Portable Artificial Kidney System with Adsorbents

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It is well known that conventional dialysis equipment requires large volumes of dialysate. This fact poses plumbing and power problems. This shortcoming of the system is a serious obstacle to bedside dialysis in hospital, and to home dialysis.

The purpose of the present research is to re-evaluate the quantities of dialysate necessary for the removal of various substances and to design a small dialysate supply system which utilises less dialysate and adsorbents.

A comparative study on removal efficiency between two systems was made; one a single pass system with 210L of dialysate and the other a recirculating system with 30L of dialysate which utilises 500 g of activated charcoal and 200 g of alumina.

MATERIALS AND METHODS

Comparison was made of remaining rates, namely the serum concentration (C_B) divided by the initial serum concentration (C_{BO}), between the two different types of dialysate supply systems for the evaluation of dialysate volume. They were (1) 210L of dialysate flowing single pass into a Kiil dialyser at a rate of 500 ml/min for a 7 hour dialysis; (2) 30L of dialysate, recirculated, flowing at the same rate for the same length of time as in (1). Taking the volume of body fluid as 30L, we then obtained the relationships between reduction rate and molecular weight using urea, creatinine, uric acid, sucrose, vitamin B_{12} and inulin.

After the evaluation of various adsorbents, activated charcoal and alumina were selected on the basis of their adsorption rate of creatinine, uric acid and inorganic phosphate at an equilibrium state. The elution of toxic metals from these adsorbents was tested: 12.5 g of charcoal or 5 g of alumina was extracted with 750 ml of dialysate for 15 hours by shaking, and the metals extracted were examined by atomic absorption spectrophotometry.
A solution containing creatinine (5 mg/dl), uric acid (5 mg/dl), and sodium phosphate (2.5 mg/dl as P content) in dialysate solution was passed through two columns, one packed with activated charcoal (3g, 1 x 9.5cm), the other with alumina (1.5g, 1 x 3.7cm), at a flow rate of 5ml/min. The amount of leakage of each solute in the eluate was determined as time passed, and the total adsorbed amount was obtained. Adsorbabilities of methyl guanidine and guanidinoacetic acid were also examined.

Dialysis was performed for a total of 46 months on patients with chronic renal failure on a dialysis system using 30 l of recirculated dialysate, 500g of activated charcoal and 200g of alumina. A comparative study was conducted on reduction rates between a machine with a small volume of recirculated dialysate and adsorbents and another with a large volume of single pass dialysate, as well as on the increase of membrane permeability with the introduction of adsorbents. Finally the evaluation of mass transfer through the membrane was made when antibiotics were added to the dialysate.

RESULTS

Dialysis efficiencies were compared for 210 l of single pass dialysate and 30 l of recirculated dialysate. Reduction rates with a standard Kiil dialyser after a 7 hour dialysis were calculated by the following formulae. Body fluid was regarded as a single bath in these calculations.

1) Single pass

\[
\frac{dC_B}{dt} = -PA (C_B - C_D)
\]

\[
\ln \left( \frac{C_B}{C_{BO}} \right) = 1 \left( \frac{PA}{V_B} \right)t
\]

2) Recirculation

\[
\frac{dC_B}{dt} = -PA (C_B - C_D)
\]

\[
C_B V_B + C_D V_D = m : \text{constant}
\]

from (3) and (4)

\[
\frac{C_B (V_B + V_D) - m}{V_D (C_{BO} - C_{DO})} = \exp \left( \frac{-PA}{V_B \cdot V_D} \right) \frac{V_B + V_D}{V_B \cdot V_D} t
\]

\[
V_B \quad \text{body fluid volume} = 30 \text{ l}
\]

\[
V_D \quad \text{dialysate volume} = 30 \text{ l}
\]

\[
C_{BO} \quad \text{initial serum concentration}
\]

\[
C_B \quad \text{serum concentration}
\]

\[
C_{DO} \quad \text{initial concentration in dialysate}
\]

\[
P \quad \text{mean permeability of Kiil dialyser (dialysate flow rate}
\]

500ml/min, blood flow rate 200ml/min)

\[
A \quad \text{membrane surface area}
\]

\[
t \quad \text{dialysis time} = 7 \text{ hours}
\]
Table I. The relationship between molecular weights of several substances and the remaining rates after 7 hours of dialysis with a standard Kii dialyser

<table>
<thead>
<tr>
<th>Substance</th>
<th>Molecular weight</th>
<th>Permeability ( \times 10^{-4} \text{cm/min} )</th>
<th>Remaining rate Single Pass (S)</th>
<th>Remaining rate Recirculation (R)</th>
<th>( S/R )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>60</td>
<td>102.9</td>
<td>0.237</td>
<td>0.528</td>
<td>0.45</td>
</tr>
<tr>
<td>Creatinine</td>
<td>113</td>
<td>68.6</td>
<td>0.380</td>
<td>0.570</td>
<td>0.67</td>
</tr>
<tr>
<td>Uric acid</td>
<td>168</td>
<td>51.4</td>
<td>0.454</td>
<td>0.602</td>
<td>0.75</td>
</tr>
<tr>
<td>Sucrose</td>
<td>342</td>
<td>33.1</td>
<td>0.630</td>
<td>0.700</td>
<td>0.90</td>
</tr>
<tr>
<td>( V_{\text{B12}} )</td>
<td>1355</td>
<td>14.9</td>
<td>0.815</td>
<td>0.831</td>
<td>0.98</td>
</tr>
<tr>
<td>Inulin</td>
<td>5200</td>
<td>7.4</td>
<td>0.910</td>
<td>0.910</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Theoretical reduction rates under these conditions calculated from (2) and (5) are shown in Table I. The table indicates that the permeability of the membrane decreased with increasing molecular weight. Hence the difference in dialysis efficiency becomes insignificant between single pass and recirculating systems for substances of large molecular weights, and the difference is hardly observable for substances with molecular weights of 300 and above. On the strength of this observation we conceived the idea of removing substances with molecular weights of less than 300 by adsorbents. After a series of careful experiments activated charcoal and alumina were chosen. The adsorbents hardly adsorb Na, K, Ca, Cl and urea and only 30% of Mg and glucose were adsorbed. The amounts adsorbed within seven hours were, 100 mg of creatinine and 103 mg of uric acid on 3 g of charcoal, and 24 mg of phosphate on 1.5 g of alumina. If the average excretion of normal adult a day is assumed to be 1.8 g of creatinine, 0.8 g of uric acid and 1.5 g of phosphate, 108 g and 48 g of charcoal for creatinine and uric acid, and 188 g of alumina for phosphate are required for two days.

The results indicated that over 90% of creatinine, over 95% of uric acid, and over 85% of phosphate were adsorbed on the column within three hours. Methylguanidine and guanidinoacetic acid were dissolved in the dialysate in a concentration of 0.7mg/dl, and the solutions were circulated through a column. As shown in Figure 1, the time-course of adsorption of these guanidine derivatives proved that over 90% of methyl guanidine and guanidinoacetic acid were adsorbed within three hours. Table II shows the results of release testing of adsorbents. All the substances released are found in higher concentrations as compared to the standards for tap water in Japan. In Japan tap water is so pure that it can be used directly for dialysis.

Clinical reduction rates by a dialysate supply system comprising 30 l of dialysate with 500 g of activated charcoal and 200 g of alumina, and a hollow fibre kidney were calculated. Of 600 dialyses, on 43 of which laboratory blood examinations were conducted, the average reduction rates were
creatinine 58%, uric acid 67%, and P<sub>1</sub> 58% (Figure 2). These figures are satisfying, but the value for urea, 40% is less than in single pass. A possible rise in BUN level was a source of concern in an anuric patient undergoing 7 hour dialysis, three times a week during the 14 months of treatment. But the BUN level eventually fell, the latest concentration being 65 mg/dl. With
a haematocrit value of 23%, this patient has no severe complications such as neuropathy or cardiac failure.

For the purpose of reducing dialysis time, testings of 3 hour dialyses with the present system and 2 hollow fibre kidneys were conducted. As seen in Figure 3, it is surprising that the predialysis BUN level began to fall after starting 3 hour dialyses and the values remain around 50 mg/dl after one and a half months. On the other hand, there was a slight rise in creatinine level, but remarkable improvement has been made clinically and the patient is now fully rehabilitated. There is no neuropathy, the haematocrit
value is 25%, and skin pigmentation is reduced. It can be said on this evidence that patients may be kept in good condition even with 3 hour dialyses. Also in this patient, predialysis BUN level tended to fall in spite of a protein intake of 1.2 g - 1.6 g/kg of body weight/day and oliguria. The fall is noteworthy since it occurred in two other patients as well.

When adsorbents were added to the dialysate, adsorbable substances such as uric acid showed greater tendency to pass through the membrane than in the single pass system. It seems that this phenomenon is caused not only by diffusion of the substances, but some other active force. Furthermore, when streptomycin and aminobenzyl penicillin are added to the dialysate, permeability of the membrane for uric acid, creatinine, and $P_i$ increased.

**DISCUSSION**

The problems concerning dialysate volume reduction have not been fully explored. At present the majority use large volumes of dialysate despite the need to make the system less bulky. However, our results show that 30 l of dialysate is sufficient for the removal of substances with molecular

![Figure 4. Home dialysis training using this small system with adsorbents and two hollow fibre kidneys](image-url)
weights of 300 and above and the introduction of adsorbents greatly adds to
dialysis efficiency as compared to conventional systems. A system which
utilises charcoal, urease, zirconium phosphate and other materials as
adsorbents (Gordon et al, 1968) has proved to be satisfactory for the removal
of urea. However, since it employs little dialysate, the removal of unknown
substances is open to question. Our present system using 30 l of dialysate
is not different in size, and is far safer than the type mentioned (Maeda et al,
1972). When further comparison is made with direct haemoperfusion through
charcoal the question concerning the removal of unknown substances is also
left open. The technique is not capable of controlling electrolytes or water
(Yatzidis, 1964; Chang et al, 1972).

CONCLUSION

It can be concluded that our present system of 30 l of dialysate with 500g of
activated charcoal and 200g of alumina, when used in combination with a hol-
low fibre kidney is capable of sustaining a 3 hour dialysis without causing
disequilibrium, and is readily available for bedside dialysis in the ward and
home dialysis (Figure 4), for adults and children.

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OPEN DISCUSSION

E DENTI (Saluggia): Three years ago a similar piece of equipment was con-
bstructed in Italy and has been commercially available since 1972. It works
by means of a charcoal and aluminium cartridge. It differs from your machine
in that in order to avoid bacterial contamination the water is supplied through
a millipore filter and there is no ultra violet sterilisation.

Charcoal is an industrial product normally heavily contaminated: the
degree of contamination depends on the production method. What is your
washing procedure to avoid this contamination? My next question is —
aluminium oxide is more active when contaminated by sulphate. What method
do you employ to avoid sulphate release?
MAEDA: We sterilise by means of ultra violet irradiation, and I do not know how to wash the activated charcoal and alumina: Takeda Chemical Company supplied these products ready to use. I believe the charcoal and alumina are pure enough for our purpose.

DENTI: I think that this type of apparatus is very useful for treatment of acute renal failure. With the limited amount of solution, one avoids the problem of rapid removal of urea and the disequilibrium syndrome. Have you had any experience with your apparatus in acute renal failure?

MAEDA: I think that this type of apparatus is very useful for treatment of acute renal failure. I prefer it to the conventional type, when I treat acute patients, because there are no side effects during dialyses.

D N S KERR (Newcastle upon Tyne): One possible explanation for a falling BUN and a rising creatinine is putting on muscle mass. Were your patients so fit that they took lots of exercise and became very muscular?

MAEDA: They did take lots of exercise, but their muscle mass was not changed.