**[Oxidative Stress, Mitochondrial Dysfunction, and Hemodialysis effects on Patients with Chronic Kidney Disease]**

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**The question to be determined is, what is a leading problem for Chronic Kidney Disease (CKD)? The proposition is that there are mitochondrion abnormalities in skeletal muscle, as well as dysfunctional mitochondria. 27 varying subjects, broken up into 17 controls and 10 with stage 5 of CKD on hemodialysis, were tested for mitochondrial volume density, mitochondrial DNA copy number, PGC1α protein expression, and BNIP3. These tests were facilitated for the purpose of discovering if mitochondrial function and structure worsens with the severity of CKD. “Muscle biopsies from patients with CKD stage 5 revealed lower mitochondrial volume density and lower mtDNA copy number.” (Gamboa; pg 9). These results are important because it shows that mitochondria are a contributing factor to the severity of CKD, oxidative stress and mitochondrial dysfunction to be precise. “The mitochondrial abnormalities that are common in skeletal muscle from patients with stage 5 CKD can possibly explain why this muscle dysfunction is associated with sarcopenia and frailty.” Continuing studies are highly crucial to assess mitochondrial function and structure in patients with varying stages of CKD.**

**Introduction**

Mitochondria’s main job is to take in nutrients and break them down; creating a goal of this system to create energy rich molecules for the cell. When mitochondrion does not work as a proper system, it is considered dysfunctional mitochondria. This dysfunctional mitochondrion is a major contributing factor to oxidative stress. Oxidative stress is an imbalance among the production of free radicals and the body’s ability to fight back. It is thought that this may contribute to cardiovascular disease in individuals with CKD. “Sarcopenia and frailty are mutual among individuals with CKD, as well as being associated with higher rates of mortality.” (Bao; pg. 1071-1077). Frailty is better understood as weak, fragile, and easily damaged. Sarcopenia is the shrinking in muscle mass.

“Cardiovascular mortality as well as morbidity is higher in patients with CKD compared to the general population that does not have CKD.” (Foley; pg. 516-520). Those in a select group with CKD do not have the risk factors such as smoking to explain the increase in cardiovascular morbidity; however, elevated levels in oxidative stress have been suggested as further risk factors for cardiovascular incidents in patients with CKD.

“Prior studies have shown that patients with CKD exhibit skeletal muscle mitochondrial dysfunction” in comparison to people who are healthy. (Kemp; pg. 1520-1527). These studies revealed a decrease in activity of mitochondrial enzymes such as the longer extensions of time phosphocreatine recovery takes after exercise from CKD patients. On the other hand, no experiment has been created to measure the mitochondrial number in the human skeletal muscles from people with CKD.

**Recent Progress**

“Mitochondrial dysfunction is connected with increased oxidative stress and inflammation.” (Lopez-Armada; pg. 106-118). There have been studies to show the correlation among mitochondrial dysfunction and atherosclerosis. This is yet another key factor to understanding that there is a contribution to cardiovascular diseases from compromised mitochondrial function. In prior years, research showed “mitochondrial abnormalities in peripheral blood mononuclear cells from individuals with CKD.” (Granata; pg. 388).

The scientiests examined vastus lateralis muscle biopsies from patients with stage 5 CKD that are being treated with maintenance hemodialysis for abnormalities within their mitochondria. The focus of this study was to test if mitochondrial function decreases with the different stages of CKD, as well as if mitochondrial number decreases in skeletal muscle. Lactate levels were tested because they are used as an indicator for anaerobic metabolism prompted by mitochondrial dysfunction.

The results show intracellular lipofuscin granules were abundant in patients undergoing hemodialysis, indicating oxidative damage in mitochondria and lysosomes. Lipofuscin granules are lipid-covering deposits of lysosomal digestion. There was a lower amount of mitochondria in patients with stage 5 CKD. What was interesting about this result was that it was variable to age as well as race; however, more tests must be run to further establish this as a concrete fact.

**Discussion**

This study set out to test oxidative stress, mitochondrial volume density, and mitochondrial dysfunction. The results from this experiment reveal that patients with a higher stage of CKD are more apt to have microbial dysfunction and oxidative stress than those patients at stage 3 and 4. For patients with CKD in a lower stage, they also had decreased numbers for mitochondrial DNA. This suggests that the alterations in mitochondrial DNA happens prior end-stage renal disease. Structural abnormalities were discovered in skeletal muscle mitochondria linked to those with normal kidney function.

This is the first study to demonstrate suppressed mitochondrial volume density in skeletal muscle in individuals proceeding through hemodialysis. “They also exposed mitochondrial DNA quantity is lower in muscles of patients going through hemodialysis,” which concur with experiments done in 2012. (Lewis; pg. 72-78). Largely speaking, the abnormalities in mitochondrial structure could be a reason leading to poor mobility in patients with CKD. It may also explain the amplified commonness of frailty and sarcopenia in this population of stage 5 CKD. “The etiology of these abnormalities is not clear, but a trial in an animal model of CKD suggests that lessening in muscle mitochondria go before the loss of muscle volume and muscle power.” (Tamaki; pg. 1330-1339). These results are exceedingly important because it advances our knowledge into understanding how we can slow down CKD from taking over one’s life. ”Lactate levels reflect anaerobic metabolism. The latest community‐based cohort study found that increased lactate levels were associated with higher risk of heart failure and all‐cause mortality.” (Matsushita; pg. 401-409). The study showed that there are higher levels of lactate in patients with stage 5 CKD on hemodialysis. This is important because there may be further linkage between the lactate levels and the mitochondrial dysfunction. Further studies need to be done to evaluate if muscle mitochondrial reduction happens before the onset of sarcopenia.

This study did not evaluate mitochondrial function in skeletal muscles. In the future it is crucial to prove that there is association between the function in skeletal muscle and mitochondrial structure of individuals that have CKD in all stages. Through study it was determined that there was not a connection between elevated blood pressure levels and the amount of mitochondrial DNA.

It still remains unknown how to directly inhibit the dysfunction of mitochondria as well as keep elevated levels of mitochondrial DNA in CKD patients. More studies are necessary to establish a relationship between lactate and mitochondrial dysfunction.

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