The Clearance of Middle Size Molecules

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The square meter hour hypothesis formulated by Babb et al (1971) proposes that the rates of removal of large molecular weight solutes are not appreciably affected by variations in either blood or dialysis fluid flow within the usual clinical range, but are dependent upon the usable surface area times the number of hours per week that the blood is exposed to the surface. If this hypothesis is correct, the implications on future dialyser design and efficiency are profound. As the clinical strategies which Babb and Scribner have proposed to test the hypothesis are unlikely to provide clear confirmation in the near future we have felt it necessary to introduce middle molecular clearance into our dialyser evaluation programme.

METHOD

In vitro clearances have been calculated from the formula

\[
\text{Clearance} = \frac{\text{Blood flow} \times (\text{arterial concentration} - \text{venous concentration})}{\text{arterial concentration}}
\]

Concentrations of the isotope in samples are measured on a Gamma-matic counter to an accuracy of 1%. The isotopes were diluted in Physiological saline and dialysed against normal dialysis fluid under conditions of minimal transmembrane pressure and ultrafiltration.

The solutes used were \(^{125}\)I Na diatrizoate (Hypaque MW 630) and \(^{58}\)Co Cyanocobalamin (Vitamin B\(_{12}\) MW 1335). Initially \(^{51}\)Cr EDTA (MW 400) was also used but when clearances were only 10% better, we chose the cheaper Na diatrizoate as representative of solutes in the 400-700 MW range. The accuracy of Bromsulphthalein estimations has not been sufficient to allow reproducible comparison by our method.

RESULTS

The comparative in vitro clearances for small and middle size molecules at blood flow 200 ml/min are shown in Table I.
Table I. In vitro clearance of small and middle size molecules

<table>
<thead>
<tr>
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<th>Clearance ml/min at blood flow 200 ml/min</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Urea MW 60</td>
</tr>
<tr>
<td>Meltec Multipoint 1m²</td>
<td></td>
</tr>
<tr>
<td>11-12µm Standard Membrane</td>
<td>146</td>
</tr>
<tr>
<td>18µm Membrane</td>
<td>127</td>
</tr>
<tr>
<td>Meltec Multipoint 0.61m²</td>
<td></td>
</tr>
<tr>
<td>11-12µm Standard Membrane</td>
<td>112</td>
</tr>
<tr>
<td>Watson Marlow 1m²</td>
<td></td>
</tr>
<tr>
<td>11-12µm Standard Membrane</td>
<td>95</td>
</tr>
<tr>
<td>18µm Membrane</td>
<td>85</td>
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</tbody>
</table>

The Meltec Multipoint 1m² with an effective surface area of 0.95m² is 40-50% superior to the Watson Marlow Kiil (effective surface area 0.7m²) in removing both small and middle size molecules.

The Meltec Multipoint 0.61 m² is more efficient than the Watson Marlow Kiil for small molecules and equally effective in removing middle size molecules due to a similar effective surface area.

The use of 18µm cuprophan in the Meltec Multipoint 1m² results in a drop in clearance for middle size molecules to levels comparable to the Watson Marlow Kiil. The use of 13.5µm cuprophan is not accompanied by a reduction in clearance of middle size molecules (Hoenich et al, 1972). Where excessive ultrafiltration is a problem with the Meltec Multipoint 1m² the use of thicker cuprophan membranes can reduce ultrafiltration (Hoenich et al, 1972).

The use of 18µm cuprophan is not recommended in the Watson Marlow Kiil where a considerable reduction in clearance of middle size molecules results.

DISCUSSION

Our clearance data for Cyanocobalamin (Vitamin B₁₂) in the Standard Kiil is considerably higher than previous published data of Babb et al (1971) and Gotch et al (1971). It might be due to the use of a more effective Kiil or perhaps due to changes in molecule structure of B₁₂.

The characteristics of B₁₂ and Hypaque become altered by persistent exposure to light and tap water and clearances can drop to half those observed when the isotope is dissolved in physiological saline and kept in the dark. It is thus essential to run a control dialyser two or three times a day when com-
paring dialysers in terms of middle size molecules to ensure that the comparison is not coloured by deteriorating isotope labelled solutes. Comparisons between different dialysers from different units are, therefore, not comparable unless consistent and similar results are obtained for a control dialyser.

This improved performance of the Meltec Multipoint \(1 \text{m}^2\) for middle size molecular solutes as well as small size solutes could be used in two ways. If improved well being by more efficient dialysis is our aim this will be achieved by continuing to use the Meltec Multipoint \(1 \text{m}^2\) for 30 hours of dialysis per week. If reduced dialysis time is more important, then 21 hours of the Meltec Multipoint \(1 \text{m}^2\) is equivalent to 30 hours of Watson Marlow Kill dialysis if a rise in predialysis serum creatinine levels is to be avoided (Frost & von Hartitzsch, 1972). These in vitro results suggest that a change from 30 hour Kill to 21 hour Multipoint dialyser should not result in accumulation of middle molecules provided their behaviour in vivo is not affected by tight protein or tissue binding.

CONCLUSION

The Meltec Multipoint \(1 \text{m}^2\) is 40-50\% more effective than the Watson Marlow Kill in removing both small and middle size molecules. This improved efficiency could be used to improve patient's well being by continuing with 30 hours of dialysis per week, or dialysis time could be reduced to 21 hours per week and health probably maintained at its present level.

REFERENCES