Wearable Artificial Kidneys: A Historical Perspective

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Abstract- **A wearable artificial kidney (WAK) allows the patient to have a more normal life style and provides continuous fluid and electrolyte balance. Only four WAKs have been tested in patients and none marketed. Two hemofiltration WAKs used the heart as the blood pump. Neff required the patient to drink 450 ml of dialysate every hour to replace the fluid lost. Murisasco regenerated the ultrafiltrate with a miniature REDY cartridge. In both instances the artificial kidneys clotted within 5 days. Two WAKs were based on hemodialysis. Bazzato used the heart to pump the blood through a dialyzer without a casing, placed in a plastic bag. The patient changed the dialysate in the bag periodically. Gura uses a blood pump and regenerates the used hemodialysate with a REDY type cartridge. His unit has been clinically tested for only 8 hours. To develop an extracorporeal WAK, problems of clotting and possible accidental fatal disconnects need to be solved.**

A number of WAKs are under development. Lande presented a hemodialysis unit on the arm, which uses the heart as a pump by intermittently blocking the fistula. Nissenson has proposed a kidney based upon a G membrane and T membrane. The G membrane filters the blood. The T 'smart" membrane blocks undesired substances while passing desirable substances. Humes and also Saito have proposed a hybrid kidney but have not formulated a wearable configuration.

Two peritoneal-based kidneys are under development. Ronco uses activated carbon and polystyrene resins for the removal of creatinine, β2 microglobulin and angiogenin from used dialysate. Other metabolites such as urea and phosphate were not addressed. Lee and Roberts use a REDY type cartridge for complete regeneration of used peritoneal dialysate. Use of peritoneal dialysis eliminates the problem of clotting and accidental fatal disconnects.

Keywords- **Peritoneal Dialysis, Wearable kidney, Wearable Artificial Kidney, Hemodialysis, Hemofiltration.**

Ever since it became possible to maintain end-stage renal disease (ESRD) patients by hemodialysis in the early 1960's, investigators have attempted to develop a wearable artificial kidney. Potentially, a wearable kidney operating 24 hours a day and 7 days a week will allow an ESRD patient to live a relatively normal life. The patient could be gainfully employed full time. Chemistries would be stable and more optimal treatment can be provided. Restrictions on diet and fluid intake could be relaxed. There would be fewer requirements for hypertensive and anemia drugs, and phosphate binders.

Today most ESRD patients are treated with hemodialysis at designated centers. This requires the patient to travel to a dialysis center for 3-4 hour treatments, three times a week, which seriously interferes with their quality of life and their ability to be fully employed. Numerous studies have shown that more frequent dialysis will improve the patient's quality of life. However, this will increase cost, use up more of the patient's time, and require patients to treat themselves at home.

Patients at home on either hemodialysis or automated peritoneal dialysis (APD) need to set up their machines before treatment and take themselves off the machine after treatment. This requires 30 minutes to an hour. Patients on continuous ambulatory peritoneal dialysis (CAPD) are required to exchange the dialysate in their peritoneum every 4 hours during the day. At night the dialysate is allowed to remain in the peritoneal cavity. Each exchange takes 30 minutes and must be done under relatively sterile conditions. Patients on CAPD find the 4-hourly exchanges tedious and frequently switch to APD.

Between exchanges, CAPD patients can go about their normal activities while the dialysate in their peritoneal cavity is removing metabolic toxins and excess fluid from their blood. On this basis CAPD may be considered a wearable artificial kidney. Thus, CAPD is the only wearable artificial kidney available since there are no other wearable kidneys on the market. However, CAPD provides sub-optimal dialysis, particularly in anuric patients. CAPD can be made more effective by increasing the frequency of dialysate exchanges and/or by increasing the amount of dialysate for each exchange. Increasing the frequency of exchanges

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make the treatment more tedious, while increasing the dialysate volume increases intra-abdominal pressure, which may be associated with back pain and the development abdominal hernias.

All wearable artificial kidneys proposed and/or developed have been based on either hemodialysis, hemofiltration, or on peritoneal dialysis. Hemodialysis or hemofiltration involves extracorporeal blood circulation, which requires the use of anti coagulants to prevent clotting of the extracorporeal circuit. So far no one has demonstrated the capability of preventing clotting in an extracorporeal circuit containing a dialyzer or hemofilter for longer than a week. Further, accidental disconnects of the wearable kidney can result in fatal bleeding. If the patient is anticoagulated, internal bleeding can result. The interaction of blood with artificial membranes result in the release of inflammatory agents.

Wearable artificial kidneys based upon peritoneal dialysis require the use of an osmotic and/or oncotic agent to promote ultrafiltration. Ultrafiltration failure is a major reason for shifting a patient from peritoneal dialysis to hemodialysis. Approved osmotic and oncotic agents are glucose, amino acids and icodextrin. CAPD has demonstrated that glucose can be used long term. However, in many patients the peritoneal membrane changes so that the patient becomes a high transporter and fails to ultrafilter adequately. Amino acids have not been used exclusively long term. A combination of glucose and amino acids would provide calories and the building blocks for proteins. This combination has not been used long term. Icodextrin used exclusively could result in the accumulation of excess maltose in the patient. Peritoneal membrane changes could limit the number of years a patient could use the peritoneal dialysis-based wearable kidneys.

Hemodialysis-Based Wearable Kidneys

A number of wearable kidneys based upon hemodialysis have been clinically tried. Kolff et al. (4) clinically evaluated a hemodialysis machine to be worn on the chest. The machine was connected to a 20 L dialysate container. The patient could disconnect from the container and then would be relatively mobile. However, within 15 minutes the dialysate would reach equilibrium with the blood and no further dialysis would take place. The hemodialysis machine was designed to be used a few hours a day and only a few days a week. Thereby, providing no better dialysis than standard hemodialysis treatment. Bazzato et al (1) prepared a machine-less wearable kidney by removing the casing from a dialyzer and placing the hollow fibers in a plastic bag. The fibers were connected to an artery and vein while the plastic bag was filled periodically with dialysate by the patient. No clinical data was reported. Davenport et al (2) have developed a wearable kidney based on hemodialysis. The spent hemodialysate is regenerated with a REDY type cartridge. The wearable kidney was used in 8 patients for 4-8 hours. Two patients had clotting problems due to an inadequate amount of heparin and one patient had an accidental blood circuit disconnect.

Hemofiltration-Based Wearable Kidneys

Neff et al. (8) placed a hemofilter on the arm and connected the hollow fibers to an artery and vein. The rate of hemofiltration was adjusted to 7 ml/min in the daytime and 0 ml/min at night. The average hemofiltration rate was 5 ml/min. The ultrafiltrate was collected in a bag and discarded. The patient had to drink about ½ L of dialysate per hour during the daytime to replace the ultrafiltrate that was discarded. The patients found it difficult to drink so much dialysate every hour. In addition, although anticoagulants were used, the system clotted within 5 days. Murisasco et al. (7) used a hemofilter and regenerated the ultrafiltrate with a miniature REDY cartridge. The regenerated ultrafiltrate was returned to the venous line. A portion of the ultrafiltrate, necessary to maintain the patient's fluid balance, was removed from the ultrafiltrate stream and pumped into the patient's bladder for storage. This allowed the patient to have normal urinary function. The extracorporeal circuit clotted within 5 days

Proposed Hemodialysis-Based Wearable Kidney

Lande et al. (5) have proposed a wearable kidney located on the forearm near the wrist. Blood is pumped through a miniature dialyzer by periodically blocking the fistula and thereby creating a pressure drop between the arterial and venous side of the fistula. A low blood flow will be used with only the extracorporeal circuit anti coagulated. A miniature REDY type cartridge will regenerate the dialysate

Proposed Wearable/Implantable Kidney Based Upon Nanotechnology

Nissenson et al. (9) have proposed a wearable/implantable kidney consisting of 2 membranes, a G membrane and a T membrane. The G membrane will filter the blood allowing only protein-free ultrafiltrate to pass through. The G membrane will be biocompatible so no clotting will occur. The T membrane will contain "smart" pores, which will allow only desired substances to pass through, while holding back uremic wastes. Thus for example, water and sodium will pass through, while urea will be blocked. Since at least 90 % of the water must be returned to the patient to maintain the patient's fluid balance, the urea concentration will be increased ten fold on the blocked side of the T membrane. The fluid on the blocked side of the T membrane containing all the undesirable substances will be discarded. The blood remaining after passing the G membrane and the filtrate from the T membrane are returned to the patient.

Biohybrid Kidneys

Ding et al. (3) have developed a biohybrid kidney utilizing a hemofilter to filter the blood and a hollow fiber unit with tubular cells to purify the filtrate. It has been used in acute renal failure patients. Potentially it can be developed into a wearable kidney. Saito et al. (11) have developed a similar kidney

Proposed Peritoneal Dialysis-Based Wearable Kidneys

Ronco et al. (10) have proposed a wearable kidney based on peritoneal dialysis. A sorbent column consisting of activated carbon and a sorbent for middle molecules regenerates the spent peritoneal dialysate. Creatinine and middle molecules are removed but urea, phosphate and other uremic toxins remain in the regenerated dialysate. Lee and Roberts (6) have proposed a peritoneal dialysis based-wearable kidney currently under construction. A REDY type sorbent cartridge regenerates the spent dialysate. The urease in the cartridge is chemically bound to prevent displacement by proteins in the spent dialysate. The use of peritoneal dialysis instead of an extracorporeal system eliminates the problem of coagulation and fatal accidental disconnects.

References.

1. Bazzato G, Coli U, Landini S, Lucatello S, Fracasso A, Morachiello P, Righetto F, and Scanferla F. Bag-filter dialysis: a new therapeutic modality for uremic patients. ***Life Support Syst*** **1 Suppl 1: 170-173, 1983.**

2. Davenport A, Gura V, Ronco C, Beizai M, Ezon C, and Rambod E. A wearable haemodialysis device for patients with end-stage renal failure: a pilot study. ***Lancet*** **370: 2005-2010, 2007.**

3. Ding F and Humes HD. The bioartificial kidney and bioengineered membranes in acute kidney injury. ***Nephron Exp Nephrol*** **109: e118-122, 2008.**

4. Kolff WI, Jacobsen SC, Stephen RL, and Ron D. Toward a wearable artificial kidney. ***Kidney Int.*** **10:S300-S304, 1976**

5. Lande AJ, Resig PP, Avin CM, Anderson RD, Ward T, and Zwischenberger JB. Forearm worn artificial kidney demonstrates "blood" flow modulation, "plasma" filtration and A/V pressure amplification for absorbents cartridge perfusion. ***J Amer Soc Nephrol*** **19:458, 2008**

6. Lee DB and Roberts M. A peritoneal-based automated wearable artificial kidney. ***Clin Exp Nephrol*** **12: 171-180, 2008.**

7. Murisasco A, Reynier JP, Ragon A, Boobes Y, Baz M, Durand C, Bertocchio P, Agenet C, and el Mehdi M. Continuous arterio-venous hemofiltration in a wearable device to treat end-stage renal disease. ***ASAIO Trans*** **32: 567-571, 1986.**

8. Neff MS, Sadjadi S, and Slifkin R. A wearable artificial glomerulus. ***ASAIO Trans*** **25: 71-73, 1979.**

9. Nissenson AR, Ronco C, Pergamit G, Edelstein M, and Watts R. Continuously functioning artificial nephron system: the promise of nanotechnology. ***Hemodial Int*** **9: 210-217, 2005.**

10. Ronco C and Fecondini L. The Vicenza wearable artificial kidney for peritoneal dialysis (ViWAK PD). ***Blood Purif*** **25: 383-388, 2007.**

11. Saito A, Aung T, Sekiguchi K, Sato Y, Vu DM, Inagaki M, Kanai G, Tanaka R, Suzuki H, and Kakuta T. Present status and perspectives of bioartificial kidneys. ***J Artif Organs*** **9: 130-135, 2006.**