Editorial

Evolution of Artificial Kidneys

Chronic Kidney Disease (CKD) is one of those diseases that may change the present trend in the healthcare system in future not so far. Being a relentlessly progressive disease, there is no cure. Diabetes and hypertension being the two most prevalent contributors, the burden of CKD is rising as a clow epidemic. Presently more than 10% of the world's population is suffering from CKD. Since 1990, there has been a 23% increase in prevalence and a 45% increase in mortality contributed by this disease.The scenario is worsein lower- and middle-income countries(LMIC). In India, the prevalence reported in various regions are variable ranging from 1% to 13%. Recently, data from the International Society of Nephrology's Kidney Disease Data Centre Study reported a prevalence of 17% in India.

The treatment of End stage or Stage V kidney disease or Kidney failure is renal replacement therapy. Hemodialysis is the most common modality of renal replacement therapy. However, the situation is dismal in LMICs. In India, over 90% of patients requiring RRT die because of inability to afford care and even in those who do start RRT, 60% stop for financial reasons.

The role of Renal transplantation as a permanent solution to this problem is encouraging. The actual scenario is howeverextremely non assuring. Out of almost 2 lakh new patients started on dialysis only 5,000 to 10,000 people received an organ. The average waiting period for a patient even in USA is three to five years.

To improve the overall outcome in Ens Stage Kidney Disease (ESKD), the concept of an artificial kidney started to be in vogue. This bioartificial kidney was conceptualized as a universal donor, wearable filtration device designed for mass production and use.

Only portability of the dialysis machine was not going solve the question. During covid times many commercially available portable home dialysis machine came into use. They failed to change the dialysis pattern of our society because of limited availability, cost and technical requirements. As compared tothese **Portable Artificial Kidneys (PAK)**, weighing between 8 to 10 kgs, the next generation **Wearable Artificial Kidneys (WAK)** weighed less, 5 to 6 kgs but had to be worn outside the body in a belt. The problem with WAK was a power source, dialysate regeneration system access and anticoagulation.Most of the WAK devices performed peritoneal dialysis.

In most of these designs the challenge of **regeneration of spent dialysate** was achieved through a **sorbent-based system**, the most used being **Recirculating Dialysis (REDY) sorbent system**. Uremic toxins are removed from dialysate using **activated charcoal**, **cation and anion exchange sorbents**. The most difficult part was urea removal. This was achieved by **column-fixed urease enzyme.**

The next phase of development of an artificial kidney was development of a **Renal Assist Device (RAD)** which is cultured human proximal tubular epithelial cell coated hollow fibre dialyzers replicating the secretory and absorptive functions of human renal tubules. This model was developed by Humes in US and Saito in Japan developing a extracorporeal artificial kidney.

The latest development in this field was done by the pioneering research from **Dr Shuvo Roy of University of California** and Dr William H Fissellfrom Vanderbilt university. Their research has led the path towards first **implantable Bioartificial Kidney (iBAK)**. Developed on the scaffold of silicone nanopore membrane, the used cultured conditionally immortalized proximal tubular epithelial cells. This device would be implanted in the iliac fossa and anastomosed to the iliac vessels for blood flow and to the bladder or ureter.

These devices undergoing animal trials were placed like a renal transplantation without the requirement of immunosuppressive therapy. It used the same dialysate regeneration system of previous models.

Bioengineered living membrane : Human conditionally immortalized PTEC **(ciPTEC**) has been developed which are enriched in influx and efflux transporters. These cells when cultured on hollow tubes in presence of albumin demonstrated clearance of protein bound uremic toxins.

While still a long way, this iBAK device is the closest to what we have gone to an ideal bioartificial kidney. The research is ongoing, the funding still is an issue.We hope that this conceptually correct model will ultimately solve the much sought-after solution of organ crisis.

Summary : Ideal renal replacement therapy must address few issues. **First** comes the removal of uremic toxins and maintain euvolemia with maintaining acid base balance and physiological electrolyte concentration. **Secondly** performing metabolic function of kidney by maintaining bone-mineral homeostasis and anemia correction. First function can be addressed by in center hemodialysis. But for convenience it was miniatured to PAK and later WAK. All these technologies failed to perform metabolic functions of kidney. This issue will be addressed in BAK and iRAD. All these uses **Bio-artificial Renal Epithelial Cell System (BRECS)**. It is Cryopreservable on-demand cell therapy delivery system. Progenitor stem cells are placed on high density porous disks and later seeded on to the fiber of hemofilter. iRAD contains Micro-Electro Mechanical System (MEMS) with Hemofilter with Silicon Nanopore Membrane seeded with renal tubule cell bioreactor (BRECS) with Immune isolation process.

In conclusion with improvement of tissue engineering and material science artificial kidney is ever evolving with promising future.

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