(42) / 36(58)
Educational status (primary school/ secondary school/tertiary school/university) (n)	54(87) / 3(4.9) / 4(6.5) / 1(1.6)

SD: Standard deviation

Table-2: Clinical and laboratory parameters.

Parameter	Value
Body mass index (kg/m^2)	26.31 ± 5.18
Systolic blood pressure (mmHg)	122.26 ± 24.25
Diastolic blood pressure (mmHg)	71.45 ± 11.43
BUN (mg/dL)	71.31 ± 19.88
Creatinine (mg/dL)	9.16 ± 2.69
Sodium (mEq/L)	137.27 ± 2.67
Potassium (mEq/L)	5.35 ± 0.71
Chloride (mEq/L)	105.94 ± 3.50
Corrected calcium (mg/dL)	8.64 ± 0.64
Phosphorus (mg/dL)	4.83 ± 1.27
Intact parathyroide hormone (pg/mL)	241.97 ± 188.67
Total cholesterol (mg/dL)	154.67 ± 38.66
Triglyceride (mg/dL)	152.34 ± 53.14
HDL-cholesterol (mg/dL)	37.12 ± 6.18
LDL-cholesterol (mg/dL)	90.48 ± 29.38
Serum albumin (g/dL)	3.55± 0.32
Hemoglobin (g/dL)	11.42 ± 1.34
Venous pH	7.31 ± 0.04
Venous bicarbonate (mEq/L)	18.41 ± 2.33
Anion gap	17.04 ± 2.48
spKt/V	1.50 ± 0.27
hs-CRP (mg/L)	6.63 ±0.37
Pittsburgh score	7.73 ± 3.93
Epworth score	5.21 ± 3.82

BUN: Blood urea nitrogen, hs-CRP: High sensitivity C-reactive protein, spKt/V: Single pool kinetic modeling / volume, HDL: High density lipoprotein, LDL: Low density lipoprotein.

mean PSQI score was 7.73±3.93 (Table 2). According to the PSQI score, 22(35.4%) patients were good sleepers, while 40(65.6%) were bad sleepers. Mean PSQI was 3.95±0.99 for good sleepers and 9.8±3.34 for bad sleepers. Compared to the good sleepers, the bad sleepers had a significantly higher body mass index (BMI) (p=0.02) and significantly older age (p=0.001) (Table 3).

There were 11(17.7%) patients with ESS score >9. Patients with EDS, compared to those with ESS <9, had significantly lower calcium (p=0.046), had higher creatinine (p=0.014) and were older (p=0.01). Venous pH (p=0.197) and bicarbonate (p=0.315) levels did not show any significant differences between good (PSQI ≤5) and bad (PSQI >5) sleepers. Also, there were no significant differences between patients with (ESS >9) or without (ESS ≤9) EDS with regard to venous pH (p=0.684) and bicarbonate (p=0.778) levels (Table 4).

Univariate correlation analysis showed that PSQI and ESS scores were correlated with hypocalcaemia and age (Table 5).

Age was the only independent predictor of both ESS (p<0.001) and PSQI (p=0.014) scores (Table 6).

Discussion

The current study found that pre-dialysis venous blood pH and bicarbonate levels had no effect on sleep and sleepiness and that the most significant factor associated with both sleep disturbance and sleepiness was older age.

In one study[19], which, to our knowledge, is the only study on this topic, both pH and bicarbonate levels were found to be related to sleep disturbance. Actually, the ideal blood pH and bicarbonate values in patients undergoing maintenance haemodialysis and the effect of these values on the lives of patients are very controversial issues. For example, it is known that

Table-3: Characteristics of patients according to their ESS and PSQI scores.

	≤9 ESS score	>9 ESS score	*p*	PSQI score ≤5	PSQI score >5	*p*
Age (y)	55.94 ± 12.49	66.55 ± 8.60	0.010	51.14 ± 11.98	61.50 ± 11.35	0.001
Male/Female	34/17	4/7	0.089	17/5	21/19	0.055
Educational Status (primary school/higher education)	43/8	11/0	0.330	21/1	33/7	0.240
Duration of hemodialysis (months)	59.71 ± 46.62	60 ± 48.89	0.985	57.75 ± 43.16	63.41 ± 53.21	0.651
Body mass index (kg/m2)	25.92 ± 5.22	28.11 ± 4.81	0.207	24.27 ± 4,53	27.43 ± 5.23	0.020
Systolic blood pressure (mmHg)	120.59 ± 24.52	130 ± 22.36	0.246	122.27 ± 27,76	122.25 ± 22.47	0.997
Diastolic blood pressure (mmHg)	70.98 ± 11.70	73.64 ± 10.26	0.489	71.36 ± 12.83	71.50 ± 10.75	0.965

ESS: Epworth sleepiness scale, PSQI: Pittsburgh sleep quality index.

Table-4: Laboratory results according to ESS and PSQI scores.

	≤9 ESS score	>9 ESS score	*p*-value	PSQI score ≤5	PSQI score >5	*p*-value
BUN (mg/dL)	71.37 ± 20.60	71.14 ± 17.10	0.973	72.24 ± 19.15	70.84 ± 20.52	0.794
Creatinine (mg/dL)	8.89±2.83	10.40±1.40	0.014	8.53 ± 2.55	9.50 ± 2.47	0.174
Sodium (mEq/L)	137.16 ± 2.84	137.82 ± 1.66	0.462	136.95 ± 2.42	137.45 ± 2.81	0.490
Potassium (mEq/L)	5.31 ± 0.73	5.57 ± 0.54	0.274	5.20 ± 0.68	5.44 ± 0.72	0.211
Chloride (mEq/L)	105.75 ± 3.73	106.82 ± 2.04	0.195	106.23 ± 3.07	105.78 ± 3.74	0.630
Corrected calcium (mg/dL)	8.72 ± 0.60	8.28 ± 0.60	0.046	8.80 ± 0.56	8.56 ± 0.64	0.120
Phosphorus (mg/dL)	4.70 ± 1.17	5.38 ± 1.51	0.116	4.45 ± 1.05	5.04 ± 1.33	0.075
Intact parathyroide hormone (pg/mL)	234.86±186.88	274.95±202.64	0.527	207.83 ± 149.87	261.3 ± 206.43	0.287
Total cholesterol (mg/dL)	160.86 ± 40.98	167.44 ± 30.16	0.618	154.67 ± 40.60	165.89 ± 38.28	0.274
Triglyceride (mg/dL)	149.68 ± 51.37	165.63 ± 58.45	0.356	140.83 ± 46.05	158.54 ± 55.80	0.217
HDL-cholesterol (mg/dL)	37.12 ± 6.18	37.12 ± 6.57	0.910	37.12 ± 7.34	37.12 ± 5.80	0.882
LDL-cholesterol (mg/dL)	90.48 ± 30.93	91.26 ± 20.88	0.915	86.62 ± 31.70	92.80 ± 28.22	0.456
Serum albumin (g/dL)	3.56 ± 0.34	3.54 ± 0.20	0.886	3.59 ± 0.25	3.54 ± 0.35	0.552
Hemoglobin (g/dL)	11.5 ± 1.31	11.03 ± 1.46	0.296	11.72 ± 0.77	11.26 ± 1.55	0.125
pH	7.31 ± 0.04	7.31 ± 0.03	0.684	7.30 ± 0.04	7.32 ± 0.03	0.197
Venous bicarbonate (mEq/L)	18.37 ± 2.40	18.60 ± 2.07	0.778	18.83 ± 2.07	18.19 ± 2.46	0.305
Anion Gap	17.28 ± 2.48	15.93 ± 2.28	0.103	16.81 ± 2.26	17.17 ± 2.61	0.598
spKt/V	1.48 ± 0.27	1.60 ± 0.21	0.211	1.45 ± 0.24	1.53 ± 0.27	0.224
hs-CRP (mg/L)	6.68 ± 3.01	6.39 ± 2.92	0.769	6.51 ± 2.95	6.70 ± 3.02	0.815
Score	3.75 ± 2.19	12 ± 1.89	<0.001	3.95 ± 0.99	9.80 ± 3.34	<0.001

ESS: Epworth sleepiness scale, PSQI: Pittsburgh sleep quality index, BUN: Blood urea nitrogen, hs-CRP: High sensitivity C-reactive protein, spKt/V: Single pool kinetic modeling / volume, HDL: High density lipoprotein, LDL: Low density lipoprotein.

Table-5: Variables correlation with PSQI and ESS scores.

	PSQI scores		ESS scores	
	r	*p*	*r*	*p*
Age	0.418	0.001	0.529	<0.001
Duration of hemodialysis (month)	-0.134	0.298	-0.043	0.743
Body mass index (kg/m2)	0.159	0.218	0.116	0.369
Systolic Blood Pressure (mmHg)	-0.028	0.830	0.062	0.633
Diastolic Blood Pressure (mmHg)	-0.086	0.507	0.001	0.997
BUN (mg/dL)	-0.146	0.258	-0.010	0.935
Creatinine (mg/dL)	0.125	0.333	0.227	0.076
Sodium (mEq/L)	0.049	0.703	-0.007	0.955
Potassium (mEq/L)	0.018	0.889	0.017	0.899
Chloride (mEq/L)	-0.217	0.090	-0.086	0.507
Corrected calcium (mg/dL)	0.315	0.013	0.285	0.025
Phosphorus (mg/dL)	0.206	0.108	0.262	0.040
Intact parathyroide hormone (pg/mL)	0.150	0.243	0.144	0.265
Total cholesterol (mg/dL)	0.131	0.310	0.108	0.402
Tr?glyceride (mg/dL)	0.057	0.658	0.026	0.844
HDL-cholesterol (mg/dL)	0.242	0.058	0.071	0.582
LDL-cholesterol (mg/dL)	0.098	0.450	0.023	0.860
Serum albumin (g/dL)	-0.064	0.620	0.030	0.816
Hemoglobin (g/dL)	0.014	0.912	-0.068	0.602
pH	0.233	0.068	-0.043	0.741
Venous bicarbonate (mEq/L)	-0.043	0.739	0.064	0.622
Anion gap	0.165	0.201	-0.188	0.143
spKt/V	0.064	0.624	0.220	0.086
hs-CRP (mg/L)	-0.002	0.985	-0.074	0.566

PSQI: Pittsburgh sleep quality index, ESS: Epworth sleepiness scale, BUN: Blood urea nitrogen, hs-CRP: High sensitivity C-reactive protein, spKt/V: Single pool kinetic modeling / volume, HDL: High density lipoprotein, LDL: Low density lipoprotein.

Table-6: Multivariable lineer regression analysis for the ESS and PSQI scores.

Variables	β-value	*p*-value
ESS score		
Age (y)	0.553	<0.001
PSQI score		
Age (y)	0.403	0.014

ESS: Epworth sleepiness scale, PSQI: Pittsburgh sleep quality index.

metabolic acidosis seriously affects bone and protein metabolism. On the other hand, Dialysis Outcomes and Practice Patterns Study (DOPPS) showed that moderate metabolic acidosis before dialysis had positive effects on nutritional status and caused a decrease in mortality[20] Therefore, there have been many suggested methods for correcting bicarbonate levels before dialysis initiation.[20-24] One study[25] showed that bicarbonate values before and after dialysis were not related to all-cause and cardiovascular mortality. Regarding their effects on sleep, for example, a study[19] suggested that obstructive sleep apnoea and metabolic acidosis affected the upper respiratory tract. However, another study[26] showed there was no correlation among sleep apnoea, pH, and bicarbonate values using polysomnography in non-diabetic haemodialysis patients. Another study[27] used polysomnography in 17 maintenance dialysis patients and showed that there was no correlation

between the severity of obstructive sleep apnoea and either pH or bicarbonate values. Therefore, it is apparent that there are conflicting publications on the results and causes of blood pH and bicarbonate levels in dialysis patients. The main reason for this discrepancy is likely to be that both variables are fundamentally multifactorial. There are many factors affecting mortality in dialysis patients,[28] such as advanced age, vascular access problems, hypo-albuminaemia and cardiovascular diseases, and there are also many factors affecting sleep quality and sleepiness, such as restless leg syndrome, uraemic itching, metabolic changes, inflammation, impaired sleep regulation mechanisms, symptoms and complications of chronic renal failure and comorbid diseases.[5,29]

The current study found that elderly dialysis patients were more prone to both sleep disturbances and sleepiness problems. Many studies support this finding.[30,31,32]

Today, older people tend to be more mobile than in the past, and, as a result, the frequency of trauma (e.g., traffic accidents and falls) has increased. A study[33] showed that medical problems accompanying geriatric populations increase mortality in trauma cases. It has been reported that older people fall more often than younger people.[34] Elderly patients undergoing haemodialysis have a tendency to fall due to dialysis blood pressure problems and complications such as hyperparathyroidism.[35] In addition, it is obvious that this problem is likely to increase with sleep problems, but, to our knowledge, there is no detailed study on this topic. We think that sleep disorders should be included in the history of haemodialysis patients who are referred to ED with a history of trauma.

The current study found that the calcium values of patients were associated with both sleep disturbance and sleepiness. The uraemic form of restless leg syndrome is one of the most important factors contributing to sleep disturbance in haemodialysis patients, and there are studies showing that 62% patients have these problems.[36] In haemodialysis patients, changes in many laboratory parameters, such as anaemia, decreased ferritin, reduced iron, and changes in calcium metabolism (low and high calcium levels, phosphate and parathyroid hormone levels), have been shown to be the potential causes of the development of restless leg syndrome.[37,38] We think that the relationships between calcium and both sleepiness and sleep disturbance found in the current study may result in the development of restless leg syndrome.

The study also found a relationship between EDS and phosphate, and we believe that this relationship may have developed on the basis of arterial calcification and endothelial dysfunction due to high phosphate levels as cited in literature.[39]

Our study found that sleep deficiency incidence was 64.5% and sleepiness incidence was 17.7%. In literature, the sleep disorder frequency is reported to be 45-80% in patients undergoing maintenance haemodialysis treatment.[40,41] When Epworth sleepiness rates were taken into consideration, the incidence of insomnia in several studies ranged 12-41%.[30,41,42] As can be seen, the frequencies of sleep disturbances vary significantly. This variation may be due to reasons such as cultural differences, ethnic differences, dialysis modalities, metabolic problems, emotional problems, and drug use. The aetiology of sleep disorders in dialysis patients is multifactorial but is not yet fully understood. Restless leg syndrome, uraemic itching, metabolic changes, inflammation, impaired sleep-regulating mechanisms, symptoms and complications of the chronic renal failure and comorbid disorders can lead to sleep problems.[5]

The current study has some limitations. The PQSI and ESS are subjective evaluation methods, and more objective assessment methods, such as polysomnography or the multiple sleep latency test (MSLT), were not used. Also, because it was a cross-sectional study, it failed to show the cause-effect relationship. Finally, all measurements were one-time values as it was not possible to perform follow-ups.

Conclusion

There was no correlation of the sleep quality and sleepiness levels of haemodialysis patients with their bicarbonate or venous pH values. There is a need for multi-centre studies with larger samples.

Disclaimer: None.
Conflict of Interest: None.
Source of Funding: None.

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