A Simple Relationship Between Dietary Intake, Techniques of Treatment and Body Fluid Chemistry in Routine Haemodialysis

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The waste solute products from cell metabolism accumulate continuously in the total body water of an anuric patient with chronic renal failure at rates depending on the dietary intake and body size. Average data on this (from Leonard, 1965, in particular) gives production rates of 20 and 0.7 gm/day respectively for urea and uric acid for a 60 gm/day protein diet and 2 gm/day of creatinine for an average body weight.

EFFECT OF TREATMENT ON PRE-DIALYSIS SOLUTE CONCENTRATION

The net effect of routine haemodialysis is to restrict the level of the concentration \( C_b \) of any solute in the body fluid to a limiting predialysis level \( C_{b0} \). In the following theory a single pool model for the body fluid is assumed; in addition the small effects of ultrafiltration and of solute production rate on the kinetics of haemodialysis are neglected.

A simple mass balance, in which the solute produced by cell metabolism over a long interval of time is exactly balanced by removal during haemodialysis in the same time interval, leads to the following expression:

\[
\text{Pre-dialysis solute conc. } (C_{b0}) = \left( \frac{\text{solute production rate } (ps) \times (\text{body fluid volume } V_b)^{-1}}{\text{treatment frequency } (n) \left\{ \frac{-\text{clearance (C)} \times \text{treatment time } (t^*)}{1 - e^{\frac{\text{treatment time } (t^*)}{\text{body volume } (V_b)}} \right\}} \right) \ldots (1)
\]

This expression shows that the equilibrium pre-dialysis concentration is:

a. linearly proportional to the dietary intake,
b. inversely proportional to the frequency of treatment,
c. as a first approximation (i.e. for values of \( C t^*/V_b \ll 1 \)),
   inversely proportional to both the total treatment time and the dialyser standard.
VARIABLES AFFECTING TREATMENT TIME 
AT A FIXED PRE-DIALYSIS CONCENTRATION

A. At a fixed frequency (see Figure 1)

At a fixed frequency, equation (1) shows that a given solute production rate and pre-dialysis concentration must be associated with a constant value of (dialyser clearance x treatment time). Present day treatments based on Kill dialysers, for which the urea clearance is typically 100 ml/min, need
on this rationalized basis, treatment times of 10 hours three times weekly to balance a 60 gm diet (Figure 1). Doubling the clearance level would result in significant savings in time. What limitations are imposed by the extracorporeal circuit?

A typical in vivo variation of urea dialysance (D) with blood flow ($Q_b$) for an experimental coil dialyser, is shown in Figure 2. At low blood flows the performance is limited by blood flow, i.e. by perfusion and hence the experimental points are asymptotic to a line $D = Q_b$.

At high blood flow rates the dialysance is diffusion limited and, from Renkin's formula $D = Q_b \left[ \frac{-S}{1 - \frac{1}{e} \frac{Q_b}{R_e}} \right]$ has a maximum value of Surface Area ($S$) over Total resistance to transfer ($R_e$)

At a blood flow equal to $S/R_e$ the dialysance is thus given by $Q_b (1 - e^{-1}) = 0.632 \dot{Q}_b$, and the performance is equally limited by perfusion and by diffusion. At this condition the performance of a dialyser, thus optimised for one solute, is only limited by the blood flow attainable in the extra-corporeal circuit.

Present levels of blood flow and red cell effects therefore restrict the maximum usable clearance to around 120-200 ml/min for urea.

**The effect of a varying frequency**

Figure 3 shows that as the frequency of treatment is increased the predicted total treatment time decreases rapidly if the pre-dialysis concentration and dialyser standard are kept constant. This effect is the result of an increasing average body solute concentration both during and between treatments as the treatment time is shortened.

![Figure 3. Effect of treatment frequency on total treatment time](image_url)
An alternative method of comparison would be to keep the average body solute concentration constant as frequency is increased: this is shown by the dotted line in Figure 3 and there is clearly no advantage in going to a frequency greater than 4 treatments/week.

Some centres are already reporting the use of short 'daily' dialyses (for example de Palma et al., 1969).

REMOVAL OF SOLUTES OF HIGHER MOLECULAR WEIGHT

The simple theory, already given, shows that for normal dialyser treatments the pre-dialysis concentration of creatinine and uric acid will stabilise out at levels between 10 and 20% greater than the equilibrium pre-dialysis level for urea factored by the ratio production rate of solute. As the frequency of production rate of urea treatment is increased, with corresponding reductions in treatment time, the above percentage increase rises to a limiting value given by

\[
\frac{\text{urea clearance}}{\text{solute clearance}} - 1 \times 100
\]

Other factors which are likely to restrict the use of fast frequent haemodialysis are:

a. the removal of high molecular weight solutes from the intracellular compartment and associated osmotic disequilibrium. Data on intracellular to extracellular mass transfer coefficients is so sparse for solutes, other than urea (for example Rastogi et al., 1968) as to prohibit numerical predictions.

b. the removal of water without causing post-dialysis fatigue, and orthostatic hypotension (see Shimizu et al., 1967). To remove 5 kg of fluid per week at a restricted ultrafiltration rate of 4 ml/min sets the minimum treatment time at 21 hours/week. Careful dialyser design is necessary to avoid penalising solute transfer at low ultrafiltration rates.

CONCLUSIONS

1. Reductions of up to 50% in total treatment time compared to current Kill treatment could be attained by a combination of an improved dialyser standard, with a clearance of more than 150 ml/min and a higher frequency of treatment of the order of 5 times weekly.

2. The realisation of this worthwhile target depends critically on the design of the dialyser and the extracorporeal circuit.

3. The response of a patient to this proposed standard of treatment needs further investigation, particularly in respect of disequilibrium.
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REFERENCES