Abstract

Hemodialysis access recirculation is an important cause of inadequate dialysis delivery to individual patients. It is important to diagnose recirculation in order to optimize dialysis delivery. In addition, screening for recirculation may be used as a surveillance technique for the early detection of fistula stenosis, the correction of which may prevent thrombosis.

The presence of access recirculation should be suspected when there is an inadequate reduction in the BUC, as shown by the post-dialysis BUC exceeding 40 percent of the pre-dialysis BUC. Therefore high degrees of access recirculation in long term can lead to significant inadequate dialysis. It is well established that inadequate dialysis is an important contributor to lower overall survival among these patients.

It is also suggested that the presence of access recirculation is one of the surrogate markers of A-V fistula inflow problems among HD patient and early detection and treatment of these problems improves long-term access patency rates. Therefore, periodic assessment of access recirculation may have an important effect in the management of ESRD patients undergoing maintenance HD.

Any access recirculation should be considered abnormal and if it is exceeding 10% in the urea-based method or exceeding 5% in the non-urea based dilutional method, prompt investigation should be performed for discovering its causes. Doppler ultrasound offers the advantage of a non-invasive bedside procedure with lower costs and with no need for radio-contrast in order to assess the vascular access. It is also recommended that fistulography should be performed in elevated levels of access recirculation to determine whether stenotic lesions are impairing access blood flow.

In our study we aimed at studying the arterio-venous fistula recirculation in patients with maintenance hemodialysis to evaluate the prevalence and the causes of recirculation in the studied population.

One hundred patients were enrolled in this study, the AVFs were assessed for recirculation by two needle urea based equation and then patients were divided into 2 groups based on the percentage of recirculation. Patients with recirculation percentage equal or less than 10% were classified as group I, while patients with recirculation percentage more than 10% were in group II. The both groups were subjected to clinical and laboratory assessment. Patients in group II were assessed to find the causes of recirculation by investigating the patients with Echo and AVF Doppler.

According to our study the access recirculation was a common occurrence with high prevalence rate of 55% and it does not dependent on age, number or site of failed fistula but more frequent in female. Improper arterial and venous needle placement and close proximity between needles were identified as most important causes of recirculation. Left ventricular ejection fraction had no significant association with recirculation. Low Flow fistula was detected by Doppler ultrasound in three patients in present study. The small number of patients that had poor flow using AVF Doppler did not permit assessment of flow contribution to AVF recirculation.

Keywords: Arterio-Venous Fistula Recirculation in Hemodialysis: Causes and Prevalence

INTRODUCTION

End-stage renal disease (ESRD) is an irreversible condition for which patients require renal replacement therapy with dialysis or kidney transplantation to survive. Hemodialysis (HD) is one of the main modalities of renal replacement therapy ***(El-Sheikh and El-Ghazaly, 2016)***.

The dialysis prescription must ensure that an adequate amount of dialysis is delivered to the patient. Inadequate dialysis is an important contributor to lower overall survival among patients undergoing maintenance dialysis. Therefore, assessment of dialysis adequacy is a central issue in the management of these patients ***(Zeraati et al., 2013).***

It is well established that one of cause of inadequate dialysis in HD patients is arterio-venous (AV) fistula access recirculation (AR) ***(Shayanpour and Faramarzi, 2015).***

Hemodialysis AR is suspected when the blood urea concentration in arterial line is lower than that of systemic circulation, indicating that dialyzed blood returning through the venous needle reenters the HD machine through the arterial needle ***(Tonelli et al., 2001).***

It is also suggested that high degree of AR is one of the surrogate markers of AV fistula inflow problems and periodic assessment of AR can be used as a screening tool for early detection of this problem, which improves long-term AV fistula patency rates ***(Tentori et al., 2007).***

An accurate assessment of access fistula recirculation can be made by urea-based method as well as nonurea-based techniques using ultrasound dilution technique, conductivity, or potassium-based dilutional method ***(Brancaccio et al., 2001).***

Any access recirculation is abnormal. Recirculation exceeding 10% using the recommended two-needle urea-based method, or 5% using a non-urea based dilutional method, should prompt investigation of its cause ***(K-DOQI Clinical Practice Guidelines, 2006).***

AIM OF THE WORK

This study is designed to:

- Determine the prevalence of arterio-venous fistula recirculation.
- Assess the potential causes leading to arterio-venous fistula recirculation.

HEMODIALYSIS ADEQUACY

HEmodialysis (HD) is the main therapy available for patients with end-stage renal failure. Adequate dialysis improves patient survival, quality of life and biochemical outcomes as well as minimizes disease complications and hospitalizations ***(Adas et al., 2014).***

Adequacy of HD is defined as the dose of HD that is needed to maintain the healthy and functional status of the patient. Measuring the solute clearance which accumulates in uremic patients is the mainstay for assessing the dialysis dose and determining its adequacy ***(Himmelfarb and Ikizler, 2010)***.

If hemodialysis efficiency is not adequate, the level of blood toxins and the clinical symptoms of the patient will not be controlled which lead to increase the mortality and morbidity of patients, and the cost of dialysis ***(Oshvandi et al., 2014).***

Inadequate HD results in complications such as malnutrition, nausea, vomiting, anorexia, hypoalbuminemia, restless leg syndrome, insomnia, hypertension, pericarditis, electrolyte imbalance and headache, all reducing quality of life and may even result in death ***(Salehi et al., 2016).***

Many factors can increase adequacy of HD including use of high flux dialyzers, increasing blood flow rate (BFR), increasing flow of dialysate and dialysis time; some of these methods cannot be used routinely due to their economic impact and poor patient compliance ***(Borzou et al., 2009).***

The potential benefits of increasing the dialysis times to be three times per week for 6-8 hours per session is documented in some dialysis centers. It was found that the blood pressure is controlled better, the need of medications of hypertension is reduced and the episodes of intra-dialytic hypotension and mortality rates become less in some studies ***(Daugirdas, 2013).***

The high flow rate of the dialysate results in apparent increase in the dialyzer surface area and enhancing the dialysate penetration through the hollow-fiber bundle leading to increase the effective surface area of the dialyzer and subsequently enhance the dialysis efficiency ***(Leypoldt and Cheung, 2001)***.

It has been suggested that increasing blood flow rate by 15–20% of previous flow rate is effective in achieving dialysis adequacy in HD patients with low Kt/V ***(Kim et al., 2004).***

The use of high flux dialysis membranes improves the removal of a wide spectrum of uremic toxins including middle molecules and large size molecules which may improve the adequacy of dialysis and the quality of life of HD patients ***(Oshvandi et al., 2014).***

Removal of middle molecules (e.g. β2-microglobulin) results in better improvement of the metabolic alterations that is associated with uremic condition. This associated improvement includes decreasing in chronic inflammation and prevention of pro-inflammatory cells and protein pathway activation ***(Locatelli and Canaud, 2012)*.**

Optimal HD quality requires extracorporeal circuit (ECC) with full patency as coagulation system disturbance results in considerable morbidity and mortality. Although removal of uremic toxins during HD decreases the risk of bleeding, the interaction between the artificial surfaces and the blood leads to coagulation pathway activation. This disturbance decreases the efficiency of dialysis so appropriate anticoagulation is required without over or under heparinization ***(Kessler et al., 2015)***.

Adequate hemodialysis plays an important role in improving anemia and reducing the erythropoietin-stimulating agent (ESA) dosage required for anemia correction. This benefit may due to the correction of oxidative stress, and the removal of molecules that inhibit erythropoiesis and erythrocyte G6PD activity. This beneficial effect of hemodialysis adequacy on anemia improves the general status of ESRD patients by reducing the morbidity associated with anemia ***(Ayesh et al., 2014).***

As mentioned before that HD adequacy is related directly to the quality of life of the patient, morbidity and mortality. Malnutrition is considered one of the most leading factors to mortality and morbidity in hemodialysis patients. Malnutrition may be due to appetite loss with dietary limitations, hypermetabolism, metabolic acidosis, depression, decreased physical activity and comorbidities ***(Kaya et al., 2016).***

The nutritional intervention is effective when it is targeted at improvement of the protein status and includes anti-inflammatory properties. A scientific interest to omega -3 fatty acids application to the dialysis patients is growing as it prevent cardiovascular disease, decrease the pro-inflammatory response, improve the lipid level and the endothelial function in addition to its antithrombotic properties ***(Daudzam et al., 2012).***

The delivered dose of HD should be measured regularly at least every 8 weeks to be sure that urea is cleared from the patient as prescribed ***(Jindal, 2006)***.

The expression of clearance should include the patient's treatment time (t) and adjustment for patient size. The most convenient measure that satisfies these requirements is Kt/V. Several methods have been used to calculate Kt/V; these methods include simplified explicit formulas, multi-compartment models, and on-line conductivity measurements (OCM), not all of which generate the same value ***(KDOQI Guidelines update, 2015)*** .

Kt/V, is expressed as clearance (K) multiplied by time of treatment (t) divided by volume of urea distribution (V) and describes the fractional urea removal per dialysis treatment ***(Kemp et al., 2001)***.

The single-pool *Kt*/*V* (*spKt*/*V*), determined from the pre- and postdialysis urea concentrations and the equilibrated *Kt*/*V* (*eqKt*/*V*), have been used for some time to measure the efficiency of a single session of intermittent dialysis. The standard *Kt*/*V* (*stdKt*/*V*) is used to measure the relative efficiency of the whole spectrum of dialytic therapies, whether intermittent, continuous, or mixed ***(Diaz-Buxo and Loredo, 2006).***

Calculation of Kt/V based on single pool urea kinetics with a variable distribution volume was initially proposed by Sargent and Gotch. Numerous difficulties with the Gotch formula have been previously noted. On a practical basis, in dialysis facilities computers are needed to perform Kt/V assessments with the Gotch formula. Using computer simulation, a simple and precise equation was developed by Daugirdas to compute Kt/V based on predialysis and postdialysis plasma urea nitrogen (UN), ultrafiltrate (UF) volume in liters, time (t) of dialysis in hours, and postdialysis patient weight (W) in kg (R is postdialysis UN/predialysis UN): $spKt/V = -\ln(R - 0.008 \times t) + (4 - 3.5 \times R) \times UF/W$. This formula for single pool Kt/V (spKt/V) was further simplified by assuming dialysis time to be equal to 3.75 hours, thus $Kt/V = -\ln(R - 0.03) + (4 - 3.5 \times R) \times UF/W$. A minimum Single-pool *Kt/V value* of 1. 2 is recommended by KDOQI adequacy guidelines ***(Goldfarb-Rumyantzev et al., 2002)***.

According to the United States Renal Data System (USRDS), increasing Kt/V by 0.1 can result in reducing partial risk of cardiovascular and infectious diseases and each 0.1 reduction of Kt/V can increase the mortality rate by *5-7%* in dialysis patients ***(Borzou et al., 2009).***

Since both spKt/V and stdKt/V are normalized by V, the patient's urea (water) volume, both are potentially underestimated in small patients and in women. Substitution of body surface area (BSA) for V in the denominator reduces the error as BSA depends more on height than weight. BSA is more commonly used as a denominator for physiologic functions, including basal metabolism, cardiac output, and glomerular filtration ***(Ramirez et al., 2012)***.

The relatively rapid removal of BUN during hemodialysis causes BUN concentration disequilibrium between intracellular (ICF) and extracellular (ECF) fluid spaces. The ECF BUN concentration rebounds in a logarithmic fashion for 30-60 minutes after the hemodialysis treatment as BUN equilibrates between the ICF and ECF. Since Kt/V calculation is based partially on the post-hemodialysis BUN level, urea rebound has a significant impact upon the calculation of the delivered dose of hemodialysis ***(Goldstein et al., 2006).***

Many equations have been developed to adjust the Kt/V for urea rebound which happens in the first 30-60 minutes postdialysis. The resultant Kt/V is called equilibrated Kt/V(eKt/V). KDOQI guidelines recommend that eKt/V value is usually less than spKt/V by 0.2 units ***(Mehta and Fenves, 2010)***.

There are different methods and devices that measure the *Kt*/*V* on-line. All deliver *Kt*/*V* measurements before the end of treatment, overcoming the drawback of the blood-sampling method. These measurement systems can be classified to three groups according to the technical principle: conductivity-based methods, urea sensors, and spectrophotometric methods ***(Castellarnau et al., 2010).***

The online Conductivity measurement(OCM) is based on the observation that urea and sodium chloride are similar regarding the osmotic distribution volumes and the molecular weight, so the ionic dialysance (ID) is considered to be equivalent to the urea clearance ***(White, 2013)***.

The online measurement of ionic dialysance is performed by using of a conductance probe in the dialysate waste and regular set perturbations of inlet dialysate conductivity, which enables the software to measure the movement of ions across the dialysis membrane. This allows the depurated volume to be measured at 30 min intervals throughout dialysis, and for Kt/VID to be recorded ***(Al saran et al., 2010).***

As a result of the changes in a patient's condition during the session of dialysis, the Kt/VID by OCM is not accurate.

Hypotension episodes, reduction of blood flow rate and the colloid or crystalloid infusion between measurements are the factors that decrease the accuracy ***(Tam, 2004)***.

According to the European Best Practice guidelines on hemodialysis, online clearance should not be replaced by measurements of equilibrated Kt/V, though it is an acceptable method for calculating hemodialysis on a treatment-by-treatment basis ***(European Best Practice Guidelines, 2007).***

Spectrophotometric methods are based on that many substances present in the uremic serum are active in the ultraviolet (UV) range of the light spectra. Monitoring UV-absorbing compounds in spent dialysate not only offers enough data to tightly monitor a dialysis treatment, but also eliminates the need for V, by directly obtaining the ratio K/V from the decaying absorbance curve ***(Castellarnau et al., 2010).***

The urea reduction ratio (URR) is another measure of delivered dose of HD. the measurement of URR is expressed as follows:

$$URR = (BUNpre \_ BUNpost)/BUNpre$$

Where BUNpre is concentration of pre-dialysis urea and BUN post is concentration of post-dialysis urea. By convention, the value is expressed as a percentage. It is also called percentage reduction in urea (PRU). The recommendations of

DOQI guidelines include that the urea reduction ratio (URR) should be >65% ***(Mehta and Fenves, 2010)***.

When level of kidney replacement increases, especially when treatment is given daily, URR approaches zero. URR also is zero in continuously dialyzed patients or patients with normal kidney function. The disadvantages of URR include the inability to adjust the prescription accurately when the value is off target (by adjusting K or t), inability to add the effect of residual kidney function, and inability to troubleshoot by comparing prescribed with delivered dose ***(KDOQI Guidelines updates, 2006).***

There are many reasons why a discrepancy between prescribed and delivered dose of hemodialysis might exist. Failure of staff to ensure that the pre-determined treatment time is given (usually in the face of variable patient resistance) is a common failing. However, other factors such as suboptimal needle placement, hemodynamic instability, and progressive access malfunction all militate against this optimal delivery ***(K-DOQI Clinical Practice Guidelines, 2001).***

A-V fistula recirculation is one of the causes that markedly decrease dialysis adequacy resulting in the delivered dialysis being less than the prescribed so access recirculation should be assessed periodically. However, most of the HD centers seem to neglect making a periodic assessment for their patients ***(Zeraati et al., 2013)***.

VASCULAR ACCESS

Hemodialysis is a transient procedure for treating those patients who are waiting for kidney transplantation and a permanent procedure for the end-stage kidney disease patients with no plan of transplantation. Hemodialysis requires a vascular access with blood flow of 350 ml/min at least. Without a proper vascular access, the efficacy of dialysis is reduced with increased the morbidity and mortality rates ***(Hajbagheri et al., 2014)***.

Effective hemodialysis needs a reliable vascular access. Criteria for an ideal VA: to be safe, acceptable to the patient, inexpensive to create and maintain with a reliable performance and free of complications ***(Francais, 2005).***

The main types of the vascular access are arteriovenous fistula (AVF), AV graft (AVG) using synthetic material (*e. g.*, polytetrafluoroethylene (PTFE), and central venous catheter (CVC). AVF is the first best choice for chronic HD. The fistula use is recommended strongly by the guidelines in different countries as its morbidity and mortality association is the lowest. An arteriovenous graft is an alternative for maintenance HD. CVCs have become an important adjunct in maintaining patients on HD ***(Santoro et al., 2014).***

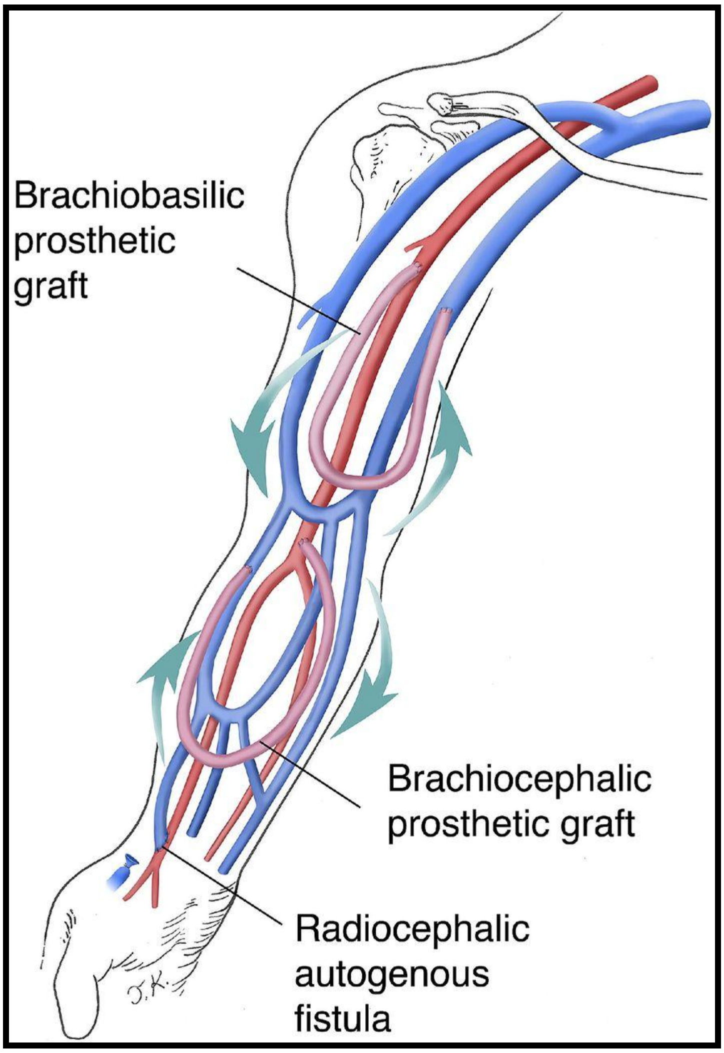

Figure (1): Composite Illustration of Access Anatomy of the Right Arm.

The preferred sites for AV fistula creation are the wrist (radiocephalic) followed by the elbow (brachiobasilic). The preferred graft site and type is a forearm curved radio cephalic followed by an upper arm straight one while the least preferred grafts are the straight radial cephalic in forearm and looped thigh grafts ***(Jindal et al., 2006).***