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Effect of Dialysis on Maximum Inspiratory and Expiratory Pressures in End Stage Renal Disease Patients

Sasan Tavana[1], Seyed Mohammadreza Hashemian[2], Fatemeh Kazemi Jahromi [2]

[1] Department of Pulmonary Medicine, Shaid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2] Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Correspondence to: Tavana S
Address: Department of Pulmonary Medicine, Shaid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Email address:sasan.tavana@yahoo.com

Background: Muscle weakness especially weakness of the respiratory muscles is a complication of chronic kidney disease. The cause of muscle weakness is the accumulation of excessive amounts of urea and other toxins. The aim of this study was to assess the effect of hemodialysis on respiratory muscle strength by measuring maximum inspiratory (PI max) and expiratory pressure (PE max).
Materials and Methods: A cross sectional study was carried out on 31 patients with chronic kidney disease at Modarres hospital in 2012. Before hemodialysis, patients had their PI max and PE max taken by using a manovacuometer. After that, the patients were connected to the dialysis machine. At the end of the hemodialysis, the patients had their PI max measured again. Data were assessed by the multivariate regression test.
Results: Before dialysis, PI max and PE max were lower than normal levels. After the hemodialysis session, repeat PFT revealed an increase in PE max and no significant change in PI max. There were strong correlations between hypoalbuminemia, anemia, hypercalcemia, hyperphosphatemia, hyperparathyroidism and decreased respiratory muscle strength. Also, the respiratory muscle strength decreased in the elderly and women.
Conclusion: Respiratory muscle weakness is a complication of chronic kidney disease; hemodialysis can improve muscle strength and PI max.

Key words: Chronic kidney disease, Respiratory muscle strength, Dialysis

INTRODUCTION

Chronic kidney disease is an evolving problem in modern countries. In 2010, 520,000 patients had routine dialysis. Each year, new patients (4.1%) are added to dialysis patients. Although hemodialysis has increased life expectancy of these patients, they suffer from many complications including restricted physical activity, muscle weakness, anemia, osteoporosis and metabolic disturbances. Chronic renal failure predisposes patients to large volume shifts and electrolyte imbalance that could affect muscle force. Besides, structural changes in muscle morphology occur in patients under dialysis (1). Other studies have shown abnormal mitochondrial function and muscle wasting, but normal contractile efficiency in hemodialysis patients (2). Muscle weakness is manifested as generalized weakness and particularly respiratory muscle weakness. Measurement of respiratory muscle strength is useful to detect respiratory muscle weakness and quantify its severity. In patients with severe respiratory muscle weakness, vital capacity is reduced; however, it is a non-specific and relatively insensitive measure. Conventionally, inspiratory and expiratory muscle strength has been assessed by PI max and PE max sustained for 1 second during maximal static maneuver. The most widely applied tests of global inspiratory and expiratory muscle strength are PI max and PE max measurement (3). Conventionally, PI max is measured from Residual Volume (RV) although this has the

theoretical disadvantage that recoil of the chest wall contributes to the value obtained. Portable inexpensive mouth pressure meters allow immediate measurement of the PI max and PE max at bedside or in the clinic (4). PI max >80 cm H_2O and PE max>90 cmH_2O are of great value in excluding clinically important inspiratory muscle weakness (5). Dialysis has been shown to change muscle weakness but whether it could improve respiratory muscle weakness or not is still unknown.

This study aimed to determine if patients' PI and PE max improve post-dialysis compared to pre-dialysis.

MATERIALS AND METHODS

Patients undergoing dialysis were included in this cross-sectional study. Patients were scheduled for dialysis three times a week and each time for six hours. Our data sheet was composed of three parts. First part contained demographic information including age, sex, weight, height, duration of disease and duration of hemodialysis treatment. Second part included underlying diseases including diabetes, hypertension, congenital diseases or other accompanying diseases. Third part included diagnostic workups such as spirometry and blood tests.

Exclusion criteria

The exclusion criteria were age less than 18 years, pregnancy, hemodialysis for less than one month, chronic lung diseases, cardiac diseases, severe generalized edema, and severe weakness. Complete physical examination was conducted prior to the hemodialysis session. Blood tests including urea, creatinine, calcium, phosphorous, hemoglobin, parathyroid hormone (PTH) and albumin were measured pre-dialysis.

Measurements of PI and PE max

PI and PE max were measured using calibrated spirometry at sitting position pre and post-dialysis. To measure PI max, a nasal clip was inserted into the patient's nose and the patient was asked to deeply inhale and then hold his/her breath for one second and then blow at maximum speed in a vacuometer. Maximal static inspiratory pressure was measured at residual volume and PE max was measured at total lung capacity. Each measurement was repeated three times.

RESULTS

A total number of 40 patients with hemodialysis enrolled in this study. Out of 40 patients, two died and seven did not give their consent. Therefore, 31 patients remained in the study; 22 patients were males and nine were females. The mean age of patients was 62.23±11.84 years and the mean BMI was 24.98±5.31 kg/m^2. The underlying diseases included hypertension and diabetes in 45.2%, hypertension alone in 41.9%, diabetes alone in 6.5% and polycystic disease in 6.5%. The mean duration of hemodialysis in our patients was 40 months.

The mean albumin level was 3.97±0.29 gr/dl, the urea reduction ratio (1-[post-dialysis BUN/pre-dialysis BUN]) of 0.67±0.07 and Kt/v: dialyzer clearance of urea ;(k: obtained from the manufacturer in mL/min) (t: duration of dialysis in minutes) (v: volume of distribution of urea in mL) of 1.4±0.42. Also, 85% of patients were anemic and the mean hemoglobin was 11.01±1.53 gr/dL. The mean calcium level was 9.1±0.82 mg/dl and the mean phosphorous level was 5.05±1.28 mg/dl. Moreover, the PTH level was high in 72.5% of patients with a mean value of 512.3±450.9 pg/mL. The mean urea and creatinine levels were 123±27 and 7.17±1.77 mg/dL. The mean uric acid level was 6.28±1.14 mg/dL. The mean pre-dialysis weight was 69.6±16.27 Kg and the mean post-dialysis weight was 67.47±15.85 Kg (Table 1).

Table 1. Demographic information of patients

Variable	Min.	Max.	Mean± SD
Age (years)	32.0	80.0	62.23±11.84
BMI(kg/m2)	17.20	35.40	24.98±5.31
Alb (gr/dl)	3.00	4.60	3.97±0.29
URR*	0.46	0.79	0.67±0.07
Kt/v	0.67	3.14	1.40±0.42
Hb (gr/dl)	8.00	13.70	11.01±1.53
Ca (mg/dl)	6.70	10.50	9.10±0.82
Ph (mg/dl)	2.90	9.00	5.05±1.28
PTH (pg/ml)	79.0	1950	512.3±450.9
Urea (mg/dl)	80.00	181.0	123.0±27.0
Cr (mg/dl)	2.50	11.00	7.17±1.77

* Urea Reduction Ratio

PI max was 43.07±16.42 pre-dialysis (range: 20-69.70), which insignificantly increased to 60.31±7.31 (range: 50-70) cmH_2O post-dialysis (P=0.15). Pre-dialysis PE max (52.61±16.50 cmH_2O) (range: 32-75) increased post-dialysis (97.77±7.82) (range: 86-110) (Figure 1).

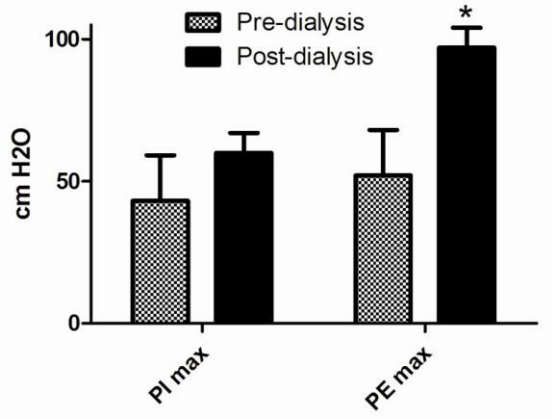

Figure 1. PI max and PE max pre- and post-dialysis.

In univariate analysis, there was no significant difference between pre and post-dialysis PI max (P=0.40). Besides, there was no significant difference between pre- and post-dialysis PE max (P=0.80). The mean weight significantly decreased after dialysis (P=0.0001). There was no linear correlation between PI max and PE max in pre- and post-dialysis with Hb, Ca, P, and PTH levels.

Age was reversely correlated with PI max and PE max (P=0.001) (r=-0.731 and -0.736, respectively). In fact, PI max and PE max decreased significantly with increase in age. PI and PE max were significantly higher in men compared to women (P=0.31, and P=0.04).

In multivariate regression analysis, PI max and PE max differences pre- and post-dialysis were adjusted for other variables including age, sex, weight and other laboratory parameters and they were extracted from the regression model using the backward method if they were not significant. This model helped determine the effect of dialysis on PI and PE max. The constant of this model determined the differences between the pre- and post-dialysis PI and PE max.

Regarding PE max and patient-related variables: when age, sex, weight, and blood test variables were adjusted for, pre and post-dialysis PE max difference was 45.16 cmH_2O, which was statistically significant (P=0.002). With one year increase in age, post-dialysis PE max decreased to a coefficient of 0.078 (regression coefficient) from pre-dialysis PE max (Table 2). Males had greater difference between pre- and post-dialysis PE max compared to female patients (P=0.02). The difference between the pre and post-dialysis PE max significantly increased with shorter duration of disease (P=0.03), lower urea level (P=0.015), higher hemoglobin level (P=0.035), higher albumin level (P=0.034), lower calcium level (P=0.021) and lower phosphorous level (P=0.04).

Table 2. Correlation of PE max with variables

Variable	Regression coefficient	P-value
Age	0.078	0.020
Gender (Male)	1	0.02
Albumin	1	0.034
Hb	0.915	0.035
Ca	-0.928	0.021
Ph	-0.3	0.04
Urea	-0.028	0.015

Regarding PE max and patient-related variables: Pre and post-dialysis PI max difference was 17.24 cmH_2O, which was not significant (P=0.447). Albumin had a significant effect on the PI max difference (P=0.030); however, increase in urea decreased the difference in PI max pre- and post-dialysis (P=0.001). Increase in calcium, phosphorous and PTH level decreased the difference in PI max (P=0.04). URR and kt/v had no significant effect on PI and PE max differences (P=0.3, P=0.24; respectively).

DISCUSSION

This study aimed to determine the respiratory variables of PI max and PE max in hemodialysis patients before and after dialysis as a determinant of respiratory muscle weakness in these patients. Our results showed that PI and PE max were significantly lower pre-dialysis compared to post-dialysis in these patients. It seems that dialysis can help significantly improve muscle weakness.

PI max and PE max increased post dialysis compared to pre-dialysis. This increase was significant for PE max

but not significant for PI max. In a study by Dipp et al, (6) in 2010, respiratory muscle weakness in hemodialysis patients was noticed by lower than normal PI and PE max. Patients with Chronic Renal Failure (CRF) undergoing dialysis showed impaired functional capacity and lung function that were not completely reverted in kidney transplant patients (7). Analysis of PE max and PI max showed that respiratory muscles in uremic patients were weak (8). Forced expiratory flow between 25% and 75% of vital capacity was slightly below normal in the dialysis patients.

Several mechanisms have been suggested for improvement of muscle strength post-dialysis. Other studies showed that lung volumes frequently decrease in chronic renal failure but remain essentially stable during the dialysis procedure (9). Preservation of diffusion capacity of the lung for carbon monoxide was noted in the hemodialysis group. More pronounced weight gain in the interdialytic period is associated with worsening of lung function, which is almost fully reversible by hemodialysis. In addition, longer duration of hemodialysis is associated with decreased respiratory muscle strength (10). Acute effects of hemodialysis on the lungs showed that acute fall in lung diffusing capacity for CO (DLCO) takes place early in the dialysis, and it returns to the pre-dialysis value by the end of a six-hour dialysis (11). In a study by Karacan et al (12), the pre-hemodialysis PI max and PE max were much lower than normal values (67.4% and 36.3%, respectively). After the hemodialysis session, repeat PFT revealed a small increase in expiratory flow rates, and a significant drop in PI max. There was a strong correlation between PI max and PE max ($r=0.567$, $P<0.01$) pre- and post-hemodialysis, indicating that common mechanism(s) are responsible for impairment of both inspiratory and expiratory muscle strength. Chronic vascular congestion may be another explanation for decreased pulmonary compliance.

Although our results showed that dialysis improved PI and PE max, reversibility or irreversibility of changes is a matter of controversy. Abnormal lung function is common in renal disease, and the main change is a reduction in carbon monoxide transfer that persists after transplantation. The likeliest explanation is that subclinical pulmonary edema progresses to fibrosis before transplantation. The fibrosis may further worsen to decrease the residual volume in the recipients of grafts (13). The spirometry results revealed significantly higher residual volume and total lung capacity in the hemodialysis and peritoneal dialysis groups than in the transplantation group in this study.

General concept is that both inspiratory and expiratory muscle strength decrease and dialysis can improve both. In our study, only PE max increased significantly after dialysis. Other studies such as the one by Saiki et al. showed that PE max increased more than PI max after dialysis, which is consistent with our study result (14). Bark et al. (15) indicated that there was an impairment of respiratory muscle strength and endurance in patients with CRF, which may predispose patients to respiratory muscle fatigue. They showed that there was a significant correlation between PI max and PE max ($r=0.827$, $P<0.001$), indicating similar involvement of both inspiratory and expiratory muscles. The principal of PI max measurement is based on residual volume (RV), and PE max is based on total lung capacity. The main involvement of lungs in end stage renal disease (ESRD) is restrictive which affects total lung capacity more significantly; dialysis improves total lung capacity and thus PE max more than PI max which is compatible with our results.

Carpenter et al. showed that increase in age was accompanied with a decrease in respiratory forces (16). With increase in age, PI and PE max and their differences pre and post dialysis more significantly decreased. The more prominent increase in PI and PE max in older age indicates the increase in respiratory muscle atrophy. Dipp et al. (6) also showed an increase in muscle atrophy in advanced age and its association with decrease in PI and PE max.

Male gender was associated with higher maximal inspiratory pressure (MIP) and maximal expiratory

pressure (MEP) (17). Patients on long-term hemodialysis show a significant decline in FVC following five years of treatment. Although the spirometry changes in chronic hemodialysis patients are reversible during the first years of renal replacement therapy, five years later these changes become irreversible (18).

Our study showed that increase in albumin is associated with increase in PI and PE max. Besides, the correlation between pre- and post-dialysis difference in PI and PE max significantly increased with shorter duration of disease (P=0.03), lower urea level (P=0.01), higher hemoglobin level (p=0.03), lower calcium level (P=0.02), and lower PTH and phosphorous level (P=0.04). It is speculated that decrease in albumin induces interstitial edema and decreases the pulmonary function. Bush and Gabriel (19) showed the same results and reported a decrease in albumin and decrease in pulmonary functions.

Our results showed that increase in urea decreases respiratory muscle force due to uremic myopathy and dialysis decreases urea and improves pulmonary function. Other study showed that the uremic myopathy induces loss of respiratory muscle bulk and decreases oxidative metabolism and muscle proteins. Therefore, dialysis seems to improve these indices by a decrease in urea (20).

In our patients, increase in calcium and phosphorous in accordance with serum PTH decreased PI and PE max. Puy et al. (21) described that hypercalcemia, hyperphosphatemia, alkalosis and alveolar damage, which predispose patients to pulmonary calcifications were associated with chronic kidney failure and decrease in pulmonary function. Another study reported a case of a uremic dialysis patient with severe secondary hyperparathyroidism, proximal muscle weakness and impaired respiratory muscle strength, the latter being assessed by maximal inspiratory pressure. After subtotal parathyroidectomy, they observed a marked improvement in respiratory muscle strength (27 vs. 87 cm H_2O) and disappearance of proximal muscle weakness.

In conclusion, chronic renal failure can decrease respiratory muscle strength and function. Dialysis can improve respiratory muscle strength and their function. The PE max improves more significantly after dialysis. The amount of this improvement post-dialysis is correlated to other factors such as calcium, phosphorus and albumin levels. Further studies with larger sample sizes are recommended.

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