Kaohsiung Journal of Medical Sciences (2018) xx, 1–9

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.kjms-online.com

Original Article

Effect of blood purification on serum miR-126 and VEGF levels in the process of atherosclerosis in uremic patients under maintenance hemodialysis

Dong Zhao, Hong Shao*

Department of Nephrology, Jining No. 1 People's Hospital, Jining, Shandong, China

Received 27 October 2017; accepted 13 April 2018

KEYWORDS
Blood purification;
Maintenance hemodialysis;
Uremia;
miR-126;
VEGF

Abstract This study aims to study the influence of different blood purification approaches on the expression of miR-126 and VEGF serum levels in the development of atherosclerosis in uremic patients under maintenance hemodialysis (MHD). A total of 207 MHD patients with uremia were divided into HD (hemodialysis, n = 60), HDF (hemodiafiltration, n = 72), and HD + HP (hemodialysis + hemoperfusion, n = 75) groups based on different purification approaches. Eighty individuals who underwent physical examinations during the same period constituted the healthy controls. The serum levels of miR-126 and VEGF were examined by qRT-PCR and ELISA both before and after treatment, and the intima media thickness (IMT) value and plaque area were evaluated by color Doppler ultrasound. The serum miR-126 level was down-regulated in MHD patients compared with healthy controls, and this was negatively linked to VEGF. The post-treatment expression level of serum miR-126 in the HDF and HD + HP groups was remarkably increased, but VEGF was decreased in MHD patients, and especially significantly in the HDF group. In addition, IMT and plaque area were obviously improved in the HD group after treatment. Pearson correlation analysis showed a negative correlation of miR-126 with IMT and plaque area, but a positive association between VEGF and IMT and plaque area. miR-126 and VEGF are expected to become a valuable biomarker for monitoring the progression of atherosclerosis in uremic patients undergoing MHD.

Conflicts of interest: All authors declare no conflicts of interests.

* Corresponding author. Department of Nephrology, Jining No. 1 People's Hospital, No. 6, Jiankang Road, Rencheng District, Jining, 272011, Shandong, China.
E-mail address: shshsh0405@163.com (H. Shao).

https://doi.org/10.1016/j.kjms.2018.04.004

Please cite this article in press as: Zhao D, Shao H, Effect of blood purification on serum miR-126 and VEGF levels in the process of atherosclerosis in uremic patients under maintenance hemodialysis, Kaohsiung Journal of Medical Sciences (2018), https://doi.org/10.1016/j.kjms.2018.04.004

Introduction

Uremia, literally "urine in the blood", is a serious clinical complication of chronic kidney disease or end-stage renal failure, leading to fluid, electrolyte, and hormone imbalances, as well as metabolic abnormalities [1]. Patients with uremia usually suffer from an unfavorable prognosis with many complications, and they incur high disease-related costs, imposing heavy burdens on human health systems [2,3]. At present, blood purification is the main treatment for uremia, clearing away toxic substances accumulated in the body to alleviate clinical symptoms of uremic patients. Purification treatments include hemodialysis (HD), hemofiltration (HF), hemodiafiltration (HDF), and hemoperfusion (HP) [4–6]. Although the overall survival rate and quality of life of MHD patients have improved to some extent with the advancement of dialysis techniques, dialysis-related complications increase with long-term dialysis therapy [7]. Atherosclerosis (AS), one of the most common complications, can lead to cardiovascular disease and is the leading cause of death in MHD patients, with an incidence rate of approximately 80%. The mortality rate of these patients was 10–20 times that of the general population [8]. In this regard, it is of great significance to explore how to improve the quality of life of MHD patients, to reduce the incidence of complications and to lower their mortality rate.

MicroRNA-126 (miR-126), an endothelial-cell-specific miRNA, has unique characteristics to help regulate vascular integrity and angiogenesis. Thus, its deficiency will result in a loss of vascular integrity and defects, consequently leading to the changes in the morphology and function of the blood vessels [9,10]. Previous studies have noted the correlation of miRNA-126 with a series of cardiovascular diseases such as hypertension [11] and heart failure [12]. Meanwhile, Pan X et al. found that miR-126 was involved in the development and progression of AS [13]. On the other hand, vascular endothelial growth factor (VEGF) is a potent stimulator of angiogenesis that plays important roles in endothelial cell proliferation, migration, vascular permeability, and other endothelial functions [14,15]. Evidence revealed that the expression of VEGF in serum might be a useful tool to predict the degree of vascular endothelial cell injury in MHD patients [16].

Given the above, we hypothesized that in MHD patients, miR-126 and VEGF levels might be useful biomarkers for monitoring atherosclerosis. Three blood purification treatments, namely, hemodialysis (HD), hemodiafiltration (HDF), and hemodialysis and hemoperfusion (HD + HP), were conducted in our study, to investigate their influence on miR-126 and VEGF levels, as well as their association with the atherosclerotic lesions.

Materials and methods

Ethics statement

This study was approved by our hospital, and all procedures were conducted properly and strictly in accordance with the Helsinki Declaration [17]. All patients signed an informed consent form prior to the study.

Subjects of study

From December 2013 to December 2016, we recruited 207 uremic patients undergoing blood purification in our hospital as subjects of the study. The inclusion criteria were as follows: all patients were in stage 5 of chronic kidney disease (CKD5) according to the Kidney Disease Outcomes Quality Initiative proposed in 2001 by the National Kidney Foundation [18]; patients were treated with blood purification and regular dialysis for more than 3 months, and were in stable condition. The exclusion criteria were as follows: primary diseases such as autoimmune disease, active infection/hepatitis and liver damage, gastrointestinal bleeding, malignant tumor, and documented cardiovascular diseases. According to the different methods of blood purification, uremic patients were classified into the HD group (hemodialysis, n = 60), the HDF group (hemodiafiltration, n = 72), and the HD + HP group (hemodialysis combined with hemoperfusion, n = 75). Seventy uremia patients in CKD stage 5 who were just about to begin dialysis and matched in age and gender to the above groups were considered as the uremia group, and 80 healthy individuals undergoing physical examinations in our hospital during the same period were selected as the control group. Individuals who suffered from hypertension, diabetes, hyperlipidemia, coronary atherosclerotic heart disease, malignant tumor, and liver and kidney diseases were all excluded.

Blood purification treatments

All patients were given 6 months of continuous treatment. Patients in the HD group were treated 3 times per week, for 4 h each time with apolyethersulfone (PES) hollow fiber membrane (Diacap H7HPS, Fresenius Co., Bad Homburg, Germany). Patients in the HDF group were given hemodialysis twice per week and hemodiafiltration once per week for 4 h each time by using the polyethersulfone (PES) hollow fiber membrane (DiacapHIPS18, Braun, Melsungen, Germany), with membrane area 1.8 m^2, ultrafiltration coefficient 55 ml/(h·mmHg·m^2), dialysate flow 500 ml/min, and a blood flow rate of 220–300 ml/min. In the HD + HP group, hemodialysis and hemoperfusion were performed 3 times per week by applying hemoperfusion for 2 h in combination with conventional hemodialysis. Hemoperfusion was conducted by using an HA130-type sterile hemoperfusion apparatus (Pharmaceutical Factory of Livzon Pharmaceutical Group, Guangdong, China). Hemodialysis was performed for 2 h after removing the hemoperfusion apparatus.

Laboratory measurements

Before and after 6 months of continuous treatment, venous blood was collected in the fasting state. Then, the Olympus AU5400 automatic biochemical analyzer (Olympus Corporation, Tokyo, Japan) was utilized to determine the biochemical indexes, including serum creatinine (Scr), blood urea nitrogen (BUN), total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), serum phosphorus, Hb (hemoglobin), and ALB (albumin). ApoC3 and IL-6 levels were detected by

Please cite this article in press as: Zhao D, Shao H, Effect of blood purification on serum miR-126 and VEGF levels in the process of atherosclerosis in uremic patients under maintenance hemodialysis, Kaohsiung Journal of Medical Sciences (2018), https://doi.org/10.1016/j.kjms.2018.04.004