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Kidney: A Review on End Stage Renal Disease, Dialysis and Transplant

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ABSTRACT

As more and more people become dependent on dialysis, the incidence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) is rising globally. For people with ESRD, dialysis is a life-saving treatment, but compared to kidney transplants, long-term survival rates are still poor. There are various dialysis treatment options available, and patients often select one based on their preferences and way of life. Each type of dialysis has its advantages and hazards. Although kidney transplants are linked to higher survival rates, the likelihood of receiving one is still low due to the high demand for organ donors. Xenotransplantation is an intriguing area of transplantation, but it is still in its early phases and has several drawbacks. Future research should concentrate on these issues. This review seeks to improve understanding of kidney disease, dialysis and transplant and identify future areas of research to improve kidney outcomes in end-stage renal disease population.

Highlights:

- The ESRD population is growing rapidly in the United States and worldwide.
- Dialysis irrespective of modality remains critical and life-saving for the ESRD population.
- Kidney transplant is associated with better survival rates but the process needs to be streamlined to improve availability and affordability of donor kidneys.
- Xenotransplantation of the kidney is an early and exciting field that needs more focus for future.

Keywords: Kidney; Renal Disease; Transplant

The process of dialysis is the diffusion of molecules in solution along an electrochemical concentration gradient across a semipermeable membrane.[1] When the kidneys are unable to remove extra fluid and waste from the blood, dialysis will help.[2] Beginning in the 1970s, dialysis became the life-saving treatment for kidney failure after being

effectively utilized for the first time in the 1940s.[2] Belding Scribner and his colleagues at the University of Washington created a blood-access device in 1960 that made it easier for patients with uremia to undergo repeated hemodialysis as a life-sustaining treatment.[1]

End-stage renal disease (ESRD) in the United States:

Over 131,600 Americans began receiving treatment for ESRD in 2018, according to the Centers for Disease Control and Prevention (CDC).[3] In the US, 2 out of every 1,000 persons, or about 786,000 people, have ESRD and are either receiving dialysis or have had a kidney transplant. Three men get ESRD for every two women who do. Three non-Hispanic Black people get ESRD for every non-Hispanic White person who does. Four Hispanic people acquire ESRD for every three non-Hispanic people who do. Diabetes and high blood pressure are the major causes of ESRD in persons in the United States who are 18 years of age or older.[4,5] The two main causes of ESRD in children and teenagers under the age of 18 in the United States are polycystic kidney disease and glomerulonephritis (kidney inflammation).

Hemodialysis:

Hemodialysis is a therapeutic modality that treats the azotemia, fluid, electrolyte, and acid-base imbalances typical of the uremic syndrome by using the extracorporeal circulation of a patient's blood.[1] Hemodialysis' main objective is to recreate the fluid environment within and outside of cells, which is essential for healthy kidney function. This is done by moving solutes from the blood, such as urea, into the dialysate, as well as moving solutes from the dialysate, such as bicarbonate, back into the blood. The main factors affecting diffusion rates are solute concentration and molecular weight.

The procedure of hemodialysis:

Tiny molecules like urea disperse quickly, whereas larger, compartmentalized molecules like phosphate, albumin, and 2-microglobulin, as well as solutes coupled to proteins like p-cresol, diffuse much more slowly.[6] In addition to diffusion, solutes may also move through membrane pores by ultrafiltration, a convective process driven by hydrostatic or osmotic pressure gradients. No solute concentrations are altered during ultrafiltration, which is mostly used to remove extra body water.

Complications during Hemodialysis:

The most frequent adverse reaction during dialysis is hypotension.[7] The most significant reason is ultrafiltration-induced volume depletion, however, other aspects may also be involved. It's interesting to note that certain hypotensive patients have a paradoxical withdrawal of reflex sympathetic nervous system activity during dialysis, which is accompanied by a drop in heart rate, a reduction in vascular resistance, and a blood pressure collapse.[8] In addition to ultrafiltration, the dialysis procedure itself can occasionally result in hypotension. Several elements are crucial besides the extracellular volume reduction brought on by osmolar changes. For instance, dialysis at 37°C is linked to excessive heat retention in some people, which might lead to vasodilation and lower blood pressure.

Increased peripheral vascular resistance, elevated plasma norepinephrine levels enhanced cardiac contractility, and stable blood pressures are all effects of using a reduced-temperature dialysis bath (35°C). It is crucial to understand that pericardial effusion with tamponade, arrhythmia, or cardiac ischemia can all cause hypotensive episodes. The most common methods for successfully treating hypotensive episodes include decreasing the rate of ultrafiltration, giving intravenous saline, or both.

Survival and risk factors:

For people with ESRD, the overall life expectancy is still under ten years.[7] The primary cause of morbidity and mortality in patients receiving hemodialysis (HD) for end-stage renal disease (ESRD) is cardiovascular disease (CVD).[9,10] Although diabetes mellitus and hypertension usually cause ESRD, it has been hypothesized that these underlying conditions are to blame for the patients' elevated CVD risk. Yet, it has been clarified how ESRD functions as a standalone CVD risk factor, unrelated to either hypertension or diabetes mellitus.[11]

Peritoneal dialysis

Today, peritoneal dialysis is a widely used kidney replacement therapy.[12] In peritoneal dialysis, the peritoneal membrane, which is made up of a vascular wall, the interstitium, and the mesothelium, allows for the exchange of solutes and fluids between the peritoneal capillary blood and the dialysis solution in the peritoneal cavity.[13] The peritoneal dialysis solutions' addition of the proper osmotic agents causes osmosis, which is what causes fluid changes. Solute mobility is governed by the physical rules of diffusion and convective transport. The peritoneal blood flow, the highly vascular membrane, and the flow rate and volume of the peritoneal dialysis solutions are the critical elements of the peritoneal dialysis system. The only variable that can be changed to achieve maximum solute and fluid removal is the flow rate of the dialysis solutions because neither the peritoneal blood flow nor the vascularity of the membrane can be altered. These transport qualities are now improved by a variety of methods and practices. The solutions also contain lactate, salt, potassium, calcium, and glucose as osmotic agents in varying amounts.[14] Since it causes sclerosing peritonitis and loss of ultrafiltration, the use of acetate as a buffer has been abandoned. Lactate-based solutions have a pH that ranges from 0 to 5. Bicarbonate, a perfect buffer for peritoneal dialysis, is thus replacing lactate in dialysis solutions. Due to the presence of glucose, the solution is hyperosmolar, unphysiological, and bio-incompatible. The most often used osmotic agent is still glucose. Although it is inexpensive, safe, and has been around for a while, its absorption causes weight gain due to the loading of 100–200 g of glucose per day, hyperinsulinemia, hyperlipidemia, and short-lived ultrafiltration. The mesothelium and macrophages are negatively impacted by the solution's hyperosmolarity and low pH. The peritoneum is further harmed by advanced glycation end-products created by the glycation of stromal proteins. The hunt for a different osmotic agent has taken a lot of time and effort. Even at dwell times of up to 12 hours, Icodextrin (glucose polymers) induces ultrafiltration via colloid osmosis and is isosmotic to uraemic plasma.[15] The alternative is a combination of amino acids, which is marketed primarily as a protein supplement for undernourished people. These

two drugs, however, should only be used in sporadic combinations with regular glucose. All future exchanges must be conducted with these osmotic agents and bicarbonate mixes since they are more physiological than the solutions now in use.

Peritoneal dialysis complications:

For peritoneal dialysis patients, peritonitis continues to be a severe complication (PD). According to the CANUSA survey, peritonitis is one of the leading causes of hospital admission, accounting for 23% of admissions.[16-18] The most common reason for dialysis failure and catheter loss is peritonitis.[19] Independent of other considerations, patients with recurrent peritonitis have a higher risk of dying.[20] Abdominal pain, cloudy effluent, or most frequently both, are the typical signs and symptoms of peritonitis. The level of pain can vary greatly or not at all. The lack of pain in a patient with limited experience may cause them to initially overlook the hazy effluent, delaying presentation and subsequent treatment. If the effluent is even slightly hazy, all patients need to be instructed to contact the right away. If the white blood cell (WBC) count in the effluent is b00/p.b or above, with at least 50% polymorphonuclear cells, peritonitis is evident. The percentage of polymorphonuclear cells (i.e., more than 50%) is a more reliable indicator of peritonitis than the absolute quantity of WBC if the sample was acquired from a brief cycle, an aspirate from a drained abdomen, or from a patient who was already taking antibiotics.[19]

Hernias

There is an increase in intra-abdominal pressure when dialysis fluid is present in the peritoneal cavity (IAP). As more dialysate is injected, the pressure inside the abdomen rises in proportion.[21] For a given volume of intraperitoneal fluid, the supine patient generates the lowest IAP. Intraperitoneal pressure corresponds with the amount of dialysate infused even in supine patients undergoing automated peritoneal dialysis.[22,31] Pressures spike intermittently as a result of coughing and straining. Moreover, individuals who are older and fatter produce higher IAP for a particular activity.

Genital and Abdominal Wall Edema

A severe PD consequence is edema of the labia majora, scrotum, and penis.[23] Genital edema was once thought to affect up to 10% of CAPD patients, however more recent studies show that this problem occurs less frequently. It seems that vaginal edema affects women far less frequently than it does men. The processus vaginalis being more frequently patent in males may be the cause of this differential, or labial swelling may not be as obvious as swelling around the penis and scrotum. Nevertheless, dialysate seldom dissects through the Douglas pouch, the vaginal vault, or even passes through the Fallopian tubes and manifests as vaginal leaking.

Hydrothorax

Dialysis fluid leakage from the peritoneal cavity, across the diaphragm, and into the pleural space can be caused by increased IAP.[24] Hydrothorax refers to the buildup of dialysis fluid in the pleural cavity. How frequently hydrothorax happens in PD patients is unknown. The incidence is typically estimated to be less than 5%, which

would make it less common than abdominal hernias. The incidence in one research reached 10%. Yet, if the patient is asymptomatic or if modest complaints of shortness of breath are disregarded, it is likely that hydrothorax does occur much more frequently but does not come to medical notice.

Kidney Transplantation

If a patient with end-stage renal disease is determined to be a candidate for a transplant, the superior survival benefits of transplantation versus prolonged dialysis are generally well described.[25] As of December 2018, there were 229,887 functional kidney transplants and 554,038 end-stage renal disease patients on long-term dialysis in the United States. Over 91,000 individuals required kidney transplants as of February 2021. Improvement of long-term survival is an important priority for academics, physicians, and patients because some kidney transplants ultimately fail, typically after several years. With time, both patient and graft survival have increased.[26] The 10-year total graft survival percentage for kidneys from dead donors was 42.3% from 1996 to 1999 and rose to 53.6% from 2008 to 2011.

The long-term survival rates recorded by American registries are lower than those reported by registries outside of the United States. For instance, primary kidney transplants from deceased donors and living donors had 5-year graft survival rates in the United States of 72% and 85%, respectively, compared to 81% and 90% in Australia and New Zealand, 79% and 87% in Europe, and 81 and 91% in Canada. Except in cases of death, alloimmune damage and recurrent glomerulonephritis are the main causes of transplant failure. The decrease in clinical acute rejection rates, improved pretransplantation cross-matching methods, prudent use of paired-exchange transplants for candidates with incompatible living donors, viral infection monitoring, and efficient antiviral prophylaxis have all been linked to the observed improvement in long-term outcomes.

Xenotransplantation:

The lack of transplantable human organs has led to one of the most promising solutions: xenografts from genetically altered pigs.[27] Hyperacute rejection has been a problem in this model.[28] In a study, pigs have been produced with subcapsular autologous thymic tissue and an alpha-1,3-galactosyltransferase gene deletion to prevent this. Two brain-dead human recipients, whose circulatory and respiratory activity was maintained on ventilators throughout the study, received kidney transplants from these genetically altered pigs. To evaluate renal function and xenograft rejection, repeat biopsies were done, and tracked the flow of urine and kinetic estimated glomerular filtration rate (eGFR) were in brain-dead human patients for 54 hours, genetically altered pig kidney xenografts remained alive and functional with no symptoms of hyperacute rejection.

This study's main drawback was its brief follow-up, which was caused by the practical constraints placed on its design while using the technique on recently deceased individuals. Both under optical and electron microscopy, we observed maintained histologic architecture and the absence of significant immune-mediated damage. In this study, electron microscopy was carried out 54 hours after reperfusion and revealed completely intact architecture with

preserved glomerular basement membrane and podocytes in the two xenografts, in contrast to the development of proteinuria and nephrotic syndrome that have been reported in pig-to-baboon renal xenotransplantation studies.

Lastly, although the PERV virus has never been transmitted to humans, the possibility of infection from the virus' presence in the pig genome has traditionally raised questions.[29,30] The exclusive herd of porcine employed in this investigation was routinely screened for all known zoonotic diseases. Although this danger is regarded to be extremely low, future research with longer exposure to xenografts may be able to assess the long-term safety of xenotransplantation. This analysis of two successful renal xenotransplantations shows that the danger of hyperacute rejection was low and that immediate catastrophic failure was improbable when using kidneys from alpha-1,3-galactosyltransferase-knockout pigs with a low or negative cytotoxic xeno-crossmatch. Longer-term research using recently deceased persons or human clinical trials are necessary for an evaluation of the resilience of beneficial effects in this paradigm as well as adaptive immune responses.

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