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Mathematical Modeling and Simulation of the Kidney Hemodialysis

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Abstract
For an organism to survive, it needs to get rid of metabolic waste materials, as well as maintain proper concentrations of various necessary materials. As these materials are metabolized or broken down, certain waste products are produced, such as carbon dioxide, water, urea and related nitrogenous compounds, salts, and various minerals. If these metabolic waste products remain in the body, they rapidly change the body's homeostasis. To avoid this change in homeostasis, the body must get rid of (excrete) the waste products quickly and efficiently. In a healthy human being, kidney is the organ which maintains homeostasis thereby ensures the process of removal of these toxic wastes from the body. For a patient with severe loss of kidney function dialysis is the only means of preventing excessive fluid gain and accumulation of these toxic chemicals. Currently, the painstaking hemodialysis procedure is necessary for patients with kidney failure; where patients undergo frequent extensive treatments. In an effort to improve and reduce the duration of dialysis, in this work, a mathematical model of kidney hemodialysis procedure was developed in which the kidney was modeled using two-compartment model. The model was evaluated using MATLAB based on the clinical data obtained from sixteen (16) kidney patients in Aminu Kano Teaching hospital (AKTH), Kano State, Nigeria. The model was validated using the collected data by comparing goodness of fit of data collected to the model predictions. Hemodialysis adequacy was also investigated based on the results of the model to determine the best duration of dialysis. It was found that dialysis procedure twice per week with five hours per session is the optimum.

Keywords: Hemodialysis, Kidney, dialyser, diabetics, diseases, modeling

1.0 Introduction

For an organism to survive, it needs to get rid of metabolic waste materials, as well as maintain proper concentrations of various necessary materials. For example, human food consists of carbohydrates, fats, proteins, various salts, and water. As these materials are metabolized or broken down, certain waste products such as carbon dioxide, water, urea and related nitrogenous compounds, salts, and various minerals (Mark, 2008), are produced. To avoid this change in steady state, the body must get rid of the waste products quickly and efficiently. The kidneys are very important organs within the human body because they are essential to maintain the steady state condition of the body. Blood flow through the kidneys allow them to assist in the regulation of blood pressure, stimulate red blood cell production, maintain calcium levels in the body and regulate the composition of the blood by keeping the pH, concentration of various ions, and the volume of water constant. The kidneys filter wastes (urea, ammonia, salts, water and other toxic substances) from the blood stream in order to keep the blood clean and chemically balanced. If these metabolic waste products remain in the body, they rapidly change the body's homeostasis

or steady state thereby giving rise to diseases like diabetics, hypertension or any kidney related diseases.

Hemodialysis is blood purifying therapy in which the blood of a patient is pumped around a continuous circuit from an artery to a dialysis machine and then back to a vein. On reaching the dialysis machine, the blood is fed into a hollow-fibre dialyser, a small cylinder containing multitudes of minute hollow fibres with small pores. On the other side of these pores, in contraflow, is pumped an acetate- or bicarbonate-based fluid of prescribed composition known as the dialysate. In standard dialysis treatment the composition of the dialysate is maintained constant. As the blood traverses the dialyser, water and solutes (ions and nitrogenous products of normal metabolism) diffuse both ways across the porous membrane in accordance with concentration gradients and an applied hydraulic pressure. On reaching the end of the dialyzer, the blood is pumped back into the body. If continued indefinitely, and without pressure gradients, the blood concentrations would eventually equilibrate (osmotically) with those of the constant dialysate. In practice, dialysis sessions are time constrained, although equilibrium may be achieved for some solutes (Casino, *et al.,* 2004). Current hemodialysis procedure inconveniences patients by requiring frequent extensive treatments. In an effort to improve and reduce the duration of dialysis, a mathematical model is needed to monitor the behavior of a patient with different conditions. Hemodialyzer can easily be optimized using mathematical models to reduce the time needed by a patient to undergo dialysis.

2.0 Methodology

Clinical data was obtained from Aminu Kano Teaching Hospital (AKTH), Kano for sixteen (16) patients with End Stage Renal Disease (ERSD) for this study. Each patient undergoes dialysis for three sessions per week and this weekly data for each patient were considered in this study.

2.1 Model Development

When kidneys fail, dialysis is necessary to remove waste products such as urea from the blood. By itself, urea is only mildly toxic, but a high urea level means that the levels of many other waste products that are more harmful and not as easily measured are also building up. During dialysis the patient is regarded as composed of two fractional urea distribution volumes; the intracellular fluid (ICF) and the interstitial and intravasal fluid, both forming the extracellular fluid (ECF). The urea concentration within both of these aqueous distribution spaces of the body, for an End Stage Renal Disease (ESRD) patient is inhomogeneous during dialysis. This is due to strong concentration gradients generated by dialysis. Dialysis has only access to the ECF, because the patient is connected via the cannula positioned within his arterio-venous fistula or graft. Urea once removed by dialysis from extracellular space will be refilled by an osmotic gradient across the cell membrane. This is a non-instantaneous process. Typically, it takes 30 minutes to equilibrate 95% of an initial urea gradient over the cell membrane if the gradient is not perpetuated by further dialysis. This effect, usually referred as rebound, is the measurable trace of the delayed urea mass transfer across the cell membrane.

The Urea generating components is the liver, both the intra- and extracellular pool each with a given buffer volume and the urea eliminating processes; like a residual clearance of the native kidneys and the urea removal performed by the dialysis machine, Figure 1 illustrates this interaction. The liver excretes urea with a generation rate G to the ECF space of volume $Ve(t)$ and concentration $Ce(t)$. The extracellular volume interferes with the intracellular volume by the inter-compartment clearance $k_{i,c}$, driven by osmotic pressure and expressed as a fluid shift rate per concentration gradient. $k_{i,C}$ is reported to be in the order of 760-1000 ml/min (Schneditz, et al., 2001) and for the purpose of this work 800 ml/min has been selected. Some ESRD patients may have retained a fraction of residual clearance (Kr) and filtration (Qv) that is only affecting ECF. Dialysis as the life-preserving treatment of the ESRD patient is the only path a substantial amount of urea can leave the body via the extracellular space. Dialysis is not applied continuously and frequently interrupted by alarms, therefore $k_d(t)$, the dialysis clearance applied by dialysis is time dependent, as Qv(t)*Ce(t), the amount of urea extracted by convection. All these interactions of the different processes, overlaid by a time dependence of the variables linked to each other like clearance, volume and concentration, make the mathematical description sophisticated and the analytical mathematical solution extremely complicated if not impossible. The numerical approach with assistance of a computer is much more practical and has been chosen to integrate the equations.

The system can be described by the mass balance formulation assuming no particle can vanish or appear in a compartment without entering or leaving another. Using continuity equation of the form;

$$\begin{Bmatrix} Rate\ of\ accumulation \\ of\ solute\ in\ the\ system \end{Bmatrix} = \begin{Bmatrix} rate\ of\ solute \\ entering\ the\ system \end{Bmatrix} - \begin{Bmatrix} rate\ of\ solute \\ leaving\ the\ system \end{Bmatrix} + \begin{Bmatrix} rate\ of\ generation \\ of\ solute \end{Bmatrix} \quad (1)$$

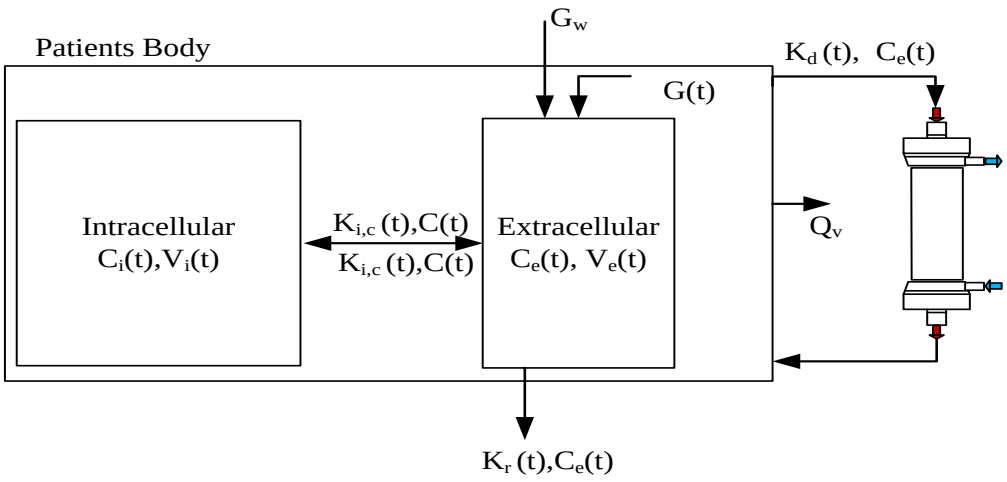

Fig. 1: A simplified representation of the participating constituents of the two pools urea kinetic model of ESRD patient.

The concentration of the solute in the extracellular and intracellular compartments is given by Eqns. (2) and (3) respectively:

$$\frac{dC_e}{dt} = \frac{G+k_{ic}(C_i(t)-C_e(t))-C_e(t)(K_d+K_r+\alpha(G_w-Q_v))}{\alpha V} \quad (2)$$

$$\frac{dC_i}{dt} = \frac{k_{ic}(C_e-C_i)-C_i(1-\alpha)(G_w-Q_v)}{(1-\alpha)V} \quad (3)$$

2.2 Model Parameters

The Parameters in Equations 2 and 3 can be classified as inputs, outputs, and constants as shown in Table 1.

S/N	Parameters	Inputs	Outputs	Constants	values
1	intracellular urea concentration (C_i)		✓		*
2	Extracellular urea concentration (C_e)		✓		*
3	urea generation rate (G)	✓			**
4	inter-compartment transfer coefficient (k_{ic})	✓			300ml/min
5	dialyzer clearance (k_d)	✓			150ml/min
6	kidney clearance (k_r)			✓	0
7	treatment time (t)	✓			
8	total Body water (V)	✓			**
9	ultrafiltration rate (Q_v)			✓	**
10	water intake rate (G_w)	✓			**
11	Body water proportionality constant (α)			✓	0.63

*: calculated by the model; **: obtained from the dialyzer

Model Assumption

- No particle can vanish or appear in a compartment without entering or leaving another.
- There is a perfect mixing in the two compartments
- The concentration of urea in the dialysed blood is zero
- Total body water (TBW) is the summation of both extracellular and intracellular compartments

A numerical tool (ODE45) of the MATLAB software was used to solve Equations (2) and (3). The solution converges in 5sec with 21 iterations. The unknown hypothetical functions: *Ce*(*t*) and *Ci*(*t*), should be correctly approximated. This general solution contains constants related to both the compartment and interval being modeled. Among these alternate forms, the most useful clinically predicts extracellular (blood) urea concentrations during dialysis, used by the curve fitting algorithm to estimate Kd, V, and Kdt/V on the basis of intradialytic Blood Urea Nitrogen (BUN).

3.0 Results and Discussion

The model developed in this study based on two pool model reported by Mahar, et al. (2008) as given in Equation (2) and (3). These models were used to predict solute (urea)

concentrations in a patient undergoing hemodialysis. The prediction from the model was validated using data collected from the hospital. Urea concentration of each patient versus time of dialysis were plotted and compared with the model results as shown in Figure 2. From these results, it can be seen that the model agrees with the clinical data.

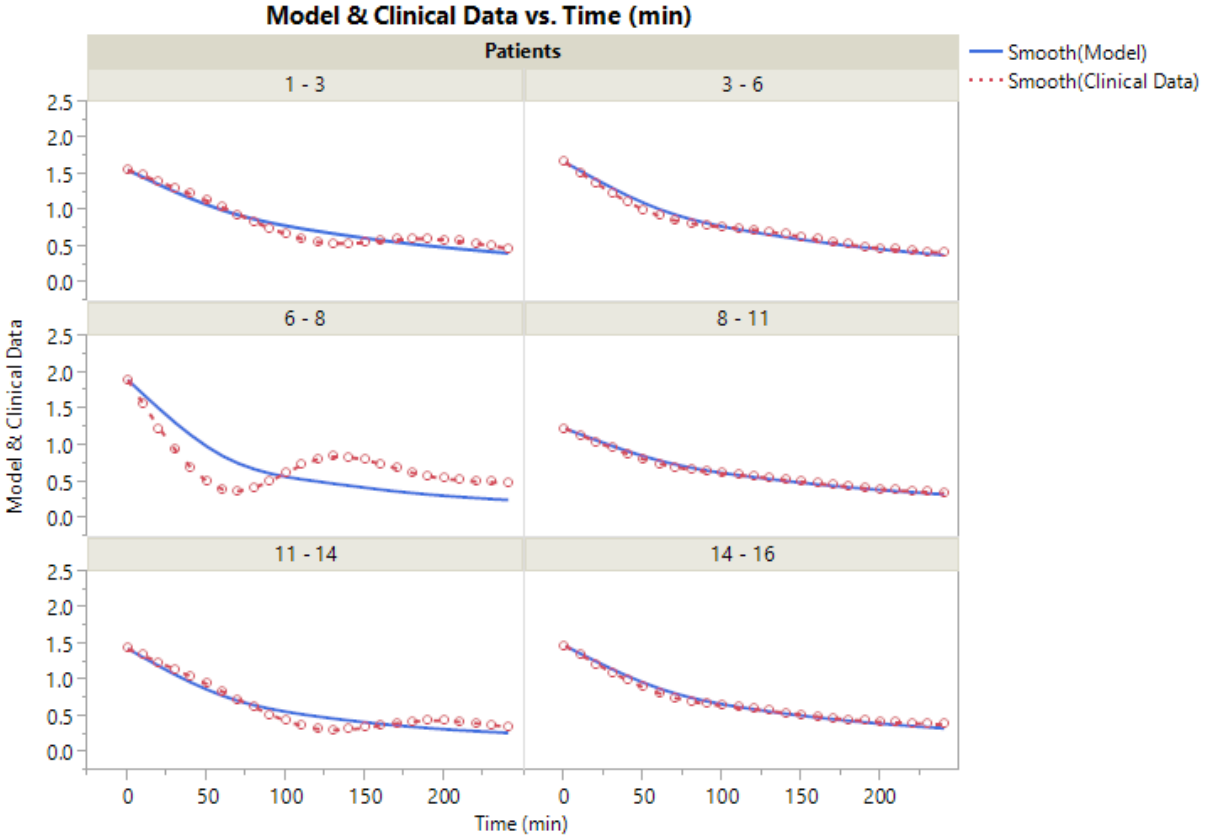

Fig. 2: Urea Concentration Profile of the 16 kidney Patients

3.1 Goodness of Fit

The goodness of the fit was also investigated; under 95% prediction bound level, *t-test* value of 0.3147 was obtained which is greater than 0.05 and standard error of 0.02 with mean difference of 0.0097. Since large t-value was obtained the model performance is satisfactory as evident from the correlation of the model with the data is (93%) which makes the model good enough to represent the clinical data.

3.2 Hemodialysis Dose and Adequacy

Two methods are generally used to assess dialysis adequacy, Urea Reduction Ratio (URR) and Kt/V. The model was used to obtain urea profile of a typical patient (patients 3 was considered in this case) for 2, 3, 4 and 5 times a week respectively. URR and kt/V of these profiles was then determined and the average is tabulated in Table 2.

Table 2: Weekly Hemodialysis Adequacy Based on kt/v and URR

S/N	Sessions	Time Schedule (h)	Kt/V	URR (%)
1	2 times/week	$2 \times 5h$	1.378481	69.14
2	3 times/week	$3 \times 5h$	1.384706	69.39
3	4 times/week	$4 \times 3h$	0.832434	50.49
4	5 times/week	$5 \times 2h$	0.487478	31.23

According to the National Institute of Diabetes and Digestive and Kidney Diseases (National Diabetes Data Group (US), 1995), patient's average URR should exceed 65 percent and average Kt/V value should be at least 1.2. From Table 4.1, it can be seen that 2-times/week and 3-times/week are the only schemes that agree with NIDDK guidelines. Even though 3-times/week has the highest URR, 2-times/week is considered the optimum because it required lesser time with slightly different kt/V and URR as compared to the 3-times/week.

4.0 Conclusion

In this study, mathematical model of the kidney hemodialysis was developed based on two- compartment model. The two-compartment model was simulated based on the clinical measurement for the kidney patients in Aminu Kano Teaching hospital, Kano (AKTH), and the parameters of the model were evaluated. The model was validated by comparison of the goodness of fit of the clinical data collected to the model predictions.
Finally, hemodialysis adequacy investigated based on the results of the model showed that the optimum frequency and duration of dialysis were twice per week with 5-hour sessions respectively.

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