CHAPTER 5

Discussion

The purpose of this study was to investigate the effects of hemodialysis on REE and hemodynamics among pre-, during, and post-hemodialysis periods in CKD patients. The main finding of this study found that VO_2 was significantly higher in post-hemodialysis when compared to pre- hemodialysis. RER at during hemodialysis was higher than post-hemodialysis. Hemodynamics parameters, which were SV, HR, CO, and EF during hemodialysis were lower than pre-hemodialysis, whereas TPR, SBP, and DBP during and post-hemodialysis were higher than those in pre-hemodialysis. All hemodialysis patients in this study had hypertension. Values were in a normal range for BMI, resting HR, resting SBP, resting DBP, Kt/V_{urea}, hemoglobin, hematocrit, and TSH. All details for these results are described below.

1. Characteristics of patients

Blood pressure recommendations for hemodialysis patients with hypertension were SBP less than 160 mmHg and DBP less than 90 mmHg (117). The hemodialysis patients in this study had resting SBP approximately equal to 141 mmHg and resting DBP equal to 80 mmHg. Therefore, all hemodialysis patients in this study had controlled hypertension. Kt/V_{urea} was an indicator of adequacy of dialysis to remove urea and the value should be equal to or higher than 1.2 (118). Hemodialysis patients in this study had Kt/V_{urea} approximately equal to 2.25; thus, all hemodialysis patients had adequate

dialysis. The hemoglobin and hematocrit recommendations for hemodialysis patients were hemoglobin equal or higher than 10 g/dl and hemoglobin equal or higher than 30% (119). Hemodialysis patients in this study had hemoglobin and hematocrit approximately equal to 10.79 g/dL and 32.80%, respectively; therefore, the patients had no anemia. The normal of TSH was 0.27–4.20 uIU/mL (120). Hemodialysis patients in this study had TSH approximately equal to 2.01 uIU/ml; therefore, the patients had a normal TSH level.

2. Resting energy expenditure

Telemetry gas analysis (Oxycon, SensorMedics, USA): Oxycon Mobile was a battery-operated, portable, and wireless metabolic system measuring gas exchange breath-by-breath and was attached to the body in a vest system (115). A flow sensor unit was connected to a face mask detecting air flow by the rotation of a low-resistance, bidirectional turbine, which allowed the determination of ventilation (115). Oxycon Mobile measures important ergospirometric key parameters, such as ventilation (VE), oxygen consumption (VO_2), carbondioxide product (VCO_2), anaerobic threshold, respiratory exchange ratio (RER), and heart rate (HR) (115). This study used Oxycon Mobile to measure REE in hemodialysis patients. Oxycon Mobile was validated against the Douglas bag method regarding gas exchange, and good agreement was reported for oxygen uptake and carbon dioxide release in the physiological range (115, 116). Until now, validation of Oxycon Mobile has only been performed for gas exchange parameters (115).

The hemodialysis patients in this study had VO_2 approximately equal to 204 ml/min and VCO_2 equal to 180 ml/min. Thus, all hemodialysis patients had VO_2 and VCO_2 less than healthy subjects (121). VO_2 and VCO_2 were an indicator of the rate at which oxygen was used by tissues (121). Hemodialysis patients had RER approximately equal 0.89. The RER of 0.70 indicators that fat was the predominant fuel source; RER of 0.85 suggests a mix of protein, and a value of 1.00 or above was an indicator of carbohydrate being the predominant fuel source (122). Therefore, the hemodialysis patients used energy from protein. Hemodialysis patients in this study had resting REE approximately equal to 1463.40 kcal/day; thus, the patients had REE higher than healthy subjects (9).

Hemodialysis patients in this study exhibited differences in VO_2, RER and REE among pre-, during, and post- hemodialysis periods. VO_2 was significantly higher in post-hemodialysis when compared to pre- hemodialysis. RER at during hemodialysis was higher than post-hemodialysis. REE was significantly higher in post-hemodialysis when compared to pre-hemodialysis. REE during hemodialysis was significantly lower at the 150^{th}, 210^{th}, and 240^{th} min than in post-hemodialysis. Consistent with a previous study, Cargill et al. (121) studied the oxygen consumption of the normal and the diseases human kidney. Their reported reduced oxygen consumptions during the period of decreased blood flow were associated with apparent urine formation in nephrons and suggested the possibility that renal oxygen consumption depends upon the relative proportion of tubular tissue actively functioning in the formation of urine from glomerular filtrate (121). The previous study found that during hemodialysis, RER was significantly higher than post- hemodialysis (9). The rise in RER in pre-hemodialysis and during hemodialysis procedure probably reflects the preferential metabolism of

carbohydrates during these periods. In contrast, the decrease of RER in post-hemodialysis was associated with the utilization of protein and fat stores for fuel metabolism (9). This is consistent with our results in that RER was higher in pre-hemodialysis and during hemodialysis when compared to post-hemodialysis. Ikizler et al. (11) studied the potential effects of hemodialysis on protein and energy metabolism. Their study evaluated 11 chronic hemodialysis (CHD) patients before, during, and after hemodialysis sessions. The results showed that post-dialysis energy expenditure was significantly higher than that in the pre-dialysis period and during dialysis. They speculated that the increase in energy expenditure post-dialysis due to whole body protein breakdown continued to be elevated by 11% after dialysis when compared with the pre-dialysis period (11). Moreover, their results found that whole-body protein synthesis in the post-dialysis period was also statistically significant higher compared with pre-dialysis period and during dialysis (11). Because protein synthesis and breakdown require energy, part of this energy increase might be due to the increased protein turnover (11). In contrast to the previous study, Ikizler et al. (10) studied energy expenditure in hemodialysis patients by using a whole-room indirect calorimeter. Their results showed that during dialysis, REE was also significantly higher than in the post-dialysis period. This increment in REE was probably related to the hemodialysis procedure (10). It is possible that the increase in REE during hemodialysis might be due to the negative nitrogen balances that result from the dialysis procedure, which might remove the amino acids, peptides, and glucose metabolites, resulting in losses of amino acids in dialysate and increased protein catabolism (7, 8). Moreover, the hemodialysis procedure impacts protein, fat, and carbohydrate metabolism because this procedure

increases catabolism of muscle protein. There was a lack of adequate compensatory protein anabolism during hemodialysis (11). These mechanisms involved an increase in REE during hemodialysis (11).

Therefore, the present study found that higher VO_2 in post-hemodialysis than in pre-hemodialysis. RER at during hemodialysis was higher than post-hemodialysis. REE was significantly higher in post-hemodialysis when compared to the pre-hemodialysis period and during hemodialysis.

3. Hemodynamics

PhysioFlow® Hemodynamics Redefined (Manatec, France): PhysioFlow® Enduro is an original system for noninvasive cardiac monitoring, which provides hemodynamic parameters using analysis of thoracic electrical bioimpedance signals (TEB) (112). More precisely, PhysioFlow® Enduro allows the assessment of the hemodynamic state and the ventricular function of patients by determining hemodynamic parameters (113). PhysioFlow® Enduro computes the following parameters: stroke volume/index, cardiac output/index, systemic vascular resistance, systemic vascular resistance index (systemic vascular resistance multiplied by the body surface area), left cardiac work index, ejection fraction, and end-diastolic volume. This study used PhysioFlow® Enduro to measure hemodynamics in hemodialysis patients. PhysioFlow® provides enhanced sensitivity and better correlation with invasive methods compared to analogic and similar conventional impedance cardiology (ICG) technologies (114). Moreover, the previous study validated the PhysioFlow® thoracic bioimpedance monitor for the noninvasive determination of CO against the thermodilution method as a reference

standard. There is good agreement between the PhysioFlow® monitor and pulmonary artery catheter for determination of the CO. A comparison of the PhysioFlow® monitor to cardiac output by the Fick method is in progress (112, 114).

Hemodynamics parameters of pre-hemodialysis in this study were in the normal range. SV, HR, CO, and EF during hemodialysis were lower than in pre-hemodialysis. In a previous study, Gadegbeku et al. (123) studied hemodynamic responses of dialysis treatments in 27 stable subjects with ESRD receiving chronic hemodialysis. Their results showed that SV and CO progressively declined by 19% to 17% ($p < 0.001$) with a concomitant increase in systemic vascular resistance by 22% from 1654 ± 88 to 2020 ± 121 dynes · sec · cm^{-5} ($p < 0.001$). Additionally, their study observed a significant reduction in small artery compliance from 4.7 ± 0.5 to 3.3 ± 0.4 mL · mm Hg^{-1} · 100 ($p = 0.01$). These findings suggest that changes in small artery vascular compliance contribute to an elevation in systemic vascular resistance during dialysis. Goss et al. (124) studied hemodynamic changes during hemodialysis and found that most hemodynamics changes during hemodialysis might be associated with a decrease in central blood volume (124). Patients had a decrease in CO, which was the result of a decrease in blood volume and central blood volume in post-hemodialysis (124). In addition, reductions in CO and SV were primarily a result of fluid loss (125). The present study found that EDV did not change in the pre-, during and post-hemodialysis procedures. Therefore, the reduction in EF in the present study might be due to decreased SV during hemodialysis.

However, TPR, SBP, and DBP during hemodialysis and in the post-hemodialysis period in the present study were higher than in the pre-hemodialysis period. The present study

found that an underlying disease for all hemodialysis patients was hypertension. A previous study found that 90% of ESRD patients had hypertension when starting dialysis (126). Excess sodium or extracellular volume was the primary factor of hypertension in ESRD (126). Extracellular overhydration was an important factor in the pathogenesis of dialysis-related hypertension (127). Fluid state was considered to be a major determinant of BP in hemodialysis patients (126). Hypertension has been linked to excess cardiovascular and cerebrovascular adverse events in hemodialysis patients (128). Hypertension in hemodialysis patients was characterized by an increase in systemic vascular resistance, which is the result of the hemodynamic response to volume loading (129). According to this theory, cardiac index increases after volume loading, causing an increase in tissue blood flow (129). As a homeostatic response, the bodies keep tissue blood flow constant and induce pre-capillary vasoconstriction by involuntary mechanisms. Therefore, an increase in peripheral vascular resistance occurs as a direct result of volume overload (129). Hampers et al. (114) studied a hemodynamic evaluation of bilateral nephrectomy and hemodialysis in hypertensive men. Their study showed that an increased TPR plays an important role in maintaining elevation of BP after nephrectomy (114). The rise in TPR appeared to be mediated by changes in small artery compliance (123) due to activation of the sympathetic nervous system (123). Thus, increases in TPR in this study might be due to decreases in CO and increases BP during hemodialysis. In addition, this study found that hemodialysis patients had an average ultrafiltration rate of approximately 2363.64 ml per 4 hours. Hemodialysis patients had decreases in blood volume during ultrafiltration (130). During hemodialysis, water in excess of normal or dry weight should be removed and

fluid loss should occur, resulting in a reduction in CO and SV (125). The previous study found that pre-hemodialysis or high ultrafiltration volume had SBP and DBP higher than post-hemodialysis or low ultrafiltration volume (131). This is consistent with our results in that SBP and DBP were significantly higher in pre-hemodialysis when compared to post-hemodialysis.

Therefore, this study found that hemodialysis patients had lower SV, HR, CO, and EF during hemodialysis than in pre-hemodialysis. However, TPR, SBP, and DBP during and post-hemodialysis were also higher than in pre-hemodialysis.

3. Conclusion

Hemodialysis patients had significantly REE and hemodynamics alterations at pre-hemodialysis, during hemodialysis and post- hemodialysis procedures. Food intake and hemodynamics changes should be considered during hemodialysis.

4. Clinical application and future study

The results of this study can be used as preliminary data of REE and hemodynamics in this patient group. Moreover, the results might be useful for basic knowledge and might contribute to understanding hemodynamics and metabolism during hemodialysis. Therefore, health professionals may consider adding interventions to hemodialysis treatment such as a specific exercise program during a hemodialysis procedure. The results in this study found that lower SV, CO, and EF and higher BP during hemodialysis than in pre-hemodialysis. Cardiovascular exercise such as cycling during the first 1 to 1.5 hours of treatment might be safe, does not interfere with treatment, and also can help control hemodynamic parameters.

5. Limitations and suggestions

There were some limitations in this study. Firstly, the level of physical activity was not assessed in this study. In a future study, physical activity levels should be measured to investigate the relationship between the physical activity level and REE because increased REE was associated with a physically active lifestyle, and energy requirements decrease because of a decline in physical activity. Secondly, this study did not estimate food intake that might confirm REE because of the food intake effect on REE. A measurement of food intake is recommended in a future study.