Research Article

Osteoprotegerin in Chronic Hemodialysis Patients and its Relation to Age and Gender

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Abstract
Introduction: Cardiovascular disease (CVD) is a major cause of death among chronic hemodialysis (HD) patients. Gender and age belong to its classical risk factors. **Aim of the work:** The aim of this work is to evaluate the srum levels of osteoprotegerin (OPG), in HD patients and 16 healthy volunteers in relation to gender, age and the other clinical and laboratory parameters. **Patients and Methods:** This observational cross sectional study included 80 chronic renal failure patients on maintenance hemodialysis, in nephrology unit, Nephrology and Urology university hospital and 16 healthy volunteers, in the period from January 2016 to June 2016. **Results:** Demographic data of the two studied groups are given in table (5) as following: Group (1): Consists of 80 chronic renal failure patients on maintenance hemodialysis; 40 males (50%) and 40 females (50%), their mean age (45.93±12.45). Group (2): Consists of 16 health volunteers served as control group; 6 males (37.5%) and 10 females (62.5%), their mean age (47.7±10.01). **Discussion:** Chronic kidney disease (CKD) can be defined in a variety of ways. The US Preventive Health Service defines it as decreased kidney function, with size-adjusted estimated glomerular filtration rate (eGFR/1.73 m2) <60 mL/min, or as abnormalities of kidney structure or function, present for 3 months, with implications for health (KDIGO, 2012).
Keywords: OPG: Osteoprotegerin, CKD: chronic kidney disease, VC: Vascular calcification

Introduction
Cardiovascular disease (CVD) is a major cause of death among chronic hemodialysis (HD) patients. Gender and age belong to its classical risk factors. In El-Minia governorate causes of death were 53% due to cardiovascular diseases and 14% were due to cerebrovascular accidents[(1)]

Osteoprotegerin (OPG) is involved in connecting bone and vascular remodeling. (OPG) regulates bone mass by inhibiting osteoclast differentiation and activation, and plays a role in vascular calcification and elevated levels of serum OPG may be associated with atherosclerosis and all-cause mortality in patients with chronic kidney disease (CKD)[(2)].

Among classic markers of renal osteodystrophy is parathyroid hormone and alkaline phosphatase (Mazzaferro, et al. 2014). Fractures are common in men and women with (CKD) but the best tool to identify those at high risk is unknown.

Increased circulating (OPG) is associated with fractures in postmenopausal women[(3)].

Patients with (CKD) are at a particularly high risk for cardiovascular disease. Vascular calcification (VC) is considered a cardiovascular risk marker, so in CKD patients screening for the presence of VC is suggested in current guidelines[(4)]

Aim of the work
The aim of this work is to evaluate the srum levels of osteoprotegerin (OPG), in HD patients and 16 healthy volunteers in relation to gender, age and the other clinical and laboratory parameters.

Patients and Methods
This observational cross sectional study included 80 chronic renal failure patients on maintenance hemodialysis, in nephrology unit, Nephrology and Urology university hospital and 16 healthy volunteers, in the period from January 2016 to June 2016.

Inclusion criteria:

1. Chronic renal failure on maintenance hemodialysis for more than 6 monthes.

Exclusion criteria:

1. Chronic liver disease (decompensated liver cirrhosis and ascites).
2. Acute renal failure.

All patients were subjected to:

1- Full history taking:

1. Age.
2. Sex.
3. Duration of hemodialysis.
4. History of diabetes or hypertension.
5. Etiology of ESRD..

2- Clinical parameters:

1. Pre and post hemodialysis blood pressure.
2. Dry weight.
3. Dialysis treatment parameters (frequency, session length, intradialytic weight loss (pre-post weight), and type of vascular access).
4. Prescribed medication (phosphate binding agents, erythropoietin stimulating agents (ESAs).

Results

Demographic data of the two studied groups are given in table (5) as following:

Group (1): Consists of 80 chronic renal failure patients on maintenance hemodialysis; 40 males (50%) and 40 females (50%), their mean age (45.93±12.45).

Group (2): Consists of 16 health volunteers served as control group; 6 males (37.5%) and 10 females (62.5%), their mean age (47.7 ±10.01).

Table (1): Heamatological indices in hemodialysis patients and control group

	Group 1 Cases (n=80)	Group 2 Control (n=16)	P value
Hb (g/dl): M±SD	9.9 ± 1.81	11.5 ± 1.58	<0.001*
Platelet count ($\times 10^3$/µl): M±SD	200.2 ±70.81	320.5 ± 50.4	<0.001*
Total leucocyte count($x10^9$/L): M±S D	5.5 ± 1.08	4.8 ±1.51	0.421

Table (2): OPG levels in hemodialysis patients and the control group

	Group 1 Cases (n=80)	Group 2 Control (n=16)	P value
OPG(pg/ml) M±SD	480.55 ± 167.05	147± 20.26	<0.001*

Discussion

Chronic kidney disease (CKD) can be defined in a variety of ways. The US Preventive Health Service defines it as decreased kidney function, with size-adjusted estimated glomerular filtration rate (eGFR/1.73 m2) <60 mL/min, or as abnormalities of kidney structure or function, present for 3 months, with implications for health.

Chronic kidney disease (CKD) is a leading cause of morbidity and mortality worldwide, affecting 5–10% of the world population with an ever-increasing prevalence. It is characterized by features that include progressive loss of kidney function, cardiovascular disease (CVD), disturbance of ion and water metabolism, gastrointestinal disorders and premature death. Disturbances in mineral and bone metabolism (MBM) are well known complications of CKD that can have a significant impact on morbidity; these complications are often manifested with increased vascular calcification, which is a major risk factor of CVD and cardiovascular mortality[5].

The Kidney Disease: Improving Global Outcomes (KDIGO) organization coined the term "chronic kidney disease mineral and bone disorders" (CKD-MBD) covering a wide spectrum of clinical syndromes that manifest as a systemic disorder of MBM due to CKD. CKD-MBD comprises a group of inter-related abnormalities of serum biochemistry [calcium, phosphorus, parathyroid hormone (PTH), or vitamin D metabolism], bone (bone turnover, mineralization, volume, linear growth or strength) and the vasculature (arterial stiffness and calcification) associated with CKD[6].

Vascular calcification an independent and strong indicator of cardiovascular risk is frequently found in CKD patients. It is defined as the inappropriate and pathologic deposition of mineral in the form of calcium phosphate salts into the vascular tissues. While this can happen with normal aging, it is accelerated in certain disease states including diabetes mellitus, cardiovascular disease, and specific genetic diseases. One of the most common causes of vascular calcification is chronic kidney disease (CKD)[6].

Recommendations

1- Higher OPG levels in HD women compared to age matched HD men indicate the necessity of more careful screening towards the presence of CVD and bone-mineral disorders in older female population.
2- Higher OPG levels in longstanding hemodialysis patients, so renal transplantation is the treatment of choice.
3- Old age is considered as a risk factor for cardiovascular disease and osteoporosis in hemodialysis patients, so more careful screening is important.
4- Control of hyperlipidemia should be done to reduce the risk of cardiovascular diseases.
5- Our study has several limitations. First, the sample size was relatively small. Thus, a larger patient cohort is necessary to confirm our findings. Secondly, this study was of a cross-sectional design and lacks repeated measurements of both OPG levels and valvular calcification limiting our ability to determine a causal relationship between them. However, since we adjusted for multiple risk factors in our analysis, these limitations do not affect our conclusions.
6- An age related change in the production or the clearance of OPG could also be an explanatory factor for this finding. However no previous studies looked at this relation.
7- We think that there is a need to look at the OPG expression or action outside the bone, more particularly in the adipose tissue, muscle or liver.
8- More studies are to be done to clarify more factors responsible for OPG elevations, to tell us about how to control these factors to improve quality of the life in CRF patients.

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