Portable or Wearable Peritoneal Devices—The Next Step Forward for Peritoneal Dialysis?

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Peritoneal dialysis can be considered a “wearable” dialysis therapy. However, patients typically require 3 or 4 daily exchanges, each taking 20 – 40 minutes and potentially increasing the risk of infection by repeated disconnection and reconnection. Although peritoneal dialysis cyclers allow patients to be “free” from their machine for 13 – 15 hours, they similarly need a supply of fresh dialysate. Several groups have therefore explored the possibility of trying to minimize dialysate exchanges by recycling dialysate. However, that approach introduces not only a series of challenges, including regeneration of the spent dialysate, maintenance of acid–base and electrolyte balance and adequate ultrafiltration, but also new hurdles to be overcome, including monitoring the sorbents to determine when capacity is exceeded.

The proposed Vicenza Wearable Artificial Kidney system consists of a continuous-flow peritoneal dialysis system that combines sorbents in series and urease to regenerate dialysate during the day, and a 7.5% icodextrin exchange overnight.

Key words
Sorbents, ultrafiltration

Introduction
As we know it today, peritoneal dialysis (PD) can be described as a “portable” or “wearable” mode of dialysis. However, when first introduced in the 1960s, PD was used only for patients with acute renal failure, whose treatment consisted of insertion, by sharp metal trocar, of hard catheters, followed by instillation of sterile dialysate supplied in 1-L glass bottles, typically continuing for more than 24 hours. Over the subsequent decade, PD began to be introduced as a treatment for chronic kidney disease, initially in a form similar to that used for treating acute renal failure, but then progressing to hospital admission thrice weekly for overnight PD treatment sessions in patients who required a new catheter insertion for each treatment. In many centers, PD was therefore a temporary treatment modality until patients could be established on intermittent hemodialysis.

After a number of key technical advances, including introduction of the indwelling silicone catheter and commercially available sterile dialysate in plastic bags, development of a wearable dialysis system was possible by the late 1970s (1), and patients could then dialyze at home using simple mechanical devices that regulated dialysate inflow, dwell, and outflow. However, it was only with the advent of continuous ambulatory PD, pioneered by Moncrief and Popovich (2), that PD truly became the major mode of renal replacement therapy that we recognize today (3,4), with more than 100,000 patients treated worldwide.

Given that PD is indeed an established wearable technique, why should further developments be required?

Unfortunately, despite improvements in catheter design and placement, connectology, and flush-before-fill, peritonitis remains the major complication of the PD technique (5). Transluminal and periluminal bacterial spread remain the commonest causes of infection, and even the introduction of antibiotic creams for the exit site has failed to further reduce the rate of peritonitis (6). Thus, one potential advantage of a continuous closed PD system might be a major reduction in peritonitis and consequent improved technique survival. In addition, patients have to spend time performing their daily exchanges, or setting up and dismantling cycler machines, and although the cyclers
can be transported, they are certainly not wearable. In addition, both techniques require the delivery and storage of large volumes of fresh dialysate and the subsequent disposal of packaging and waste, so that a wearable device with dialysate regeneration might potentially save on deliveries, storage, and disposal.

Discussion

Technical hurdles to overcome

The key advantages of a wearable PD device compared with hemodialysis are that blood access and continuous anticoagulation are not required (7). Although peritonitis can occur, the risk can be reduced by a combination of minimizing manipulation and disconnection–reconnection of the catheter and using antibiotic creams at the exit site (8). However, the paradigm of dialysis is a more than just a treatment designed to remove small water-soluble waste solutes (Figure 1).

Circuit design

Currently, in PD exchanges, gravity is used to drain spent dialysate and to instill a fresh volume, and although PD cyclers regulate the dialysate cycles, measuring inflow and outflow rates, volumes, and times, the machines do not actively pump fluid into or out of the abdominal cavity.

By contrast, a wearable device would have to regenerate spent dialysate rather than simply replace it. Thus, a wearable device would require a pump, powered by a rechargeable or replaceable battery. The pump could pump dialysate either into or out of the abdominal cavity, much as a single-needle hemodialysis pump does (9), or it could pump dialysate in a continuous fashion (10).

Traditional PD catheters typically have a single lumen, such that flow would be intermittent, as in single-needle hemodialysis. In this situation with a single-lumen catheter, an additional reservoir of regenerated dialysate would have to be added to the circuit to accommodate the intermittent flow, but use of a dual-lumen catheter would permit continuous flow and thus a simpler circuit design (10) (Figure 2).

To be truly portable, a wearable device has to be powered by a battery that is not only small and light, but also capable of providing energy sufficient to power all the necessary systems for a significant period of time so that the wearer is independent of a fixed electrical outlet.

The PD effluent typically contains a small amount of protein, but fibrin strands occasionally appear, and those would have to be removed by filters to prevent fibrin from blocking the pumping mechanism or the flow through the sorbents. Those filters could either be changed independently or replaced whenever the dialysate circuit is exchanged.

Dialysate

Standard continuous ambulatory PD therapy typically uses 8 L fresh dialysate daily. Thus, a wearable device requires an initial supply of fresh, sterile dialysate, in conjunction with a sorbent system that can purify and regenerate effluent, and thus avoid the need for

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Figure 1 — Dialysis prescription is a composite to achieve homeostasis and not just small-solute clearances.

Figure 2 — Schematic circuit diagram of the Vicenza Wearable Artificial Kidney (ViWAK).
repeated administration of fresh dialysate. Typical sorbents use either a combination or mixture of microporous carbon, urease, and zirconium.

The efficiency of the system will depend on the initial fill volume (typically 2 L for an average-size patient) and the timing and volume of the cycles. With a dual-lumen catheter, flows will be continuous; with a single-lumen catheter, rapid tidal exchanges will be required, with the volume of the tidal exchange being held in the reservoir.

In addition, the peritoneal transport characteristics of the patient will also affect efficiency. Short-term in vivo experiments have reported up to 17 mL/min of urea nitrogen clearance using a reservoir volume of 500 mL and a tidal exchange of 1000 mL at an exchange rate of 4 L/h. If that clearance can be sustained 24 hours daily for a week, then the scaled-up weekly Kt/V urea would reach 5.9 for a slow-average transporter and 6.5 for a fast-average transporter respectively (11).

Dialysate sorbents

Microporous carbon and zirconium do not readily absorb urea, and so most commercial sorbents use urease to metabolize urea to ammonium and carbon dioxide (12). However, ammonium is rapidly absorbed by zirconium phosphate, and so the ammonium generated can be removed by placing zirconium phosphate adjacent to or in series with a urease sorbent (13). Even so, to ensure that all the ammonia has been removed and the zirconium phosphate sorbent has not become saturated, ammonia levels must be checked before the dialysate is returned to the patient.

Carbon dioxide produced from the metabolism of urea will form micro- and macro-bubbles at the operating temperature and pressure of a wearable device, and so must be removed by a de-aerating chamber, typically made of gas-permeable plastic (14).

The advantages of microporous carbon not only include an ability to absorb creatinine, uric acid, chloramines, oxidants, other organic compounds, heavy metals, and middle molecules, including β2-microglobulin (15), but also an ability to hold and not release ions or solutes. In contrast, zirconium-based sorbents carry a charge and typically act as an ion exchanger. Thus, zirconium phosphate absorbs ammonium, calcium, magnesium, potassium, other cations and metals, and then releases hydrogen and (to a lesser extent) sodium ions. Similarly, zirconium oxide and zirconium carbonate absorb phosphate, fluoride, and heavy metals, and release sodium, the anion bicarbonate, and (to a lesser extent) acetate (13).

The PD effluent contains proteins, typically 4 – 8 g/L, but because the dialysate is continuously used in a wearable device, the protein content may well be expected to increase with time, potentially coating the sorbents and reducing their efficiency. Additional filters may therefore be required to protect the sorbents from protein deposition.

A typical 70-kg North American or European with a dietary protein intake of 1 g/kg would be expected to generate around 9 – 10 g urea nitrogen daily (16). Although urease and 250 g zirconium can readily metabolize 2 g urea each hour, that amount of urea metabolism would typically exhaust the currently available sorbent cartridges for wearable peritoneal devices, necessitating 2 – 3 cartridge exchanges daily. Although multiple exchanges may be technically feasible, they potentially increase the risk of introducing bacterial contamination, let alone the costs of supplies. However, technical problems often become the spur to newer developments such as the production of more-effective sorbents, because the sorbents used today are essentially similar to those developed several decades ago (13,17).

Dialysate regeneration

During hemodialysis, the final dialysate is made by mixing an electrolyte solution with sodium bicarbonate and reverse-osmosis water prepared for dialysis. The mechanical proportioning system in the dialysis machine from some manufacturers is supported by conductivity feedback control. In the case of wearable PD devices proposed or under development, standard dialysate is used as the initial fresh volume. That volume has to be refreshed to maintain acid–base, sodium, potassium, and divalent cation homeostasis. The systems designed to date have either suggested adding fresh dialysate or a preformed electrolyte and bicarbonate solution (18). Further investigation is required to determine whether those proposals will provide satisfactory homeostasis, because the amount of bicarbonate required will vary from patient to patient, and sodium release from the zirconium sorbents will similarly vary. Therefore, simply providing fresh dialysate may or may not provide sufficient bicarbonate or lactate base when combined with a single electrolyte mixture, because the sodium
concentration may have to be reduced to allow for sodium release from the sorbents. As such, the circuit design will have to incorporate a micropump to regulate post-sorbent infusion into the dialysate, so that the dialysate becomes regenerated. The use of sorbent cartridges that have to be regularly exchanged may help to simplify the electrolyte and bicarbonate/lactate mixture required for dialysate regeneration. Appropriate connectology will be required to permit the exchanges to be performed safely, without introducing infectious organisms and also without introducing too much air and having to re-prime the dialysate compartment of the circuit.

Ultrafiltration

Standard hemodialysis machines permit controlled ultrafiltration, but continuous ambulatory and cycler PD both depend on simple osmotic or oncotic pressure gradients to achieve ultrafiltration. Thus, wearable peritoneal devices could either rely on hypertonic glucose to achieve ultrafiltration or could add additional complexity to the circuit by inserting a mechanical pump to regulate ultrafiltration. If the same hypertonic glucose-based dialysate is simply recycled, then glucose will be absorbed over time. Possible answers for that problem would include continually refreshing the dialysate with glucose, or reverting to an additional overnight icodextrin exchange (10). Ultrafiltrate will then have to be collected in a separate pouch that can either be emptied or exchanged (9).

Current wearable peritoneal devices have opted for the simpler osmotically-driven ultrafiltration, but longer-duration studies are required to determine both the amount and rate of glucose supplementation (19) and also whether supplementation leads to excessive glucose exposure, resulting in weight gain and accelerated glycation of the peritoneum.

Summary

The Vicenza Wearable Artificial Kidney (ViWAK) is a new concept for continuous cycling PD that uses urease to remove urea, combined with sorbents in a system designed to regenerate the dialysate. The proposed system, in combination with a nighttime 7.5% icodextrin exchange, is designed to provide daytime freedom from exchanges while ensuring adequate ultrafiltration and the maintenance of electrolyte and acid–base balance. As such, fresh dialysate is required daily, together with fresh urease and sorbents, adding not only some degree of complexity, but also cost, compared with currently available PD treatments.

Disclosures

The author has no financial conflicts of interest to declare.

References


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