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SHOULD THE LOPOT-PLOT BE USED IN DAILY PRACTICE TO OPTIMISE HEMODIALYSIS TREATMENT?

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ABSTRACT

The paper presents an application of the Lopot-plot, which compares the time-averaged concentration (TAC) and the time-averaged deviation (TAD) of the weekly dialysis cycle, to comprise the results of intensive computational study. The presented case is based on 420 one-week-cycle simulations to verify the consequences implied by the change of the treatments schedule from nonuniformly to uniformly distributed over the week. The concept of steady state is explained and utilized to obtain periodical runs of the urea concentration. The presented graphs encouragingly indicate the potential of such plots in presenting results of multivariable intensive computations that should be advisably performed during the planning process of hemodialysis treatment.

KEYWORDS: intermittent hemodialysis, hemodialisys modelling, hemodialysis adequacy, Lopot-plots

1. Introduction

In the hemodialysis treatment (HD) of patients with chronic renal failure, the kinetic modelling has already been considered a useful tool for several decades [1,2,3,4]. The kinetic approach is based on the assumption that interaction between the patient and the dialysis filter may be described with satisfactory accuracy when the first is represented by two mutually connected volumes [2]. Such volumes are called compartments and are referred to as internal and external, Vi and Ve, respectively. The marker solute, typically urea, reduces its concentration in the compartments in course of the treatment according to filter function, and increases during the interdialysis intervals, as a result of the metabolic processes. The production of urea is represented by generation rate, G, while the exchange rate of the solute is described by clearances: Kc – intercompartment clearance, and Kd – dialysis filter clearance. The arrangement of the two-compartment model is presented in Figure 1, the model equations are provided in Section 2.

The dialysis filter is active only at some specific periods of time, repeatedly during consecutive weeks according to a deliberated schedule. In contrast, the healthy subject has its renal function working all the time, thus the prescribed hemodialysis treatment is also called intermittent. Because of some side effects resulting from such feature [5,6,7] it proved reasonable to assess the efficiency of HD not only with the average level of urea concentration (time-averaged concentration, TAC) but also with deviations from the average value (time-averaged deviation, TAD) [5]. The weekly HD schedule is typically presented as a dot in the graph of the relationship between TAC and TAD, and such graph is called the Lopot-plot [8]. Such graphical form makes possible to compare and study several sets of parameters and different HD schedules in a simple, comprehensive way. In [6] several options were compared, including two possible schedules: a) the treatments starting at the same time on selected days of the week, b) the treatments distributed during the week uniformly. However, in spite of the fact that the plot was presented for some other comparative options, the result of the described change in the schedule was presented only in the form of the table, and only two cases were investigated. The changes in the HD schedule were also investigated in [7], but the Lopot-plot was not utilized, as it was later showed by Korohoda et al. [8]. Considering the publications mentioned above a gap has emerged. In this paper the relevant study is described and the obtained results suggest applying the Lopot-plots to plan a hemodialysis schedule and to assess adequacy of the HD series in the daily practice.

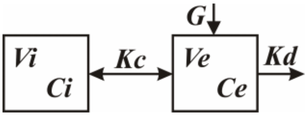

Figure 1. Two-compartment model consisting of mutually connected volumes ($\boldsymbol{Ve(t)}$ and $\boldsymbol{Vi}$) with relevant solute concentrations ($\boldsymbol{Ce(t)}$ and $\boldsymbol{Ci(t)}$), clearances ($\boldsymbol{Kc}$ and $\boldsymbol{Kd}$), and generation rate $\boldsymbol{G}$.

2. Model equations and plot parameters

The two-compartment model in its basic form is described by the following set of equations [2]:

$$\begin{aligned}
&Ve(t) \times \frac{dCe(t)}{dt} = -Kc \times \big(Ce(t) - Ci(t)\big) - Kd \times Ce(t) + G \\
&Vi \times \frac{dCi(t)}{dt} = Kc \times \big(Ce(t) - Ci(t)\big) \qquad (1) \\
&Ve(t) = Ve(0) - Q \times t
\end{aligned}$$

$$Ceq(t) = \frac{Ce(t) \times Ve(t) + Ci(t) \times Vi}{Ve(t) + Vi} \qquad (2)$$

where Q denotes the rate of volume reduction during treatment, which is compensated during the interdialysis period, when also $Kd = 0$. Ceq is time-dependent volume-averaged concentration, describing the overall patient saturation with urea. To avoid confusion, in equations (1) and (2) multiplication is marked explicitly with symbol ×.

The TAC and TAD parameters are defined by the following formulae [5]

$$TAC = \frac{1}{T}\int_0^T Ceq(t)dt \qquad (3)$$

$$TAD = \frac{1}{T}\int_0^T |Ceq(t) - TAC|dt \qquad (4)$$

3. Steady state approach

In the previously published paper [6,7] the week series had the same urea concentration at the beginning and at the end of the week cycle. In [7] the steady state approach was mentioned, which indicated that the considered cycles were obtained after some simulated weeks of transient cycles. In fact, as numerous test performed by the authors confirmed, realistic sets of parameters guarantee that after just few simulated weeks the cycle becomes periodic. Figure 2 shows examples of the concentration runs obtained for the same parameters of the model, but with different starting concentration value. In all graphs only $Ceq(t)$ is presented.

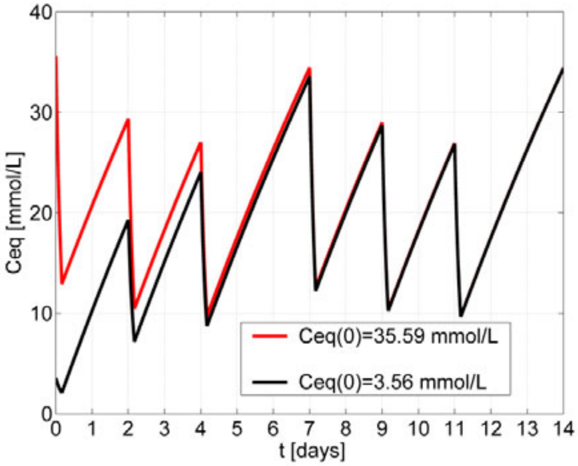

Figure 2. Example of the convergence property of the HD model, leading from different starting points to the steady state of the $\boldsymbol{Ceq(t)}$ run.

4. Experiment organization

To provide relevant generalization and show the suitability of the Lopot-plots, three schedules were selected for comparison, with 2, 3 and 6 HD treatments per week, either beginning at the same time of a day, which lead to nonuniform distribution, or distributed uniformly over all hours of a week, regardless of the daytime. The treatment time, td, was varied taking seven options: 1hr, 2hrs, 3hrs, 4hrs, 5hrs, 6hrs, and 7hrs, which covered wide range including some extreme possibilities. The remaining model parameters are presented in Table 1. Note that both the ultrafiltration rate, Q, and the relevant constant water income rate during interdialysis intervals, were computed from the assumed total water income during the whole week, ΔV.

Table 1. Parameters of the model used in the presented simulations.

Description	**Symbol**	**Value**	**Units**
Generation rate	G	7	mg/min
Intercompartment clearance	Kc	600	mL/min
Dialysis filter clearance	Kd	200	mL/min
Total weekly water income	ΔV	10	L
Water total volume*	V	35	L
External compartment volume*	Ve	$1/3V$	L
Internal compartment volume*	Vi	$2/3V$	L

*at the end of the last dialysis in a week cycle.

Each time the relevant run was obtained as the last after 10 week cycles to make sure that the steady state was reached.

5. Results

To indicate the differences between the uniform and nonuniform treatment distribution Figure 3 presents selected twelve comparisons of the $Ceq(t)$ runs, out of twenty one computed.

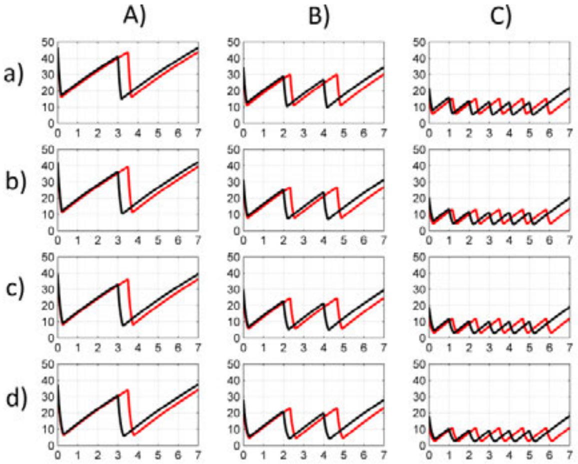

Figure 3. The week runs of $\boldsymbol{Ceq(t)}$ for several schedules: a) $\boldsymbol{td = 4}$hrs, b) $\boldsymbol{td = 5}$hrs, c) $\boldsymbol{td = 6}$hrs, d) $\boldsymbol{td = 7}$hrs; A) 2xHD per week, B) 3xHD per week, C) 6xHD per week. In each graph the vertical axis describes $\boldsymbol{Ceq(t)}$ in mmol/L and horizontal axis indicates consecutive days of a week. The comparison between uniform (red) and nonuniform (black) distribution of the treatments is provided.

Figure 4 contains the TAD/TAC graph, also called the Lopot-plot, in which it is clearly visible what consequences measured with use of these parameters should be expected when changing the schedule from nonuniform to uniform, or inversely.

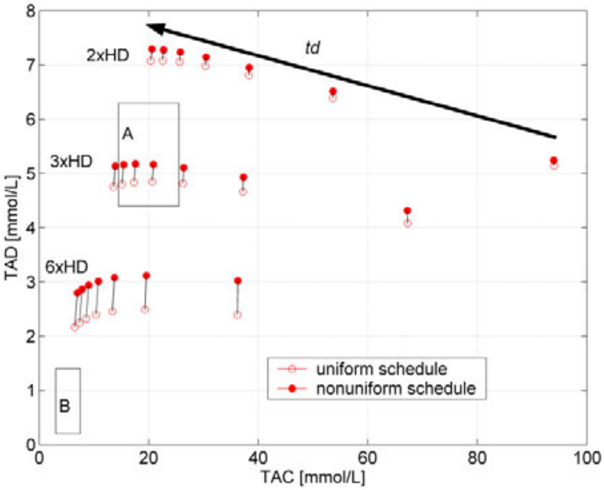

Figure 4. The TAD/TAC plot indicating the effect of changing the schedules of HD. The arrow in the upper part of the graph specifies the increasing direction of $\boldsymbol{td}$ values: 1hr, 2hrs, 3hrs, 4hrs, 5hrs, 6hrs, 7hrs. Rectangle A marks the area mentioned in [6] as expected HD region and rectangle B indicates the healthy person.

6. Concluding comments

Based on the plots presented in Figure 4 it is easy to observe that the change in the distribution profile affects mainly TAD, leaving TAC almost intact, and the differences are more noticeable for the schedules with the increased number of sessions per week, up to about 25% of its value for the so called daily HD cycle. The sensitivity to treatment time is rather negligible.

The presented results show convincingly that the TAD/TAC plots, in addition to other commonly used indexes [2,3,4], should be considered a useful tool, especially while comparing several options of the HD treatment schedule. The example with uniform vs. nonuniform distribution may be easily replaced with study of any other changes in any parameters of the model. The only challenge is the desired number of simulations, which in the presented case was $10 \times 7 \times 3 \times 2 = 420$ week cycles. It may seem time consuming, which is probably the main reason why the discussed plots have not become a standard tool in the dialysis unit practice. Nevertheless, one may think of a simple dedicated application offering such plots after entering only a few basic parameters. The results should be available within several seconds with the so common nowadays mobile devices that accept even more sophisticated software. The presented results were obtained with the University licensed Matlab Computing Software, ver. R2009a, after numerical computation of runs, without particular optimization of the program with respect to computing time. However, on the average PC (Intel CORE i5 3.0GHz) the overall computing time was less than 3 minutes. In practice, this is a time a renal nurse needs to take patient's weight and to make him/her ready to needle the fistula or to connect the double lumen catheter.

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