Post-dialysis urea concentration: comparison between one-compartment model and two-compartment model

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Abstract. The reduction of the urea concentration in blood can be numerically projected by using one-compartment model and two-compartment model with no variation in body fluid. This study aims to compare the simulated values of post-dialysis urea concentration for both models with the clinical data obtained from the hospital. The clinical assessment of adequacy of a treatment is based on the value of Kt/V. Further, direct calculation using clinical data and one-compartment model are presented in the form of ratio. It is found that the ratios of post-dialysis urea concentration simulated using two-compartment model are higher compared to the ratios of post-dialysis urea concentration using one-compartment model. In addition, most values of post-dialysis urea concentration simulated using two-compartment model are much closer to the clinical data compared to values simulated using one-compartment model. Kt/V values calculated directly using clinical data are found to be higher than Kt/V values derived from one-compartment model.

1. Introduction
End stage kidney disease (ESKD) is the result of the deteriorating function of kidneys. It is associated with accumulation of metabolic waste products such as urea in the body fluid [1]. The function can be partially accomplished by dialysis treatment. Dialysis comprises of two main modalities; haemodialysis (HD) and peritoneal dialysis (PD). PD uses the patient’s peritoneal membrane as the medium to exchange the toxins from blood into dialysate via osmotic forces while HD removes the toxins through artificial membrane housed in a dialyser via diffusion and ultrafiltration [2, 3]. Patient undergoes a haemodialysis treatment in 3-5 hours and repeated 2-3 times a week [4].

Urea kinetic modelling (UKM) had been introduced by National Cooperative Dialysis Study Group (NCDS). The introduction of UKM offered an opportunity to calculate the efficiency of a dialysis treatment [5]. In addition, it also explained the reduction in urea concentration during the dialysis treatment. UKM uses the concept of compartmental modelling which had been widely used in the analysis of physiological composition of body fluid. It visualised the compartment model as one or more compartments associated with the physiological spaces containing the body fluid. The assessment of dialysis dose is based on clinical parameter, Kt/V. K refers to the dialyser clearance, t refers to the duration of dialysis and V refers to the urea distribution volume at the end of the dialysis. A treatment is considered adequate if Kt/V achieved the minimum target of 1.2 [6].

This paper aims to compare the simulated values of post-dialysis urea concentration for both kinetic models with the clinical data obtained from the hospital and to present the difference between...
Kt/V values derived from one-compartment model with the Kt/V calculated directly using the clinical data in term of ratio. The results are useful for the physicians to predict the post-dialysis urea concentration for any patient.

2. Methods

2.1. Subjects
A total of 32 stable haemodialysis patients from Hospital Sultanah Aminah, Johor, Malaysia were selected as the subjects of study. All patients had steadily undergone dialysis for more than 5 years period. The patients aged between 20 and 80 years old and body weight varies from 30–90 kg. The clinical data; pre-dialysis urea concentration, post-dialysis urea concentration, urea generation rate, body weight and dialyser clearance for 5 years period were recorded and used in the simulation study.

2.2. Urea kinetic modelling
The modelling consists of two kinetic models; one-compartment model and two-compartment model. One-compartment model visualised the body fluid as one compartment while two-compartment model divides the body fluid into two compartments; intracellular and extracellular compartments [7, 8]. In both kinetic models, the urea is assumed to be generated outside the body fluid. The schematic diagram of the models are shown in Figure 1 and Figure 2.

\[ \frac{d(C(t),V)}{dt} = K.C(t) + G \]  
\[ C(t) = (C(0)V) = \frac{G}{K}e^{\frac{K.t}{V}} + \frac{K}{G} \]
where \( C(t) \) and \( C(0) \) are urea concentration at any time, \( t \) and pre-dialysis urea concentration respectively.

Clinical parameter, \( Kt/V \) can be estimated using one-compartment model if pre- and post-dialysis urea concentration are known. It can be simplify as in equation (3). The ratio of urea generation rate and dialyser clearance are neglected in the calculation due to its small value compared to the value of pre-dialysis urea concentration.

\[
\frac{K_t}{V} = \ln \frac{C(0)}{C(t)}
\]  

\( 2.2.2 \). Two-compartment model. In this model, the volume, \( V \) of body fluid is divided into two compartments with volume \( V_i \) and \( V_e \) represent the intracellular and extracellular volume, respectively. Urea is cleared by the kidneys and/or the dialyser in the extracellular compartment. Referring to Figure 2, the rate of change of the body fluid mass is described by a set of two differential equations.

\[
\frac{d(C_i(t), V_i)}{dt} = -X(C_i(t) - C_e(t)) + G
\]

\[
\frac{d(C_e(t), V_e)}{dt} = X(C_i(t) - C_e(t)) - K.C_e(t)
\]

where \( C_i(t) \) and \( C_e(t) \) is the urea concentration in the intracellular and extracellular compartment at time, \( t \) (mg/ml), respectively and \( X \) is the inter-compartmental clearance (ml/min).

The general solution for equation (4) is given as follows and solved using MATLAB software,

\[
C_i(t) = A_1 e^{\alpha_1 t} + B_1 e^{\alpha_2 t} + C_1
\]

\[
C_e(t) = A_2 e^{\alpha_1 t} + B_2 e^{\alpha_2 t} + C_2
\]

where \( A_1, A_2, B_1, B_2, C_1 \) and \( C_2 \) are constants. \( \alpha_1 \) and \( \alpha_2 \) are time constants.

\( 2.3 \). Simulations

In this simulation study, few assumptions were made. They are as follows: (i) the volume of urea distribution, \( V \) is assumed to be constant and \( V, V_i \) and \( V_e \) are estimated using equation (6) [9]. (ii) the residual renal clearance, \( K_r \) is approximately 0.001 which is equivalent to no urinary clearance and it is neglected in the calculation due to its small value compared to dialyser clearance [7]. (iii) inter-compartment clearance is assume to be 600ml/min [10] (iv) data such as body weight (BW), dialyser clearance (\( K_d \)), pre-dialysis urea concentration (\( C(0) \)), post-dialysis urea concentration (\( C(t=4hrs) \)), urea generation rate (\( G \)) and dialysis time (\( t_d \)) are from clinical data collected from the hospital. The simulated values were then compared with the clinical data. It is important to compare the models with the clinical data for validation purposes.

\[
V(l) = \frac{40}{70}BW(kg)
\]

\[
V_i = \frac{25}{40}, V
\]

\[
V_e = \frac{15}{40}, V
\]
3. Results and Discussion

Figure 3 shows the ratio of simulated values with the clinical data for both models. Ratio of simulated and clinical data of post-dialysis urea concentration simulated using two-compartment model were found slightly higher compared to ratio of those simulated using one-compartment model. Most of the simulated values for one-compartment model underestimate (<1.0 ratio) the clinical data. It also shows that the simulated values of two-compartment model are closer to the clinical data compared to the...
values simulated using one-compartment model. Apart from that, the ratio of simulated values of post-dialysis urea concentration for both kinetic models are also found to be increase linearly with patients’ body weight. The reduction in urea concentration are affected by the generation rate of urea. Larger patient have higher generation rate. Most of the simulated values had achieved the minimum target of urea reduction ratio (URR) ≥ 65%.

Figure 4 depicts the ratio of ocKt/V values derived from one compartment model and Kt/V calculated directly using the available clinical data. In the figure, most of ocKt/V values are found to be lower than the values of Kt/V. However, both calculation shows that they achieved the minimum target of Kt/V of at least 1.2. The SD of ocKt/V and Kt/V compared to the minimum target are 0.20 and 0.32. This shows that one-compartment model can be used to estimate the Kt/V value to determine the adequacy of a dialysis treatment.

4. Conclusion
The comparison of the values of post-dialysis urea concentration between one-compartment model and two-compartment model with the clinical data are presented. It is found that the ratios of post-dialysis urea concentration simulated using two-compartment model are higher compared to the ratios of post-dialysis urea concentration using one-compartment model. In addition, most values of post-dialysis urea concentration simulated using two-compartment model are much closer to the clinical data compared to values simulated using one-compartment model. Kt/V values calculated directly using clinical data are found to be higher than Kt/V values derived from one-compartment model.

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