



Association of serum adiponectin levels with pulmonary artery pressure in maintenance hemodialysis patients

Mohammad Reza Tamadon¹, Maryam Heidari², Saeed Mardani^{2*}

Abstract

Introduction: Abnormal pulmonary artery pressure (PAP) in hemodialysis patients is associated with significant increase in morbidity and mortality.

Objectives: Considering the significance of pulmonary hypertension in hemodialysis patients, a study was designed to assess the association of serum adiponectin levels and PAP in a group of stable hemodialysis patients.

Patients and Methods: The study was conducted on a group of non-diabetic hemodialysis patients. The study was carried out in hemodialysis ward of Shahrekord University of Medical Sciences for a period of 4 months in 2013. The studied patients had a history of dialysis from 1 to 22 years.

Results: In our study, out of 76 hemodialysis patients, 46.1% were female and 53.9% were male. The mean PAP in female hemodialysis patients was 29.74 mm Hg, which was about 9% less than the PAP observed in male hemodialysis patients. Mean adiponectin levels in all the patients, males, and females, respectively, was 10.59, 10.42, and 10.80 $\mu\text{g/mL}$ respectively. In this study a significant and positive relationship between adiponectin levels and PAP in female hemodialysis patients ($r = 0.35$, $P = 0.04$) was detected.

Conclusion: This association requires more investigation on the significant role of adiponectin in hemodialysis patients.

Keywords: Adiponectin, Pulmonary artery pressure, Hemodialysis, Pulmonary hypertension

Citation: Tamadon MR, Heidari M, Mardani S. Association of serum adiponectin levels with pulmonary artery pressure in maintenance hemodialysis patients. J Renal Endocrinol. 2017;3:e05. DOI: 10.15171/jre.2017.05.

Copyright © 2017 The Author(s); Published by Nickan Research Institute. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Abnormal pulmonary artery pressure (PAP) (pulmonary hypertension) in hemodialysis patients is associated with significant increase in morbidity and mortality (1,2). The prevalence of pulmonary hypertension in this group of patients is relatively high and varies from 17% to 49.53% as reported by different studies (1-3). In addition, end-stage renal disease patients on hemodialysis are highly prone to develop pulmonary hypertension. Furthermore, it is more common among females than males (2). According to the study by Green et al, PAP (>35 mm Hg) is associated with sudden cardiac death in dialysis patients. It shows that its pathophysiology is likely to be different in this group of patients, as compared with the general population (4).

Obesity is associated with an increased incidence and severity of asthma, as well as other lung disorders, such as pulmonary hypertension. Adiponectin, as an anti-inflammatory adipocytokine, existed at lower levels in obese individuals, which is thought to contribute to obesity-related inflammatory diseases (5). Additionally, high concentrations of adiponectin exist in serum and have anti-inflammatory and systemic vascular-protective properties. In a study, Summer et al (6) investigated the

role of adiponectin in pulmonary vascular homeostasis. They found that adiponectin localizes in the luminal side of blood vessels in lung and acts in vitro to block TNF-alpha-induced E-selectin upregulation in pulmonary artery endothelial cells. Targeted removal of adiponectin gene in mice leads to a vascular phenotype in lung characterized by E-selectin upregulation and age-dependent increase in perivascular inflammatory cell infiltration and pulmonary arterial pressures. Taken together, these findings demonstrate the important role of adiponectin in lung vascular homeostasis and suggest that adiponectin-deficient states may contribute to the pathogenesis of inflammatory pulmonary vascular disease and lead to the development of pulmonary hypertension (7-9).

Researchers reported a possible mechanism for the association between obesity and asthma and suggested a potential novel link between obesity, inflammatory lung disease, and pulmonary hypertension (5).

Walkey et al (7) conducted a trial study and measured plasma adiponectin concentrations in 816 (81.6%) participants at baseline and in 568 (56.8%) subjects at both baseline and 7 days after the enrollment. They

Received: 30 October 2016, Accepted: 15 December 2016, ePublished: 8 January 2017

¹Department of Internal Medicine, Semnan University of Medical Sciences, Semnan, Iran. ²Department of Internal Medicine, Division of Nephrology, Shahrekord University of Medical Sciences, Shahrekord, Iran.

*Corresponding Author: Saeed Mardani, Email: dr_s_mardani@yahoo.com

■ Implication for health policy/practice/research/medical education

Studies regarding prevalence of pulmonary hypertension and its associated parameters and also its impact on hemodialysis outcomes are limited. In fact, pulmonary hypertension is a disease can be caused by various underlying situations or an intrinsic modification of the pulmonary vasculature. In this study, we found a significant and positive relationship between adiponectin levels and pulmonary artery pressure (PAP) in female non-diabetic hemodialysis patients. This association requires more investigation on the significant role of adiponectin in hemodialysis patients.

detected that baseline adiponectin was inversely related to mean PAP ($\beta = -0.015$, $R^2 = 1.5\%$, $P = 0.02$), however, this association did not persist in multivariable models ($\beta = -0.009$, $R^2 = 0.5\%$, $P = 0.20$).

Objectives

Considering the significance of pulmonary hypertension in hemodialysis patients, was designed a study to assess the association between serum adiponectin with PAP in a group of stable hemodialysis patients.

Materials and Methods

Study patients

The study was conducted on a group of non-diabetic hemodialysis patients. The study was carried out in hemodialysis ward of Shahrekord University of Medical Sciences for a period of 4 months in 2013. The studied patients had a history of dialysis from 1 to 22 years (Table 1). The hemodialysis sessions were performed using a low pressure dialysis filter with complement membrane, reverse osmosis pure water, and soluble bicarbonate. Patients, who had a history of diabetes, lung or heart disease, cigarette smoking, presence of any active or chronic infections, were excluded from the study.

Study protocol

Blood samples were taken from all the patients at the beginning and end of the study before dialysis to measure serum adiponectin level.

Laboratory analysis

In order to avoid the impact of daily nutrition on serum adiponectin fluctuations, the blood samples were taken before dialysis at 7:30 AM, after at least 8 hours of fasting. Then, serum adiponectin was measured in all patients by ELISA method using Oegenium kit and laboratory protocol (Human adiponectin [Acrp30] AviBion, ELISA kit, Helsinki, Finland).

Measurement of pulmonary artery pressure

Echocardiography was conducted for all the patients. Doppler echocardiography was applied to evaluate left ventricular ejection fraction, to measure the PAP and expiratory and inspiratory inferior vena cava (IVC) diameters, and to investigate the presence of pericarditis

or pericardial effusion and valvular diseases. Pulmonary artery hypertension is characterized by systolic PAP $35 \geq$ mm Hg at rest (8,9).

Ethical considerations

The research followed the tenets of the Declaration of Helsinki. The study was approved by the research committee of Hajar hospital and School of Medicine. Additionally, ethics committee of Shahrekord University of Medical Sciences also approved the plan. Before the study, written informed consent was obtained from all patients who participated in the study. All information about individuals was coded and kept confidential.

Statistical analysis

Demographic characteristics of the patients were described using mean (\pm SD). All analyses were performed using SAS version 9.2 (SAS Inc., Cary, NC, USA). The strength of the variables was estimated by Pearson's correlation coefficient. A P value less than 0.05 was set as significance level.

Results

Out of 76 hemodialysis patients, 46.1% were female and 53.9% were male. In male patients, presence of mild, moderate, and severe PAP were observed in 34 patients (82.9%), 5 patients (12.2%), and 2 patients (4.9%), respectively. In female patients, presence of mild, moderate, and severe PAP were observed in 28 patients (80%), 5 patients (14.3%) and 2 patients (5.7%), respectively. The mean PAP in female hemodialysis patients was 29.74 mm Hg, which was about 9% less than the PAP observed in male hemodialysis patients. However, moderate and severe types of PAP were more prevalent in females than in males.

Mean adiponectin level in all the patients, males, and females, respectively, was 10.59, 10.42, and 10.80 μ g/mL, respectively. Accordingly, adiponectin level in female

Table 1. Clinical characteristics of the hemodialysis patients on hemodialysis (n=76)

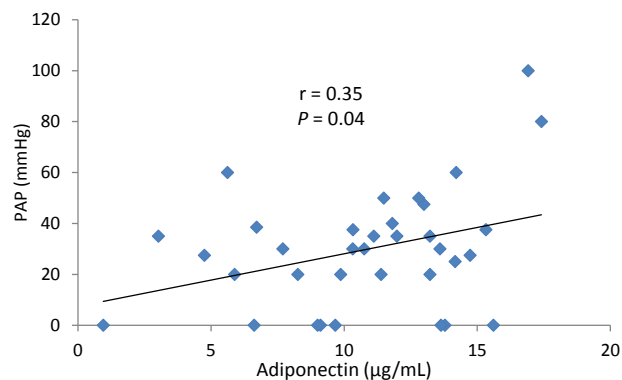
Parameters	Mean	SD	Min.	Max.
Age (y)	56.67	19.82	13	91
Adiponectin (μ g/mL)	10.59	3.82	0.32	17.41
PAP (mm Hg)	31.32	19.94	0	100
Duration of dialysis (y)	4.91	4.85	1	22
Body weight (kg)	58.36	14.17	31	103
Body mass index (kg/m ²)	21.9	3.77	14.74	33.33
Fasting glucose (mg/dL)	82.17	9.92	65	106
Total cholesterol (mg/dL)	172.57	40.59	71	283
Blood urea nitrogen (mg/dL)	64.45	18.54	26	112
Creatinine (mg/dL)	8.65	2.83	2.2	14.7
Triglycerides (mg/dL)	154.57	106.2	45	581
SBP (mm Hg)	123.95	21.79	90	190
DBP (mm Hg)	70.13	9.86	60	90

Abbreviations: PAP, pulmonary artery pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Association between serum adiponectin and pulmonary artery pressure in hemodialysis patients

	Total (n = 76)	Male (n = 41)	Female (n = 35)
PAP (mm Hg)	10.59	10.42	10.80
Adiponectin ($\mu\text{g/mL}$)	31.32	32.67	29.74
Correlation coefficient	0.22	0.09	0.35
P value	0.055	0.60	0.04

Abbreviation: PAP, pulmonary artery pressure.

**Figure 1.** Significant positive association between serum adiponectin levels and pulmonary artery pressure (PAP) in female hemodialysis patients (n = 35).

patients was 3.6% more than that in male patients (Table 2). There was a weak relationship between adiponectin levels and PAP in all dialysis patients (n = 76), but it was not significant at the confidence interval of 5% ($r = 22$, $P = 0.055$). There was also a weak relationship between adiponectin level and PAP in male hemodialysis patients (n = 41), whereas, it was not significant at the confidence interval of 5% ($r = 0.09$, $P = 0.60$). There was a significant and positive relationship between adiponectin level and PAP in female hemodialysis patients ($r = 0.35$, $P = 0.04$; Figure 1).

Discussion

In a study, it was shown that pulmonary hypertension was more common in females as it was present in 28 females (67%) and 17 males (45%), that was statistically significant ($P < 0.05$) (2).

Some studies have shown that dialysis can reduce the level of PAP (10) but in this study we did not find any significant relationship between duration of dialysis and the PAP ($r = 11$, $P = 0.53$ for women and $r = 8.5$, $P = 0.60$ for men).

Although we observed a positive relationship of adiponectin levels with PAP, in female hemodialysis patients, however, in the study by Walkey et al, which was conducted on acute respiratory distress syndrome, a negative relationship between baseline adiponectin and PAP was reported (7).

Conclusion

Studies regarding prevalence of pulmonary hypertension

and its associated parameters and also its impact on hemodialysis outcomes are limited. In fact, pulmonary hypertension is a disease can be caused by various underlying situations or an intrinsic modification of the pulmonary vasculature (11-15). In this study, we found a significant and positive relationship between adiponectin levels and PAP in female non-diabetic hemodialysis patients. This association requires more investigation on the significant role of adiponectin in hemodialysis patients.

Limitations of the study

Despite all the exertions made by the researchers, this investigation had some limitations. One of the limitations was low proportion of the patients. The study was also a single center experience. We suggest more investigations on this aspect of hemodialysis patients.

Authors' contribution

MH and SM conducted the research. MRT prepared the manuscript. All authors read and signed the final paper.

Conflicts of interest

The authors declare no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

This article is extracted from internal medicine residential thesis of Maryam Heidari. This study was supported by Shahrekord University of Medical Sciences (Grant #1302).

References

1. Shoukat, Rehman IU, Sumera, Idrees MK, Tanweer. Pulmonary hypertension and leading factors in patients undergoing dialysis. *J Coll Physicians Surg Pak.* 2014;24:836-9.
2. Mukhtar KN, Mohkumuddin S, Mahmood SN. Frequency of pulmonary hypertension in hemodialysis patients. *Pak J Med Sci.* 2014;30:1319-22.
3. Kosmadakis G, Aguilera D, Carceles O, Da Costa Correia E, Boletis I. Pulmonary hypertension in dialysis patients. *Ren Fail.* 2013;35:514-20.
4. Green D1, Ritchie JP, Abidin N, New DI, Kalra PA. The association of ECG and echocardiographic abnormalities with sudden cardiac death in a dialysis patient cohort. *J Nephrol.* 2014;27:81-6.
5. Medoff BD, Okamoto Y, Leyton P, Weng M, Sandall BP, Raheer MJ, et al. Adiponectin deficiency increases allergic airway inflammation and pulmonary vascular remodeling. *Am J Respir Cell Mol Biol.* 2009;41:397-406.
6. Summer R, Fiack CA, Ikeda Y, Sato K, Dwyer D, Ouchi N, et al. Adiponectin deficiency: a model of pulmonary hypertension associated with pulmonary vascular disease. *Am J Physiol Lung Cell Mol Physiol.* 2009;297:432-438.
7. Walkey AJ, Demissie S, Shah D, Romero F, Puklin L, Summer RS. Plasma Adiponectin, clinical factors, and patient outcomes during the acute respiratory distress syndrome. *PLoS One.* 2014;9:e108561.
8. Nasri H, Shirani Sh, Baradaran A. Pulmonary artery pressure in maintenance hemodialysis patients. *Pak J Biol Sci.* 2006;9:107-10.
9. Etemadi J, Zolfaghari H, Firoozi R, Ardalan MR, Toufan M, Shoja MM, et al. Unexplained pulmonary hypertension in peritoneal dialysis and hemodialysis patients. *Rev Port*

- Pneumol. 2012;18:10-4.
10. Havlucu Y, Kursat S, Ekmekci C, Celik P, Serter S, Bayturan O, et al. Pulmonary hypertension in patients with chronic renal failure. *Respiration*. 2007;74:503-10.
 11. Reque J, Quiroga B, Ruiz C, Villaverde MT, Vega A, Abad S, et al. Pulmonary hypertension in hemodialysis patients: Prevalence and associated factors. *Med Clin (Barc)*. 2016;146(4):143-7.
 12. Reque J, Quiroga B, Ruiz C, Villaverde MT, Vega A, Abad S, et al. Pulmonary hypertension is an independent predictor of cardiovascular events and mortality in haemodialysis patients. *Nephrology (Carlton)*. 2016;21:321-6.
 13. Abedini M, Sadeghi M, Naini AE, Atapour A, Golshahi J. Pulmonary hypertension among patients on dialysis and kidney transplant recipients. *Ren Fail*. 2013;35:560-5.
 14. Genctoy G, Arikian S, Eldem O. Pulmonary hypertension associates with malnutrition and body composition hemodialysis patients. *Ren Fail*. 2015;37:273-9.
 15. Kosmadakis G, Aguilera D, Carceles O, Da Costa Correia E, Boletis I. Pulmonary hypertension in dialysis patients. *Ren Fail*. 2013;35:514-20.