Relation between Malnutrition–Inflammation–Atherosclerosis (MIA complex) in Diabetic Patients with Peritoneal Dialysis

Seid Kazem Razavi Ratki[1], Mojgan Kord[2], Seyed Ali Sadr Bafghi[3], Nasim Namiranian[4], Mohamad Sobhan Ardekani[5], Nader Nouri-Majalan [6], Reza Nafisi Moghadam[7]

1. MD, Assistant Professor of Nuclear Medicine, Department of Radiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
2. MD, Radiologist Department of Radiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
3. MD, Shahid Sadoughi University of Medical Sciences Yazd, Iran.
4. MD, Assistant Professor Community Medicine. Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
5. MD, Assistant professor, Department of Radiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
6. MD, Nephrology Department, Shahid Sadoughi Medical University of Medical Sciences, Yazd, Iran.
7. MD, Associated professor, Department of Radiology, Shahid Sadooghi University of Medical Sciences, Yazd, Iran.

***Correspondence:**
Reza Nafisi Moghadam, MD, Associated professor, Department of Radiology, Shahid Sadooghi University of Medical Sciences, Yazd, Iran.
Email: Nafisi.moghadam@gmail.com
Tel: (98) 353 822 4000

Received: 12 June 2016
Accepted: 01 August 2016
Published in November 2016

Abstract

Objective: Atherosclerosis disease, inflammation and malnutrition have strong association with end stage renal disease (ESRD). Diabetes mellitus (DM) is the most commonly ESRD causes. Diabetic nephropathy (DN) could be associated with inflammation. Type 2 diabetic patients with advanced nephropathy show the highest levels of inflammatory markers. This study was designed to determine the association between malnutrition–inflammation–atherosclerosis (MIA complex) in Diabetic patients with peritoneal dialysis.

Materials and Methods: Fifty seven diabetic patients on peritoneal dialysis were investigated and demographic variables (age, gender, BMI and dialysis duration), Inflammatory markers (cholesterol, Albumin and CRP) were measured in routine protocol. CIMT (Carotid Intima-Media Thickness) and plaque number were evaluated by B-Mode ultrasonography (7.5 -10 MHZ probe) in supine position.

Results: the mean age (Standard deviation) of patients was 51±17.3 years. The mean time on dialysis was 26.12 ±25.42 (range 4–120) months. The mean of IMT was 5.98±1.17 mm and mean of plaques were 1.80±2.01. Results of Analysis of variance (ANOVA) showed that older patients have more carotid plaques (*P*-Value= 0.000). There was a significant relation between serum albumin and number of plaques (*P*-Value=0.043). CIMT and number of plaque revealed significant correlation with age, serum albumin and dialysis duration ($P<0.05$).

Conclusion: Our findings showed, in diabetic patients on peritoneal dialysis, carotid atherosclerosis (CIMT and Number of plaque) is associated with some inflammation, malnutrition markers.

Keywords: Carotic intima media thickness, Inflammation, Malnutration, Diabetes.

Introduction

The atherosclerotic cardiovascular disease (AVD) is significantly increased in diabetic patients with ESRD and AVD is most important mortality cause in ESRD patients. (1,2) Some clinical studies report that diabetic nephropathy (DN)

could be related to inflammation and inflammation have a potential role in the pathogenesis of DN and type 2 diabetic patient and advanced nephropathy show the highest levels of inflammatory markers (3).

DN is an important etiology of end stage kidney disease (ESRD). Inflammatory process plays an essential role in pathogenesis of DN. Inflammatory indicators such as serum albumin are higher in patients with diabetes and DN. (3) The higher frequency of DM and uremia related risk cannot completely describe increased CVD in ESRD patients. Recently numerous studies have suggested strong relationship between atherosclerosis and inflammation. (1,4)

Malnutrition is usually reported in patients with ESRD. Malnutrition is considered as a situation that fat tissue is reduced and lean body mass is initially unaffected (5,6). Malnutrition is associated with inflammatory markers. (7,8). Both malnutrition inflammation may be seen in ESRD and called malnutrition–inflammation complex syndrome (MICS) (6,9). MICS is related to the cardiovascular disease (CVD) and described as malnutrition–inflammation–atherosclerosis (MIA) complex (10).

Carotid Intima-Media Thickness (CIMT) is considered as a substitute matter for atherosclerosis and is related to the CVD (11,12). The strong relationship between coronary artery disease and CIMT was documented in previous studies. CIMT is evaluated with Carotid ultrasonography as a noninvasive and inexpensive method. (11)

The aim of this study was to determine that malnutrition inflammation complex was correlated with CIMT in diabetic patients underwent peritoneal dialysis. Key point in our study is whether an association between the inflammation severity and the degree of CIMT.

Materials and Methods

Current study is an analytic cross-sectional study. Between March and April 2002, 63 diabetic patients on peritoneal dialysis from the Nephrology Unit of Shahid Sadoughi Hospital in Yazd entered the study. Eligibility criteria were; chronic renal failure attributed to diabetic nephropathy, peritoneal dialysis as first plane and more than 4 months, clinically stability and no evidence of active infection. Patients with liver failure, autoimmune disorder, recent corticosteroid use, malignant disease and history of peritonitis in 3mounts later were excluded.

Laboratory variable including Serum LDL-cholesterol, albumin and hemoglobin were measured by standard protocol. C-reactive protein were evaluated by routine available kit. Carotid ultrasonography were done with SIEMENS X300 instrument using a 7.5 MHz high-resolution probe on supine position in a relatively dark room within 7 days after blood sampling. The carotid arteries were examined by an expert radiologist blinded to the clinical and laboratory information. CIMT was evaluated on the longitudinal projection, 1 and 2cm lower and upper portions of the bifurcation arteries and the mean value was calculated. Plaques were categorized as soft plaques and calcified plaques with bulging into the arterial lumen. Number of Plaque was calculated by maximum thickness plaques in each segment bilaterally.

All statistical analysis was performed using the SPSS 17 software. The statistical significances were considered as 0.05.Differences in means between groups were evaluated using ANOVA. Correlations were tested by Pearson correlation analysis.

Results

Fifty seven diabetic patients on peritoneal dialysis mean aged 51±17.3 years were studied. The mean time on dialysis was 26.12 ±25.42 (range 4–120) months. The mean of CIMT was 5.98±1.17 mm and mean number of plaques were 1.80±2.01. (Table1).

The differences between the group means tested by Analysis of variance (ANOVA). Results of Analysis of variance (ANOVA) showed that older patients have more carotid plaques (*P*-Value= 0.000). There was a

significant relation between serum albumin and number of plaques (*P*-Value=0.043).

CIMT and number of plaques revealed significant correlation with age, serum albumin and dialysis duration (*P*<0.05).

Spearman's correlation of CIMT and number of plaques with continuous age, duration dialysis, BMI, Hg, serum albumin and LDL cholesterol was shown in table 3.

Discussion

Recently some studies reported that atherosclerosis disease, inflammation and malnutrition have strong association with ESRD. DM is the most common ESRD causes. DN could be associated with inflammation. Inflammation has potential role in the pathogenesis of DN. In type 2 diabetic patients with advanced nephropathy the highest levels of inflammatory markers were detected (3)

MICS is associated with CAD, hard and soft cardiac events with higher mortality and morbidity prevalence (13-15). Our study findings suggested a significant correlation between serum albumin level and CIMT as well as between serum albumin and number of plaques. Serum Albumin with an oxidative function have a potential preventing role in atherosclerosis process. Decreased serum albumin is associated with increased oxidative stress and this pattern could result endothelial dysfunction and vasodilator disorder. (16,17)

Aging is an important risk factor for cardiovascular disease. In our study between CIMT, number of plaque and age statically significant association was seen.

Association between BMI and CIMT is

Table 1. Descriptive characteristics of diabetic patients on peritoneal dialysis

Variable	Maximum	Maximum	SD	Mean
Age (years)	18	91	17.34	50.98
Dialysis duration(months)	4	120	25.42	26.12
Body mass index	14.85	34.72	4.34	24.33
Hemoglobin (gr/dlit)	8.95	15.13	1.37	11.8
Serum Albunin (gr/dlit)	3.1	4.8	0.44	3.99
Cholesterol (mg/dlit)	109	341	42.03	190.89
CIMT (mm)	4	9.2	1.18	5.99
Number of plaque	0	8	2.01	1.81

Table 2. The differences between the group means tested by Analysis of variance (ANOVA)

Variable		No plaque	1-2 plaque	Plaque 3-8	*P*-Value
Age	**Mean±SD**	17.54±41.32	14.31±52.25	12.13±63.47	0.000
Dialysis duration	**Mean±SD**	30.08±27.5	24.51±25.30	20.16±25.20	0.95
BMI	**Mean±SD**	5.4±23.47	3.24±23.79	3.39±26.31	0.115
Serum albumin	**Mean±SD**	0.38±4.15	0.5±3.97	0.36±3.79	0.043
CIMT	**Mean±SD**	0.9±5.27	1.08±6.24	1.13±6.7	0.000

Table 3. Spearman's correlation CIMT and number of plaques with continuous age, duration dialysis, BMI, Hg, serum albumin and LDL cholesterol

Variable	Cholesterol	Albumin	Hg	BMI	Dialysis duration	Age
IMT Pearson correlation	0.122	-0.352	0.198	0.072	0.035	0.744
***P*-Value**	0.369	0.008	0.144	0.599	0.796	0.000
Number plaque Pearson correlation	0.191	-0.361	0.15	0.234	0.058	0.512
***P*-Value**	0.159	0.006	0.27	0.082	0.669	0.000

controversial in different studies (19) but in current study no significant association is detected.

Although our study did not confirm the association between serum CRP and CIMT, many studies suggested a strong correlation between CRP and CIMT (20,21). Also in this study there is no relationship between CRP and malnutrition markers (serum albumin, BMI and cholesterol). A challenge in this study is loss of the Quantitative CRP result. CRP result was reported positive or negative.

Major limitations in this study are included, small sample size, loss of control group and CRP result with qualitative format. Multicenter cooperative prospective research with large sample size are mandatory to clarify above findings.

Conclusion

The diabetic adolescents on peritoneal dialysis are at risk of malnutrition as well as atherosclerosis. The inflammation may contributed either conditions.

References

1. Locatelli F, Bommer J, London GM. Cardiovascular disease determinants in chronic renal failure: clinical approach and treatment. Nephrol Dial Transplant 2001;16:459-68
2. Razavi Ratki SK, Amelshahbaz A, Nafisi-Moghadam R, Sartipzadeh NH. Application of Anatomical and Functional Modalities in Detection of Silent Myocardial Ischemia in Asymptomatic Diabetic Patients- A Review Article. IJDO. 2015;7(2):73-81.
3. Dalla Vestra M, Mussap M, Gallina P. Acute-phase markers of inflammation and glomerular structure in patients with type 2 diabetes. J Am Soc Nephrol 2005;16:78-82
4. Boaz M, Iuliano L, Himmelfarb J, Matas Z, Micheletta F, McMonagle E. Baselineoxysterols and other markers of oxidative stress, inflammation and malnutritionin the vitamin e and intima media thickness progression in end-stage renaldisease (VIPER) cohort. Nephron Clin Pract. 2005;100(4):111-9.
5. Paglialonga F, Edefonti A. Nutrition assessment and management in children on peritoneal dialysis. Pediatr Nephrol 2009;24:721-30.
6. Mak RH, Cheung WW, Zhan JY, Shen Q, Foster BJ. Cachexia and protein-energy wasting in children with chronic kidney disease. Pediatr Nephrol 2012;27:173-81
7. Kalantar-Zadeh K, İkizler TA, Block G, Avram M, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences. Am J Kidney Dis 2003;42:864-81.
8. Silverstein DM. Inflammation in chronic kidney disease: role in the progression of renal and cardiovascular disease. Pediatr Nephrol 2009;24:1445-52.
9. Kopple JD. Pathophysiology of protein-energy wasting in chronic renal failure. J Nutr 1999;129(1):247-51.
10. Stenvinkel P, Heimbürger O, Berglund L, Kaysen GA, Bergström J (2000) Are there two types of malnutrition in chronic renal failure? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA syndrome). Nephrol Dial Transplant 2000;15:953-60.
11. Nafisi-Moghadam R, Namiaranian N, Karbasi M, Hojat H, Razavi Ratki S K. Assessment of Carotid Intima-Media Thickness and Infra-Renal Abdominal Aorta Diameter in Women with and Without Gestational Diabetes Mellitus-A case Control Study. IJDO. 2015;7(2):50-4.
12. Irie Y, Katakami N, Kaneto H. Maximum carotid intima-media thickness improves the prediction ability of coronary artery stenosis in type 2 diabetic patients without history of coronary artery disease. Atherosclerosis 2012;221:438-44.
13. Stenvinkel P, Heimbu¨ rger O, Paultre F. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. Kidney Int 1999;55:1899-911.
14. Zoccali C, Benedetto FA, Mallamaci F. Inflammation is associated with carotid atherosclerosis in dialysis patients. J Hypertens 2000;18:1207-13.
15. Papagianni A, Kalovoulos M, Kirmizis D. Carotid atherosclerosis is associated with inflammation and endohelial cell adhesion molecules in chronic haemodialysis patients. Nephrol Dial Transplant 2003;18:113.
16. Werver R, Boer P, Hijmering M. Nitric oxide production is reduced in patients with chronic renal failure. Arterioscler Thromb Vasc Biol 1999;19:1168-72.
17. Matsumoto A, Hirata Y, Kakoki M. Increased excretion of nitric oxide in exhaled air of patients with chronic renal failure. Clin Sci 1999;96:67-74.
18. Stompór T, Kraśniak A, Sułowicz W, Dembińska-Kieć A, Janda K, Wójcik K, et al. Changes in commoncarotid artery intima-media thickness over

1 year in patients on peritonealdialysis. Nephrol Dial Transplant. 2005;20(2):404-12.
19. Beddhu S, Pappas LM, Ramkumar N, Samore MH. Malnutrition and atherosclerosisin dialysis patients. J Am Soc Nephrol. 2004 Mar;15(3):733-42.
20. Ahmad Zaki, Safaa EL-Hefni, Alaa Saleh, Yaser Ammar, Hisham EL-Banawy. The association Between Malnutrition,Inflammation and Atherosclerosid in Hemodialysis Patients. JMRI 2008;29:150-61.
21. Papagianni A, Kokolina E, Kalovoulos M, Vainas A, Dimitriadis C, Memmos D. Carotid atherosclerosis is associated with inflammation, malnutrition, and intercellular adhesion molecule-1 in patients on continuos ambulatory peritoneal dialysis. Nephrol Dial Transplant 2004;19:1258-63.