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Original Article

The Effect of Hemodialysis on Cardiac Biomarker Levels

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Abstract

Background: According to the United States Renal Data System (USRD), the 2013 Annual Data Report indicates that patients with chronic kidney disease (CKD) have higher rates of congestive heart failure, acute myocardial infraction (MI), and cerebral vascular accidents compared to non-CKD patients.

Aim of the Study: This study aimed to investigate the effects of the hemodialysis process on cardiac biomarker levels in hemodialysis patients.

Method: A prospective study was carried conducted at Emssalata central hospital's hemodialysis department. The study involved a total of 25 individuals, 15 males and 10 females who were undergoing dialysis. A chemistry analyzer was used to measure the serum troponin I (cTn-I), creatin phosphokinase (CPK), and creatine kinase-MB (CK-MB) iso-enzyme in hemodialysis (HD) patients before and after the dialysis process.

Results: The results showed that total CPK, CK-MB, and cTn-I levels had no significant differences in CKD patients' pre and post-dialysis, with ($p = 0.989$, 0.586, and 0.284) respectively. Hemodialysis patients have none significantly higher CPK, CK-MB and cTn-I ratios after hemodialysis process when compared to the values determined to each marker before hemodialysis process.

Conclusion: The dialysis process had no effect on the levels of cardiac biomarkers (CPK, CK-MB, and cTn-I) in hemodialysis patients. The cardiac biomarker in hemodialysis patients appears to be unaffected by age, gender, or dialysis duration.

Keywords: Hemodialysis, serum total of troponin I (cTn-I), creatin phosphokinase (CPK), and creatine kinase-MB (CK-MB) iso-enzyme.

Introduction

The incidence and prevalence of chronic kidney disease (CKD) have been increased Worldwidely[1]. Chronic kidney disease is characterized by the failure of the kidney to remove waste products and excess fluid from the body[2]. It is defined by a sustained impairment of kidney function, as reflected by an abnormal excretion of urinary protein or a reduction of glomerular filtration rate (GFR)[3]. When the glomerular filtration rate reaches levels below 15 ml/ min(corresponding to a reduction in kidney function by approximately 90%), patients require Renal Replacement Therapy (RRT), which is provide in the form of dialysis or transplantation. Estimating GFR from serum creatinine is likely to avoid missing kidney disease at an early stages[4].

The etiology of CKD is heterogeneous, involving both primary kidney disease (PKD) and variety of non-renal disease, which effect the kidneys [5]. The main causes among PKD are glomerulonephritis (GN), renal vascular disease, diabetes mellitus, and hypertension. Atherosclerosis are the most frequent non-renal diseases which potentially leading to loss of the kidney function [6].

The classification and stages of CKD may help identify affected patients, possibly resulting in the early initiation of effective therapy. To achieve this goal, guidelines were proposed from the National Kidney Foundation of the United States through its Kidney Disease Outcomes Quality Initiative (K/DOQI, 2002), working group defined CKD in adults as evidence of structural or functional kidney abnormalities (abnormal urinalysis and maging or histology studies) that persist for at least three months, with or without a decreased GFR. The most common manifestation of kidney damage is persistent albuminuria, including micro albuminuria.

On the other hand, decreased GFR (as defined by a GFR of less than 60 ml/min

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per 1.73 m2), with or without evidence of kidney damage. CKD was classified into 5 stages based on the glomerular filtration rate and evidence of kidney damage, in accordance with the guidelines of the National Kidney Foundation, which include Stage 1 disease is defined by a normal GFR (greater than 90-ml/min/1.73 m2) and persistent albuminuria (1.8 % of the total United States population), Stage 2 diseases is a GFR between 60 to 89 ml/min/1.73 m2 and persistent albuminuria (3.2 % of the total United States population), Stage 3 disease is a GFR between 30 and 59 ml/min/1.73 m2 (7.7 %) of the total United States population), Stage 4 disease is a GFR between 15 and 29 ml/min/1.73 m2 (0.21%) of the total United States population), and Stage 5 disease is a GFR of less than 15 ml/min/1.73 m2 or ESRD (2.4 %) of the total United States population)[7].

The patients with CKD have non-traditional or uremia related risk factors, that occur more frequently in patients of CKD and are responsible for increase of cardiovascular disease ,Cardiovascular disease (CVD) remain the number one cause of death among patients with chronic kidney disease CKD [8]. According to the United States Renal Data system (USRD) 2015 Annual Data Report indicates that CKD patients have higher rates of congestive heart failure, acute myocardial infraction (MI) and cerebral vascular accident compared to non or CKD patients[9].

Quiroga, Borja A. 2015 survey of CK-MB in hemodialysis patients included 211 HD patients with a median age of 73 (60-80). According to the study, CK-MB is a good marker for stratifying cardiovascular risk in hemodialysis patients [10]. In an otherwise prospective study conducted by Muharrem et al. (2014) in Sanliurfa-Turkey to investigate the effect of a single hemodialysis session on echocardiographic parameters and cardiac enzyme levels, including cTn-I, CPK, and CK-MB, the study results showed that there was no significant increase in CPK and CK-MB levels after dialysis, but otherwise the findings were that post-dialysis cTn-I levels were significantly higher compared to pre-dialysis levels (p=0.03)[11], hence the present study was undertaken to evaluate the cardiac biomarker levels in

chronic renal failure patients, then estimate the effect of hemodialysis on the cardiac enzymes in chronic kidney disease patients.

Materials and methods

A cross-sectional study was conducted on HD patients in the hemodialysis center of Emssalata Hospital. Twenty-five patients on HD therapy were randomly selected for this study, regardless of gender, whether they are males or females. Three specimens were excluded due to hemolysis or elevated serum lipid levels.

Sample Collection and Measurement of Laboratory Parameters

Venous blood specimens 5 ml had been obtained from each hemodialysis patient before and after the dialysis. The samples were centrifuged at 5000 rounds per minute (RPM) for 5 minutes to separate the serum from the blood cells. Any specimens with hemolysis or high lipemic serum were excluded.

After pre-and post-dialysis serum samples were obtained from each patient, all cardiac biomarkers, including CK, CK-MB, and cTn-I, were investigated before and after hemodialysis in all patients. Bio system photometer modal (spectrophotometer) used to estimate the cardiac marker levels of creatine kinase and isoenzyme CK-MB of bio-meghrab company of chemistry analyzer, and I Chroma chemistry analyzer system was used to estimate the cardiac biomarker of troponin I.

Data collection and Statistics Analysis

The data was collected after filling structured questionnaire by each patient, these questionnaires included Gender, age, weight, length, smoking and dialysis duration of hemodialysis patients. The cardiac biomarker CPK, CK-MB were measured in clinical chemistry laboratory at the Emssalata central hospital, whereas cTn-I test was evaluated in private Alddaoun medical laboratory. All data were collected from the results of tests.

Data was analysed by using SPSS 19 version. Kolmogorov-Smirnov test was used to determine whether the data were

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normally distributed or none. Accordingly to the prevalence value of Kolmogorov-Smirnov test, all the samples of CK, CK-MB, and troponin I having a non-normality distribution, thereby the variables were presented as median (range).

The Wilcoxon signed-rank test was used to compare two paired variables having a non-parametric distribution. Prevalence value < 0.5 was considered as statistically significant. Prevalence value < 0.5 was considered as statistically significant.

Results of the Effects of Dialysis on CPK Levels

According to non-parametric statistical test called Shapiro-Wilk test (test full result was found on appendix III), all data of CPK variable has a non-normally parametric distribution (P= 0.000) and presented as a median (range), which is explained in the table 3. The Wilcoxon signed-rank test was used to determine whether there was a difference between the two paired samples.

Table 1: The Descriptive statistic of CPK levels pre and post-dialysis.

Independent Variable	Median (min-max)	St. Deviation	Sig(p.value)
CPK pre-dialysis	33(14-185)	37.50013	.000
CPK post-dialysis	10 (1-22)	47.91983	.000

According to the results of this study, the relation between the dialysis and CPK levels have been shown that there was no effect of dialysis on regarding CPK levels in haemodialysis patients (test full result was found on appendix VI), and there was not significant increase in CPK levels after dialysis compared to the values determined before haemodialysis as explained in the Table 2.

Table 2: Comparison between CPK levels pre and post-dialysis as Wilcoxon signed-rank test.

Variable	Pre-dialysis Mean ±SD Error	Post-dialysis Mean ±SD Error	P.value
CPK	47.4800 ± 7.50003	55.6800 ± 9.58397	.989

Results of the Effects of Dialysis on CK-MB isoenzyme Levels

According to Shapiro-Wilk statistic tests (test full result was found on appendix IV), the results showed that CK-MB isoenzyme has a non-normally parametric distribution (P= 0.000), as showed in the Table 3.

Table 3: The descriptive statistic of CK-MB isoenzyme levels pre and post-dialysis

Independent variable	Median (min-max)	St. Deviation	Sig(p.value)
CK-MB pre-dialysis	10 (1-24)	7.00071	.065
CK-MB post-dialysis	10 (1-22)	6.53248	.026

The Wilcoxon signed-rank test was applied to determine whether there was a differences between CK-MB isoenzyme levels before and after dialysis process, which showed that there was no effect of dialysis on CK-MB isoenzyme levels in hemodialysis patients(test full result was found on appendix VI), as well as there no significant increase in CK-MB isoenzyme levels after dialysis compared to the values determined before hemodialysis, as showed in the Table 4.

Table 4: Comparison between CK-MB isoenzyme levels pre and post-dialysis as Wilcoxon signed-rank test.

Variable	Pre-dialysis Mean ±SD Error	Post-dialysis Mean ±SD Error	P.value
CK-MB	10.48 ± 1.40014	9.44 ± 1.30650	0.586

Results of the Effects of Dialysis on cTn-I Levels

The results of this study showed that Troponin I levels in CKD has no effect on hemodialysis patients (test full result was found on appendix V). However, there was no significant difference increase in Troponin I levels after dialysis, as shown in the following Table 5.

Table 5: The descriptive statistic of cTn-I levels pre and post-dialysis.

Independent variable	Median (min-max)	St. Deviation	Sig (p.value)
cTnI pre-dialysis	.1200 (.09-.93)	.17609	.000
cTnI post dialysis	.19679 (.09-1.01)	.1200	.000

The results of this study showed that the relation between dialysis and cTn-I had no significant difference increase in cTn-I levels after dialysis. This show in the

table 8:-

Table 8. Comparison between cTn-I levels pre and post-dialysis as Wilcoxon signed-rank test

Variable	Pre-dialysis Mean ±SD Error	Post-dialysis Mean ±SD Error	p.value
CK-MB	.1736± .03522	.1800 ±.03936	.284

Discussion

The level of cardiac biomarkers that may arise from the heart was more frequently helpful in evaluating the extent of cardiac damage in predicting mortality in patients with chronic kidney disease [12]. Cardiac biomarkers including CPK, CK-MB, and troponin I were evaluated in this study. The main purpose of the current study was to determine and compare the serum level of cardiac biomarker (CPK, CK-MB, and cTnI) in predicating the outcome of hemodialysis patients on regular dialysis.

Some of the studies showed an increase in cTn-I levels, but did not do so in CPK and CK-MB [13]. The results of this study showed that the serum level of (CPK, CK-MB & cTn-I) was no statistically significant increase at post-dialysis when compared with pre-dialysis of the same hemodialysis patients.

In accordance with the results of this study showing no significant increase in cardiac biomarker for cTn-I, these results are in disagreement with H Bozbas et al (2004), a study of thirty-four patients with ESRD HD who showed that serum levels of cTn-I in 30 hemodialysis patients which was significantly increased. The study explained this for unknown reasons, it was interpreted that troponin is sometimes falsely elevated in the absence of myocardial injury. Three possible mechanisms were suggested for this elevation: expression of cardiac troponins in regenerating skeletal muscle, cross reactivity errors resulting from the measurement assay, and minor myocardial injury[14].

The results of this study showed that

there was no statistically significant increase in CPK levels on pre and post-dialysis process in HD patients, and indicated that this biomarker is not affected by the hemodialysis process, and these CPK results are not consistent with Nakai et al,(2004), which showed that CPK levels were significant increased[15].

Additionally, the results of this study showed that serum levels of CK-MB were no significant difference before hemodialysis compared to after hemodialysis. These results of CK-MB isoenzyme did not consist with uiroga B et, al (2016) study which showed that serum levels of CK-MB was significantly increased. Postoperatively increased CK-MB isoenzyme was due to the result of muscle damage [16].

Conclusion:

This study concluded that a single haemodialysis session did not cause any significant increases in CPK, CK-MB, and cTnI levels in haemodialysis patients, where the dialysis process had no effect on these cardiac biomarkers in haemodialysis patients pre and post-dialysis. More prospective multi-center studies with high sample numbers are needed to explain this issue and increase confidence in the findings.

References

1) Eknoyan, G., Lameire, N., Barsoum, R., Eckardt, K. U., Levin, A., Levin, N., Locatelli, F., MacLeod, A., Vanholder, R., Walker, R., & Wang, H. (2004). The burden of kidney disease: improving global outcomes. Kidney international, 66(4), 1310–1314. https://doi.org/10.1111/j.1523-1755.2004.00894.x.

2) Barreto, F. C., Stinghen, A. E., de Oliveira, R. B., Franco, A. T., Moreno, A. N., Barreto, D. V., Pecoits-Filho, R., Drüeke, T. B., & Massy, Z. A. (2014). The quest for a better understanding of chronic kidney disease complications: an update on uremic toxins. Jornal brasileiro de nefrologia : 'orgao oficial de Sociedades Brasileira e Latino-Americana de Nefrologia, 36(2), 221–235. https://doi.org/10.5935/0101-2800.20140033.

3) Vassalotti, J. A., Centor, R., Turner, B. J., Greer, R. C., Choi, M., Sequist, T. D., & National Kidney Foundation Kidney Disease Outcomes Quality Initiative (2016).

Practical Approach to Detection and Management of Chronic Kidney Disease for the Primary Care Clinician. The American journal of medicine, 129(2), 153–162.e7. https://doi.org/10.1016/j.amjmed.2015.08.025.

4) Kalantar-Zadeh K & Amin AN (2012). Toward more Accurate Detection and Risk Stratification of Chronic Kidney Disease. JAMA. 307(18):1976-7.
5) Mallett, A., Patel, C., Salisbury, A., Wang, Z., Healy, H., & Hoy, W. (2014). The prevalence and epidemiology of genetic renal disease amongst adults with chronic kidney disease in Australia. Orphanet journal of rare diseases, 9, 98. https://doi.org/10.1186/1750-1172-9-98.
6) Levey A.S.; Eckardt K.U.; Tsukamoto Y. et al. (2005). Definition and classification of chronic kidney disease: A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney International. 67(6):2089-2100
7) National Kidney Foundation (2002). K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Am J Kidney Dis, Vol. 39, No. 2Suppl 1, pp. S1-266.
8) Shastri, S. & Sarnak, M.J (2010).Cardiovascular Disease and CKD: Core Curriculum. Am J Kidney Dis, 56, (2): p 399-417.
9) Ouyang, L., Bolen, J., Valdez, R., Joseph, D., Baum, M. A., & Thibadeau, J. (2015). Characteristics and survival of patients with end stage renal disease and spina bifida in the United States renal data system. The Journal of urology, 193(2), 558–564. https://doi.org/10.1016/j.juro.2014.08.092.
10) Quiroga, B., Vega, A., Abad, S., Villaverde, M., Reque, J., & López-Gómez, J. M. (2016). Creatine-kinase and dialysis patients, a helpful tool for stratifying cardiovascular risk?. Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia, 36(1), 51–56. https://doi.org/10.1016/j.nefro.2015.10.004 .
11) Muharrem I1, Ebru G.O2, Tolga Y2.et.al (2014).The Effect of Hemodialysis on Cardiac Enzyme Levels. Department of Internal medicine. Int J Artif Organs. Sanliurfa, Turkey, 37(7): p513-520.

12) D'Marco, L., Bellasi, A., & Raggi, P. (2015). Cardiovascular biomarkers in chronic kidney disease: state of current research and clinical applicability. Disease markers, 2015, 586569. https://doi.org/10.1155/2015/586569.

13) Ingec, M., Oguz, E. G., Yildirim, T., Ulas, T., & Horoz, M. (2014). The effect of hemodialysis on cardiac enzyme levels and echocardiographic parameters. The International journal of artificial organs, 37(7), 513–520. https://doi.org/10.5301/ijao.5000333.

14) Bozbas, H., Korkmaz, M. E., Atar, I., Eroglu, S., Ozin, B., Yildirir, A., Muderrisoglu, H., Colak, T., Karakayali, H., & Haberal, M. (2004). Serum levels of cardiac enzymes before and after renal transplantation. Clinical cardiology, 27(10), 559–562. https://doi.org/10.1002/clc.4960271007.

15) Naka, T., Wan, L., Bellomo, R., Wang, B. Z., Jones, R., Berry, R., Angus, P., & Gow, P. (2004). Kidney failure associated with liver transplantation or liver failure: the impact of continuous veno-venous hemofiltration. The International journal of artificial organs, 27(11), 949–955. https://doi.org/10.1177/039139880402701107.

16) Quiroga, B., Vega, A., Abad, S., Villaverde, M., Reque, J., & López-Gómez, J. M. (2016). Creatine-kinase and dialysis patients, a helpful tool for stratifying cardiovascular risk?. Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia, 36(1), 51–56.