Sorbent Peritoneal Dialysis—
Initial Clinical Trials

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Summary

The initial clinical results of peritoneal dialysis utilising a sorbent system to
regenerate dialysate are presented. A 0.22 micron filter maintains sterility in
the closed system and removes particulate matter. Uraemic metabolites in
dialysate are eliminated and electrolyte balance maintained by passage through
the sorbent cartridge. Changes in glucose concentration of the dialysate are
accomplished by either adjusting the initial dialysate glucose concentration
or by varying the amount of glucose added via the infusion system. The adsorp-
tion of large amounts of glucose by the sorbent cartridge as well as the coating
of the sorbents by the small amounts of protein found in peritoneal dialysate
do not interfere with other adsorptive functions. The patients tolerated the
procedure well and experienced the same degree of solute removal as one would
expect from conventional peritoneal dialysis. The feasibility of developing an
ambulatory dialysis unit based on the principle of sorbent regeneration of
peritoneal dialysate is discussed.

Introduction

The application of sorbent technology for dialysate regeneration in haemodialysis
has permitted a dramatic reduction in the dialysate volume required for the
procedure (Gordon et al, 1971 and Lewin et al, 1972). During our recent work,
we have attempted to apply similar sorbent principles to the regeneration of
peritoneal dialysate (Lewin et al, 1974). There are several major differences
involved in the regeneration of peritoneal dialysate as compared to haemodialysate
Dialysate must be maintained sterile and free of particulate matter. The high
glucose concentration of peritoneal dialysate and the protein in spent dialysate must not interfere with either the biochemical or mechanical functions of the sorbent cartridge. Our work in experimental animals has demonstrated that a closed sorbent system can be maintained free from bacteria and particulate matter and that the glucose and protein in peritoneal dialysate does not interfere with sorbent function (Maxwell et al, 1975). In this paper we report the results of our initial studies using such a sorbent system in chronically uraemic patients.

METHOD

Our current research utilises a prototype of a closed, automated, recycling peritoneal dialysate delivery system. Its major components are the Automatic

![Diagram of Closed, Automated, Recycling Peritoneal Dialysate Delivery System]

Figure 1. Closed, automated, recycling peritoneal dialysate delivery system
Peritoneal Cycler® and an IVAC® infusion pump and a sorbent cartridge† (Figure 1). The sorbent cartridge is similar to the cartridge used in the REDY® haemodialysate delivery system (Gordon et al, 1971) but does not contain urease. The cartridge is sterilised by gamma radiation and urease is added after undergoing filtration sterilisation. The system as presently constituted utilises three 2 litre bottles of sterile commercially available peritoneal dialysate with 1.5 or 4.25 percent dextrose concentrations.

To start dialysis, solenoid pinch valve No 1 is opened and 2 litres of dialysate flows from the dialysate bottles into the warming bag where it is heated to 37°C. Valve No 1 closes and pinch valve No 3 opens and warmed dialysate flows by gravity into the peritoneal cavity. Valve No 3 then closes. After a predetermined dwell time in the peritoneal cavity, dialysate is drained by gravity through pinch valve No 2 into a 3 litre weigh bag which is monitored by an alarm system to ensure proper drainage. When drainage is complete, valve No 2 closes, pinch valve No 4 opens and the dialysate is pumped by a roller pump through the sorbent cartridge. A vacuum pressure switch automatically shuts off the roller pump when the weigh bag is empty. After passing through the sorbent cartridge, dialysate flows through a 0.22 micron filter and then into one of the original dialysate bottles for storage prior to re-use. After the filter, infusate is added to the dialysate to regulate the concentration of calcium and magnesium as well as to add additional glucose, acetate, potassium, heparin, antibiotics or other drugs as needed. The infusion of the proper amount of concentrate is assured by the use of the IVAC® infusion system. This device contains an optical drop sensor which maintains the desired infusion rate by feedback to a line clamp.

Our initial human studies with this system have been undertaken in two chronically uraemic male patients at the VA Wadsworth Hospital Center, who were undergoing peritoneal dialysis prior to a decision regarding which type of therapy would be instituted for chronic renal failure. Initially, after informed consent was obtained, four 40 minute exchanges with the sorbent system were substituted for exchanges on conventional equipment during a therapeutic peritoneal dialysis. After assuring ourselves that the patient was not adversely affected by sorbent dialysis, the amount of time spent on the sorbent system was increased. Currently, we are performing 10 to 15 exchanges of 40 minutes each with the sorbent device during the course of each peritoneal dialysis.

Blood samples were drawn at the beginning and the end of sorbent dialysis for the determination of BUN, creatinine, uric acid, electrolytes and glucose. In addition, pre and post cartridge dialysate specimens were obtained during each exchange and analysed for the same solutes. Ascitic fluid prior to dialysis, peritoneal dialysate from the last exchange and the filter within the dialysate flow line were cultured for both aerobic and anaerobic organisms. Additionally,

* Manufactured by American Medical Products Corporation
† Manufactured by CCI Life Systems, Inc
two litres of fresh peritoneal dialysate were washed through the used sorbent cartridge after it was incubated for 24 hours at 37°C. A 0.45 micron filter through which this dialysate was passed was also sent for culture. Frequent clinical observations were made. The reported results are from ten different dialyses comprising a total of 80 exchanges.

RESULTS

The changes in serum levels of nitrogenous waste products are shown in Table I. These results are represented both as the pre and post sorbent dialysis serum chemistries for dialyses of 12 or more exchanges as well as the serum chemistry

<table>
<thead>
<tr>
<th></th>
<th>Urea nitrogen (mg/100 ml)</th>
<th>Creatinine (mg/100 ml)</th>
<th>Uric acid (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dialysis</td>
<td>67.7</td>
<td>15.1</td>
<td>9.3</td>
</tr>
<tr>
<td>Post-dialysis</td>
<td>58.7</td>
<td>14.2</td>
<td>8.1</td>
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</table>

Average Serum Concentration Change per Forty Minute Peritoneal Exchange (N=80)

<table>
<thead>
<tr>
<th></th>
<th>Urea nitrogen (mg/100 ml)</th>
<th>Creatinine (mg/100 ml)</th>
<th>Uric acid (mg/100 ml)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>-0.915 ± 0.567</td>
<td>-0.136 ± 0.092</td>
<td>-0.108 ± 0.066</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Na⁺ (mEq/l)</th>
<th>Cl⁻ (mEq/l)</th>
<th>K⁺ (mEq/l)</th>
<th>Ca²⁺ (mg/100ml)</th>
<th>Mg²⁺ (mg/100ml)</th>
<th>PO₄ ³⁻ (mg/100ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dialysis</td>
<td>141</td>
<td>102</td>
<td>4.0</td>
<td>9.8</td>
<td>2.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Post-dialysis</td>
<td>142</td>
<td>101</td>
<td>3.7</td>
<td>10.5</td>
<td>1.8</td>
<td>3.7</td>
</tr>
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<th>Ca²⁺ (mg/100ml)</th>
<th>Mg²⁺ (mg/100ml)</th>
<th>PO₄ ³⁻ (mg/100ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+0.23±0.39</td>
<td>-0.25±0.92</td>
<td>-0.06±0.11</td>
<td>+0.12±0.22</td>
<td>0.0±0.03</td>
<td>+0.01±0.18</td>
</tr>
</tbody>
</table>
results for all dialyses regardless of duration, expressed as the average reduction per exchange. Each exchange was of 40 minutes duration, consisting of 20 minutes fill and dwell time and 20 minutes dwell and drain time. The changes in urea, creatinine and uric acid are similar to what one would expect in conventional peritoneal dialysis. Changes in electrolytes (Table II) are likewise similar to conventional peritoneal dialysis.

The serum glucose concentration was essentially unchanged during the course of our experimental procedures, changing from a pre-dialysis serum concentration of 164 mg/100 ml to a post-dialysis value of 147 mg/100 ml. The range of the initial glucose concentration of the peritoneal dialysate varied between 1.5% and 4.0%. Also, the amount of glucose added via the infusion system varied according to the requirements for ultrafiltration. The CO₂ content of the serum remained essentially unchanged during the course of sorbent peritoneal dialysis with a predialysis level of 19.5 mM/L and post-dialysis level of 18.8 mM/L.

TABLE III. Pre- and Post-cartridge Dialysate Concentrations (N=80)

<table>
<thead>
<tr>
<th></th>
<th>Urea nitrogen (mg/100 ml)</th>
<th>Creatinine (mg/100 ml)</th>
<th>Uric acid (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-cartridge</td>
<td>24.7 ± 9.6</td>
<td>3.6 ± 1.1</td>
<td>2.7 ± 1.0</td>
</tr>
<tr>
<td>Post-cartridge</td>
<td>1.1 ± 1.29</td>
<td>0.1 ± 0.15</td>
<td>0.6 ± 0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Na⁺ (mEq/l)</th>
<th>Cl⁻ (mEq/l)</th>
<th>K⁺ (mEq/l)</th>
<th>Ca⁺⁺ (mg/100 ml)</th>
<th>PO₄³⁻ (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-cartridge</td>
<td>136.5 ± 6.3</td>
<td>100.9 ± 12.0</td>
<td>1.2 ± 0.36</td>
<td>6.4 ± 1.7</td>
<td>0.79 ± 0.27</td>
</tr>
<tr>
<td>Post-cartridge</td>
<td>141.5 ± 7.6</td>
<td>108.1 ± 12.1</td>
<td>0.02 ± 0.04</td>
<td>0.55 ± 0.3</td>
<td>0.01 ± 0.03</td>
</tr>
</tbody>
</table>

As shown in Table III, the sorbent cartridge completely removes the urea and creatinine from the peritoneal dialysate while only a small concentration of uric acid (0.6 mg/100 ml) remains. Similarly, potassium and phosphate are completely removed by the sorbent cartridge while post cartridge dialysate concentration of calcium is only 0.55 mg/100 ml. Sodium and chloride concentrations increase slightly from the pre to post cartridge dialysate specimens due to contribution of these ions by the sorbents. The pre and post sorbent cartridge dialysate concentrations of protein are similar, in the range of 100 mg/100 ml.

For sterility studies we obtained four different specimens during each of ten dialyses. There have only been two positive cultures. Both of these were from specimens obtained after the sorbent cartridge was incubated for 24 hours at 37°C and two litres of sterile dialysate washed through the cartridge with subsequent passage through a 0.45 micron filter. The filter was then sent for
culture. The two positive cultures were from one patient and the same organism, Staphylococcus epidermidis, coagulase negative was grown. The patient did not clinically manifest signs and symptoms of peritonitis but was treated with antibiotics. Cultures during subsequent exchanges failed to reveal any growth and the patient has remained well without evidence of peritonitis.

DISCUSSION

Ever since the development of an acceptable indwelling peritoneal catheter (Tenckhoff and Schechter, 1968), there has been a resurgence of interest in peritoneal dialysis. Prior to this, peritoneal dialysis was ordinarily used only as temporary therapy for acute renal failure, certain drug overdoses, excessive salt and water retention, or for an occasional dialysis in chronic haemodialysis patients during periods when haemodialysis was contraindicated due to medical complications or difficulties with blood access. Only recently has peritoneal dialysis been utilised as a method of chronic treatment for renal failure.

There are currently several different types of equipment in use for conducting peritoneal dialysis. The simplest is the manual changing of two litre aliquots of sterile peritoneal dialysate. Because of the obvious disadvantage of this method which requires an individual to change bottles for every exchange, a peritoneal cycling device has been developed which allows for the consecutive administration of 6 to 8 two litre volumes of sterile peritoneal dialysate. Another type of peritoneal dialysate delivery equipment uses a proportioning pump to mix dialysate continuously from concentrate, glucose and reverse osmosis processed water. Volumes of dialysate are then infused according to the therapeutic parameters. The early clinical results reported here utilise sorbent regeneration and subsequent recirculation of the peritoneal dialysate.

There are advantages and disadvantages to each of the various methods mentioned above. Changing bottles by hand uses very simple equipment. However, the reduced cost of equipment is quickly lost by the increase in personnel costs as well as the expenses of the two litre containers of sterile dialysate. Also, by using individual bottles, numerous breaks in sterility occur. The automated peritoneal cycler which allows 6 to 8 bottles to be hung at one time eliminates some of the personnel costs but still requires multiple breaks in the sterile system as well as the expense incurred in purchasing sterile two litre volumes. Ten litre carboys of peritoneal dialysate (available in Europe and elsewhere) are not currently available in the United States due to concern about the maintenance of sterility in large volumes of glucose containing fluid.

The peritoneal dialysate delivery equipment utilising a proportioning pump to make up the dialysate requires a larger initial investment, but the ongoing expenses are reduced. These systems allow for prolonged dialysis without numerous invasions of the closed system. Complexities of the design as well as the necessity for reverse osmosis treatment of the water, raise questions about the reliability
of the available equipment. Home training, although generally easier than for haemodialysis still necessitates a considerable investment of time and effort on the part of the hospital personnel.

The initial expense of the sorbent system currently under development should be less than for the currently available automated equipment. The expense of the sorbent cartridge will be compensated for by the savings in the amount of commercial peritoneal dialysate necessary for the procedure. The major advantage of the sorbent system is the simplicity of design, the ease of operation and, therefore, the reduced time needed for patient education. The easy transportability of the equipment as well as the absence of the need for water treatment are added advantages.

The presented data indicate the feasibility of a sorbent system. The uraemic metabolites are removed by passage through the sorbent cartridge and, therefore, with their absence in post cartridge dialysate their mass transfer and decrease in serum concentrations are similar to what one would expect with conventional peritoneal dialysis. Electrolyte balance is likewise maintained and salt and water removal can be easily accomplished by adjusting the dialysate glucose concentration. An increase in the serum concentration of sodium may result from an exchange by the sorbent cartridge of sodium for calcium, magnesium and ammonium ion, generated from urea. This increase has been small and has not presented any clinical problems. However, it can be compensated for by reducing the initial sodium concentration of dialysate below the 140 mEq/L concentration we have been using.

In these early experiments the metabolic acidosis of uraemia was incompletely corrected. This was in part the result of using the chloride form of hydrated zirconium oxide in the sorbent cartridge rather than the acetate form of the same sorbent. With this composition an ion of chloride is exchanged for phosphate, fluoride and other anions of the precartridge dialysate. In the newer cartridges which contain the acetate form of the sorbent, a molecule of acetate is exchanged for these anions and therefore additional buffer is available to correct the metabolic acidosis. The pre and post cartridge dialysate protein concentrations are similar and may indicate that the protein loss with sorbent dialysis is less than with conventional peritoneal dialysis. However, our precision for measuring low concentrations of protein is poor and a definitive answer to the question will only be available after more precise measurements are obtained.

As we have shown previously, the carbon in the sorbent cartridge becomes saturated with glucose, the magnitude of the adsorption depending on the initial glucose concentration of dialysate. During the course of dialysis, as the glucose concentration in the dialysate falls due to peritoneal adsorption by the patient, glucose is gradually eluted from the carbon helping maintain a stable dialysate glucose concentration. The glucose concentration of dialysate can be regulated by either changing the initial glucose concentration, or varying the amount of glucose added in the infusate. The level of glucose concentration
will be dictated by the clinical requirements for water removal. The sterility of the system has been monitored throughout our clinical work. There were two positive cultures. They most likely were introduced from the abdominal wall where there was an area of infected dermatitis. The positive cultures that were obtained were from the sorbent cartridge after incubation for 24 hours at 37°C. Since the dialysate itself and a filter in the dialysate flow line were sterile during the same procedures, the inoculum of bacteria must have been very small. The sorbent system utilises a closed circuit of dialysate flow, minimising the possibility of contamination during the procedure. Since the sorbent cartridge, the filter and the dialysate are initially sterile, the opportunity for exogenous contamination is very small.

A sorbent based delivery system for peritoneal dialysis represents an advance in the available technology for the treatment of chronic renal failure. However, one must also consider future applications of this type of approach to fully appreciate its potential. Utilisation of this type of technology as a basis for the development of an ambulatory dialysis unit is feasible. With the opportunity available for longer periods of dialysis the requisite size of the sorbent cartridge will be considerably reduced, as would the amount of dialysate. With miniaturisation of mechanical equipment the whole system would be easily carried or worn.

Compared to an ambulatory mode of haemodialysis, a peritoneal system would have several advantages: avoidance of the extracorporeal circulation of blood and necessity for anticoagulants; the elimination of the need for complex and cumbersome blood pumps and pressure monitoring devices; the freeing of the extremities of mechanical encumbrances; the safety of the procedure so that if accidents occur they are unlikely to be catastrophic; the less rigid requirements for dialysate composition eliminating the need for conductivity monitors, etc.

The use of continuous flow peritoneal dialysis instead of the intermittent batch-type delivery that is currently in use will be a further advance in technology and will enable dialysis procedures to be even further simplified and the requisite equipment accordingly reduced. This technique will also increase the efficiency of peritoneal dialysis (Gordon et al, 1976). The major obstacle towards the development of this type of system lies in the absence of a double lumen peritoneal catheter allowing concurrent infusion and drainage. Such a catheter will have to minimise the amount of streamlining between inlet and outlet orifices. Designs for such a catheter are currently under study.

References

Tenckhoff, H and Schechter, H (1968) Transactions of the American Society for Artificial Internal Organs, 14, 181