DEVELOPMENT OF A SORBENT PERITONEAL DIALYSATE REGENERATION SYSTEM – A PROGRESS REPORT

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Summary

A sorbent regenerative dialysate system for peritoneal dialysis has been developed (Pericycle\textsuperscript{1}). Clinical results and data demonstrate that the sorbent system provides a suitable dialysate. The sorbents effectively remove uraemic metabolites from the dialysate. Calcium and magnesium removed by the cartridge and glucose metabolised by the patient are replaced by the infusion system.

The machine pumps regenerated dialysate into and spent dialysate out of the patients. A pressure sensor in the patient line prevents excessive inflow and outflow pressures by stopping the inflow or outflow pump respectively.

The Pericycle provides a simple, safe, portable method for conducting peritoneal dialysis in the home or hospital.

Introduction

Advances in technology, equipment design, and increased experience have made peritoneal dialysis an acceptable alternative to haemodialysis for the chronic maintenance of patients with end-stage renal disease [1,2]. Current techniques of peritoneal dialysis require large volumes of solution supplied via multiple bottles, large sterile containers, or dialysate concentrate mixed with sterile reverse osmosis water by proportioning systems. The object of our study has been to develop a peritoneal dialysis system utilising sorbents to regenerate dialysate in a manner similar to the haemodialysate sorbent regeneration system [3]. Such a system would allow a complete dialysis to be conducted with 4 L of dialysate. We report the results of our initial clinical studies using this system.

\textsuperscript{1}Trade Mark – CCI Life Systems, Inc.
Patient Population and Methods

Seven chronically uraemic male veterans, mean age of 54 years (range 46–67 years), underwent a total of 37 dialyses. Each dialysis was from 4 to 12 hours in duration. The initial three patients had a temporary Trocath\(^2\) inserted; subsequent patients had a chronic implanted Tenckhoff catheter.

Studies with the initial six patients utilised a modification of a commercially available automatic peritoneal cycler\(^3\) with an IVAC pump for infusedate and a sorbent cartridge similar to that used in the Redy Haemodialysate Delivery System [4]. The cartridge was sterilised by gamma irradiation. Filter sterilised urease was added prior to use. This system used three 2 L bottles of commercially available peritoneal dialysate. Inflow into and drainage from the peritoneal cavity was by gravity.

The chemical properties of the sorbent system have been reported [5]. Sorbents effectively remove urea and other uraemic metabolites from the dialysate. The high levels of glucose and the small amount of protein present in peritoneal dialysate do not interfere with sorbent function [6]. An infusion system is used to maintain the concentration of calcium and magnesium ions and glucose in the dialysate. Additional glucose, water, heparin, acetate or other drugs can also be infused by this system. Salt and water removal are easily accomplished by adjusting the dialysate glucose concentration.

In January 1978, studies were initiated with a peritoneal cycling device (Pericycle) designed for dialysate regeneration with a sorbent cartridge. A schematic diagram of the system is shown in Figure 1 and a picture of the

\(^2\)McGaw Labs., Irvine, California
\(^3\)AMP Cycler, American Medical Products, Fairfield, NJ

![Figure 1. Schematic flow diagram of the sorbent regeneration system for peritoneal dialysis](image-url)

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actual equipment in Figure 2. The present unit is 51 x 46 x 43 cm and weighs 25 kg. The production unit will be smaller and lighter. The Pericycle pumps warmed peritoneal dialysate into the peritoneal cavity through a 0.22 micron filter at the rate of 300 ml/min. The total volume for exchange can be varied from 0.5 to 2.5 L. Excessive pressure in the system stops the inflow pump. There is no ‘dwell’ time and at the conclusion of the inflow cycle, the outflow pump is activated and fluid is pumped out at a rate of 150 ml/min. The rate of inflow and outflow can be varied. A negative pressure monitor is incorporated into the outflow line, and an alarm is sounded and the pump is stopped if the pressure limit is exceeded before 80% of the inflow volume of dialysate has been drained. If the pressure limit is exceeded after 80% of the dialysate
has been removed the next inflow cycle is initiated. The dialysate is pumped directly from the peritoneal cavity through the sorbent cartridge. The appropriate quantities of calcium, magnesium, acetate and glucose are added, and this regenerated dialysate is stored in the warming bag. A digital display indicates a continuous ‘read-out’ of the instantaneous volume infused and drained during each single exchange. The usual dialysate exchange rate is 6 L/hr, although exchange rates up to 9 L/hr are feasible. With this system we have also conducted ‘reciprocating’ dialysis [7] with a residual peritoneal dialysate volume of 1 L and 6–9 L exchanges/hr. Since dialysate is regenerated, the amount and cost of dialysate solutions required is not a limiting factor [8,9].

**Clinical Experience**

During a typical 10 hour dialysis in the patient dialysed with the Pericycle, the concentration of sodium in dialysate increased slightly from 132 to 136 mEq/L. The chloride, bicarbonate and calcium levels remained stable. The addition of 17 g of glucose/hr maintained its level in dialysate at a concentration of 1330 mg/dl. The regenerated dialysate was free of potassium, phosphate and urea. The concentration of glucose of 1330 mg/dl creates a high ‘blank’ of 1.2 mg/dl for apparent creatinine concentration. Table I shows the

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<tr>
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<th>Drainage</th>
<th>Regenerated</th>
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<tr>
<td><strong>Urea N</strong></td>
<td>23</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Creatinine</strong></td>
<td>2.8 mg/dl</td>
<td>1.1*</td>
</tr>
<tr>
<td><strong>Phosphate</strong></td>
<td>1.2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Glucose</strong></td>
<td>860</td>
<td>1330</td>
</tr>
<tr>
<td><strong>Sodium</strong></td>
<td>132</td>
<td>136</td>
</tr>
<tr>
<td><strong>Potassium</strong></td>
<td>1.2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Bicarbonate</strong></td>
<td>30 mEq/L</td>
<td>29</td>
</tr>
<tr>
<td><strong>Chloride</strong></td>
<td>84</td>
<td>83</td>
</tr>
<tr>
<td><strong>Calcium</strong></td>
<td>3.0</td>
<td>3.3</td>
</tr>
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*high blank due to glucose

composition of the effluent and regenerated dialysate at the end of 10 hours. Since the cartridge removes all urea, creatinine, phosphate and potassium, the clearance of these substances is dependent on the permeability characteristics of the individual patient’s peritoneal membrane.

A number of problems were encountered during the development of the system. Three of the initial four patients dialysed developed bacterial peritonitis. The first patient had an extensive dermatitis with Staphylococcus epidermidis. Cracks in the gamma-irradiated sorbent cartridge developed on a number of occasions in the second patient. No obvious source of bacterial contamination
was present in the third patient, and the source of infection was thought to have been the tubing set. However, numerous cultures taken from tubing sets and sorbent cartridges from the same source and lot number, and infusate and dialysate solutions prepared in an identical manner were all sterile. Peritoneal dialysis carried out in dogs using the same solutions and supplies failed to reveal any bacterial contamination. The tubing sets used in these early studies were fabricated from several separate sterile tubing sets that were connected prior to dialysis. In addition, dialysate samples were obtained frequently by syringe and needle from the 'sterile' system. The Millipore twin 90 filter which was used in the early trials was subsequently recalled by the manufacturer because of a defect in the filter housing which could have allowed bacterial contamination. After these early experiences, the procedure for sterilisation was changed and the filter system was changed. Presently, the complete tubing set and attached sorbent cartridge are sterilised by gamma irradiation. This change, combined with a reduction in the number of dialysate samples obtained and the use of a different filter has resulted in the absence of bacterial peritonitis during subsequent trials with the Pericycle.

However, one patient developed fever, chills and abdominal pain suggestive of a typical pyrogen reaction after 4 hours of dialysis. All cultures were negative. The various components of the system were rinsed and tested by the USP rabbit pyrogen test and the limulus endotoxin test [10]. All of the components of the system, as well as the dialysate, were found to be pyrogen-free except for the sterile urease. Limulus tests on urease from six different sources were all found to be positive. After this experience, the procedure was further modified; presently, the sorbent cartridge is routinely rinsed with several litres of sterile fluid after the urease is added. Pyrogen reactions have not been encountered since this procedure was initiated. Also, a method has been developed for preparing endotoxin-free urease. Urease prepared by this method should be available in the near future and may obviate the need for pre-rinsing the cartridge.

One patient presently undergoing dialysis with the Pericycle system is somewhat unique in that he experiences peritoneal irritation with use of peritoneal dialysate of the usual pH of 5.2 to 5.5. Thus, he routinely adds sodium hydroxide to the dialysate delivery equipment used in his home. To obviate peritoneal irritation in this patient, it has been necessary to increase the pH of the dialysate to at least 6.3 by pre-rinsing the cartridge with sodium bicarbonate. A cartridge is presently being produced which will contain zirconium phosphate at a higher pH; this may eliminate the need for such pre-rinsing.

Another source of abdominal discomfort and peritoneal irritation was the filter being used. This was initially thought to be due to the peristaltic flow created by the roller pump [11]. However, dampening of the pulse wave with an air chamber did not correct this situation. This problem was alleviated when a Millipore 136 sq. cm filter was substituted for the filter originally used.

Summary and Conclusions
The clinical results and data demonstrate that the sorbent system for perito-
neal dialysis provides a suitable regenerated dialysate. Comparable clinical results should be obtained with this system as with other systems at similar cycle times and flow rates. Since fluid quantities are not a limiting factor, the sorbent system will lend itself to flow rates of 6 L per hour or greater.

Pumping dialysate solution into and out of the peritoneal cavity has not been a problem and the system has operated alarm and trouble free. Setting the acceptable drainage to 80% or greater of the inflow volume has not caused fluid accumulation in the abdomen nor alarms during outflow. Display of the volume infused or drained has been convenient in determining the status of the dialysis.

Sterilisation of the cartridge and tubing set as one unit and utilisation of a closed circuit has minimised the possibility of bacterial contamination. The use of a 0.22 micron filter in the inflow line to the patient has further decreased the possibility of particulate or bacterial contamination.

The sorbent system lends itself to simplicity of design, uncomplicated logic, and ease of operation, and therefore reduced patient training time. The machine is quiet during operation and is easily transported even during dialysis since the electrical plug can be disconnected and reconnected at another location. Potentially, the system can be miniaturised, making a wearable artificial kidney an approachable goal.

Long-term unassisted home dialysis will be conducted in several patients, when sterile non-pyrogenic urease and a sorbent cartridge at a higher pH become available. Smaller more compact dialysate delivery systems are being built. With these machines the clinical investigation will be expanded to other peritoneal dialysis centres.

Acknowledgments

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References

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Open Discussion

LOBDELL (Denver) Have you calculated the cost of maintenance peritoneal dialysis with such a system, including the cost of the sorbent cartridge?

BLUMENKRANTZ With the sorbent system only three 2 L bottles of commercially available peritoneal dialysate are used. They cost approximately four dollars each. Since the dialysate is regenerated the volume used is not a consideration and exchange rates of 6–9 L of dialysate/hour are used to optimise the clearance of small molecules. Even with the additional cost of the sorbent cartridge, infusate and disposable tubing set, sorbent dialysis is considerably less expensive than the manual exchange of 2 L bottles of dialysate. In addition to the 36 bottles of dialysate commonly used with this technique there is also the considerable cost of nursing time; a minimum of nursing effort is required for sorbent peritoneal dialysis. We have recently calculated that the total cost of a 36 hour peritoneal dialysis using the manual exchange of 2 L bottle is approximately three hundred dollars.

The sorbent peritoneal system probably will cost more than dialysate proportionating systems which mix dialysate concentrate with water prepared by reverse osmosis. But with the sorbent system, since formaldehyde sterilisation and rinse-out are not required, patient or staff time requirements will be less.

ROBSON (Toronto) I can see that we are both going in the same direction, towards portable dialysis. I just have a feeling that with this system you are introducing a lot more machinery. It sounds as though it is going to cost more than CAPD which is about five thousand dollars per year.

BLUMENKRANTZ As you know, I do not share your opinion that in the future CAPD will be the most commonly employed method of dialysis. Intermittent peritoneal dialysis performed four nights per week costs approximately ten thousand dollars a year, is very well accepted by most patients who are completely free from dialysis during the day. I would suspect that in the future most of the patients switching to CAPD will be those currently undergoing in-centre haemodialysis.