THE EFFECT OF DIFFERENT VARIABLES ON UREA CLEARANCE USING THE SKEGGS-LEONARDS HAEMODIALYSEER

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The present study was undertaken to measure the effects of changing the membrane area and thickness on the dialysing efficiency of the Skeggs-Leonards dialyser. Urea clearance was determined in vitro and in vivo with Skeggs-Leonards 12 and 18 unit packs using 300 and 150 PT cuprophane.

IN VITRO EXPERIMENTS

Ten litres of aqueous urea solution, representing the patient's blood, were dialysed against water at body temperature with venous return pressures of 30 or 150 mm. of mercury (Figure 1). Blood flow was varied from 100 to 400 ml./min. and dialysing flow maintained constant at 1000 ml./min.

At each level of 'blood' flow four to six series of samples were collected and their urea content determined by autoanalyzer. Each series consisted of samples from the 'blood' inflow, dialysate and 'blood' outflow taken at minute intervals.

Urea clearances were calculated both from the dialysate clearance and the blood extraction(1).

\[
\text{Clearance, } C = \frac{UV}{A} \quad \text{or} \quad a = \frac{(A-R)}{A}
\]

Where \( U \) = Urea concentration in Dialysate, mg. %.

\( A \) = " " in Blood inflow, mg. %.

\( R \) = " " in Blood outflow, mg. %.

\( V \) = Rate of dialysate flow, ml./min.

\( a \) = Rate of blood flow, ml./min.

The inflow urea concentration decreased from approximately 600 to 300 mg. % during each 4 hr. experiment, with no apparent effect on the clearance. Urea clearance as calculated by both methods showed reasonable agreement. Figure 2a shows the improvement in urea clearance resulting from increasing the area in dialysing membrane from 2 to 3 m^2 by using the 18 unit pack in place of the 12, with the thin cellophane in both packs. The points represent the mean values from both equations and the standard deviation is shown as a vertical line at each point. The improvement in clearance is most pronounced at the higher blood flows. Using thick cellophane similar increases were observed.

When the thin cellophane is used in place of the thick, the distance separating the blood from the dialysing fluid is halved. Figure 2b shows the improvement in urea clearance by the thin cellophane compared to the thick using the 12 pack. The improvement is again more pronounced at the high blood flows. Similar increases were observed using the larger pack.

As expected the highest clearance rates were obtained using the large pack and thin cellophane, the greatest increases occurring at the higher blood flow rates. The large pack with thick cellophane and the small

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pack with thin cellophane gave very similar results, while the small pack with thick cellophane was the least efficient.

The improvements in the percentage extraction, reflected those in the urea clearance (Figure 3).

The results obtained with high and low venous resistances, were compared. They showed that in vitro using aqueous urea solutions, changing the blood outflow pressure without changing the rate of blood flow, had no appreciable effect on the urea clearance or extraction.

IN VIVO DETERMINATIONS

The in vivo measurements were made during therapeutic dialyses of uraemic patients. As the blood flow could not be measured directly the rotary roller pump was calibrated using water, and the setting shown on the pump dial was then taken to be the rate of blood flow. The in vivo results reflected the inaccuracies in the blood flow estimation due to variations in pack resistance and venous tone. The total blood volume in the machine and patient could no longer be maintained constant. The blood flow was initially increased from about 100 ml./min. to a constant level of 200 to 300 ml./min. depending on the patient's blood pressure and clinical condition. The dialysing flow remained constant at 1000 ml./min.

Samples from the blood inflow, dialysate and blood outflow were taken as in the laboratory experiments, and the urea content and clearance values determined as before.

The results obtained from measurements during the dialyses of patients show good agreement with those made in vitro. Results were obtained from 9 patients dialysed with the 18 pack and thin cellophane and 9 patients with the 12 pack and thick cellophane (Figure 4).

Higher standard deviations were obtained from the results from clinical measurements especially at the low blood flow rates where fewer determinations were obtained. The results from 7 patients dialysed with the 18 pack and thick cellophane and 4 with the 12 pack and thin cellophane showed similar agreement with the in vitro results.

DISCUSSION

The results obtained in this study are similar to those obtained by Jørgensen\(^1\) using 14 and 21 unit Skeggs-Leonard's packs with 150 PT cellophane. Jørgensen stressed the importance of the size and number of parallel units in the pack; the mixing of the blood as it passes between units produces an improvement in the clearance. In the present investigation the channelling of blood and dialysing fluid in the larger pack probably resulted in a reduced clearance.

Renkin\(^2\) applied the Fick principle to a dialysing system. He showed that:

\[
\text{Clearance} = \frac{(\text{Blood Flow})(1 - e^{-\frac{\text{Permeability}}{(\text{Area})}})}{\text{Blood Flow}}
\]

provided the dialysing flow is considerably greater than the blood flow. Hence the clearance would be expected to increase with increase in rate
of blood flow, membrane area and permeability. The present study confirms this with respect to blood flow and membrane area. The permeability depends on three factors:

1. The rate of diffusion through the film of blood on the blood side of the membrane.
2. The rate of diffusion through the membrane.
3. The rate of diffusion through the film of dialysing solution on the dialysate side of the membrane.

The rate of diffusion through the membrane is determined by the thickness, and the pore size and frequency of distribution.

A lower overall permeability than expected, may occur with a thin membrane if the blood or dialysing film resistance is increased. Laminar flow and channelling of the blood or dialysing fluid produce relatively stagnant regions within the pack, thus increasing the film resistance on either side of the membrane.

The results from the present investigations show, that as expected increasing the area or decreasing the thickness of the dialysing membrane, leads to considerable increases in the urea clearance at the higher blood flow rates.

REFERENCES


A paper on this topic has been accepted for Clinical Science, February, 1965.
Figure 1. Diagram of in-vitro apparatus for clearance measurements.

Figure 2. Comparison of urea clearance by:

a) 12 and 18 packs with thin cellophane.

b) Thick and thin cellophane with 12 packs.
Figure 3. Comparison of urea % extraction (in-vitro).

Figure 4. Comparison of urea clearance measured in-vivo and in-vitro.
THE CHAIRMAN, F.M. PARSONS (Leeds): I should like to congratulate both speakers on their manner of presentation. It was so clear.

Are there any questions, please?

G.M. BERLYNE (Manchester): We have been running experiments on permeability of various types of cellophane, primarily to find cellophane made in England which was as good as the Cupraphane. Like the last speaker, we found that the thinner the cellophane is the greater the permeability. We can get cellophanes which are 1 thou* thick, however - that is 300 Pt which is the same as the Cupraphane 300 - which have a higher permeability to urea and a higher permeability to sodium. The ratio, of course, may not be particularly significant: the ratio of permeability mu values is 1.67 to about 1.45 for urea. We time the blood flow through the kidneys in patients in vivo, Kiil kidneys, by the Scribner technique, which is to put a small column of air into the arterial side and time the number of seconds it takes to reach the arterial side of the kidney. After dialysis we measure the volume at the same pressure through the tubing on the arterial side.

THE CHAIRMAN: Can we have this quite clear? Did you say 1 micron thick?

G.M. BERLYNE (Manchester): It is 1 thou* thick.

THE CHAIRMAN: Is that wet or dry?

G.M. BERLYNE (Manchester): This is another red herring which I ought to bring up now. At one time we used to put up all our Kiil kidneys wet, and we had quite a large percentage of mechanical failures at the beginning of, or during, dialysis. We now put them up dry, then put the fluid in, and we have had no failure in the past six weeks since we have been doing this. Previously we had 30%, 40% or 50% failures. This thickness is all measured dry. I think that all cellophane manufacturers mean by their code numbers, so far as I can gather, 300 equals 30 grammes per square metre approximately.

A.M. JOEKES (London): May I ask Dr. Fritz if he has any explanation for the fall-off of the sodium permeability with the higher flow rates in his in vitro experiments?

K.W. FRITZ (Bonn): Do you mean that the sodium dialysis was slower with higher flow rates? No, that is not right. It is only that it will not go so high with higher flow rates.

A.M. JOEKES (London): I mean relative to the potassium.

K.W. FRITZ (Bonn): Yes. If you change the composition then the sodium dialysis is slower, but it will not go down with higher flow rates.

A.M. JOEKES (London): But why does it fall off relative to the potassium?

K.W. FRITZ (Bonn): I have thought about this with physical chemists, and I have been told that this is a different affinity of the cations, potassium and sodium, to the anion, chloride. If you change the relation between sodium and chloride, the chloride as it goes through the membrane picks up more of that cation for which it has a higher affinity than it does of the

* 1/1000 inch = 25.4 micron
other, and this depends naturally upon the relationship of both cations.

J.L. FUNCK-BRENTANO (Paris): I should like to add that, by stretching the membrane one can improve the dialysis of urea. As you can see in Figure 1, stretching the same kind of cellophane to higher levels improves the dialysance of urea.

N. ALWALL (Lund): I should like to stress the importance of the quality of the cellophane membrane and to illustrate the fact by my own experience. About 1952 we made tests with our artificial kidney and got certain results. When we repeated these tests ten years later we got the same yield from the same artificial kidney with an area of 1.2 sq.m. as we had obtained with 0.8 sq.m. ten years earlier. That is to say the manufacturers had changed the tubing according to the demands of the casing manufacturers (a thick walled tubing) and not according to our demands (a thin walled tubing). So far they have not supplied us with a cellophane tubing as good as their earlier one which we used at the beginning of the 'fifties. I think it is very important to consider such facts when comparing data from the literature about artificial kidneys of different construction. I think it is necessary to make parallel tests with the same cellophane membrane when comparing different machines if you want to assess the influence of the construction of the artificial kidney.

A. HARDY-SMITH (Liverpool): I should just like to add that our technicians do not like using the thin cellophane in the larger pack so much. They find
it more difficult to make up the large packs. So we have been using the smaller pack with the thin cellophane rather than the larger one. It is just a technical thing that it is a bit more fiddly; it tends to fold over as you are making up the pack.

N. ALWALL (Lund): I believe that you are using sheets of membranes but we are using tubing. The sheets are better (thinner) than the tubing. The technique of manufacturing the tubing demands a thicker membrane.

D. N. S. KERR (Newcastle upon Tyne): Miss Hardy-Smith, when you said that there was a possibility of decreased efficiency in the larger pack, had you actually expressed your results as dialysance per square metre and shown that it really is lower per square metre in the larger pack, or not?

A. HARDY-SMITH (Liverpool): No, I have not done it as dialysance per square metre.*

THE CHAIRMAN: I should like to thank Dr. Fritz and Miss Hardy-Smith. We are always referring our results to urea, but we have no knowledge of all the molecules that accumulate in uraemia. For the majority of cellophanes in use, the maximum diameter of the molecules that pass through the pores is of the order of 17 Å. Anything larger is dialysed very slowly. I hope that sooner or later we shall hear a lot about substances of this size or greater. I am sure that the future trend will be to look more closely at these higher molecular size substances.

*Miss Hardy Smith subsequently sent the following figures for clearance per sq. m. of membrane area:

<table>
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<th>Membrane</th>
<th>Area (m²)</th>
<th>100</th>
<th>200</th>
<th>300</th>
<th>400</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 PT</td>
<td>2.18</td>
<td>38</td>
<td>59</td>
<td>70</td>
<td>76</td>
</tr>
<tr>
<td>300 PT</td>
<td>3.26</td>
<td>30</td>
<td>49</td>
<td>59</td>
<td>66</td>
</tr>
<tr>
<td>150 PT</td>
<td>2.18</td>
<td>44</td>
<td>72</td>
<td>88</td>
<td>98</td>
</tr>
<tr>
<td>150 PT</td>
<td>3.26</td>
<td>31</td>
<td>54</td>
<td>71</td>
<td>80</td>
</tr>
</tbody>
</table>

These figures show the expected fall-off in mean clearance/sq.m. as surface area is increased, particularly when the thin cellophane is used. With a dialyser of this size and efficiency there is relatively little 'return for money' when the membrane area is further increased, at least as far as urea clearance is concerned.

To test whether this small increase in effectiveness on enlarging the area is simply a factor of dialyser size, or is due to channeling or similar phenomenon in the larger model, the results were also analysed in terms of extraction ratio per sq. m. (er) from the formula \((1 - er)^n = 1 - ER\), where \(n\) is the area in sq. m. and ER the extraction ratio of the whole dialyser. With both types of cellophane the extraction ratio/sq. m. was virtually the same in large and small packs, at blood flows from 200-400 ml./min. This suggests that the results are explained on the basis of dialyser size alone.