THE UREA KINETIC MODELLING IS THE KEYSTONE FOR CONDUCTING A RANDOMIZED CONTROLLED TRIAL ON INCREMENTAL HAEMODIALYSIS

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The Residual Kidney Function

The majority of dialysis patients are currently treated with a fixed dose thrice-weekly haemodialysis (HD) (3HD/wk) regimen irrespective of whether they are starting dialysis therapy (incident) or have been receiving dialysis for some time (prevalent) and without consideration for their residual renal function (RKF). The RKF provides effective and naturally continuous clearance of both small and middle molecules; is associated with better patient survival and greater health-related quality of life; plays a major role in effective phosphorus excretion, and endogenous vitamin D and erythropoietin production. While the RKF and urine output do not measure the same physiologic quantities – the former is a clearance while the latter is just a fluid volume – they are closely related **(Figure 1)** (1). Preservation of the RKF requires a careful approach, including regular monitoring, avoidance of nephrotoxins, gentle control of blood pressure to avoid intradialytic hypotension, and an individualized dialysis prescription including the consideration of incremental HD.

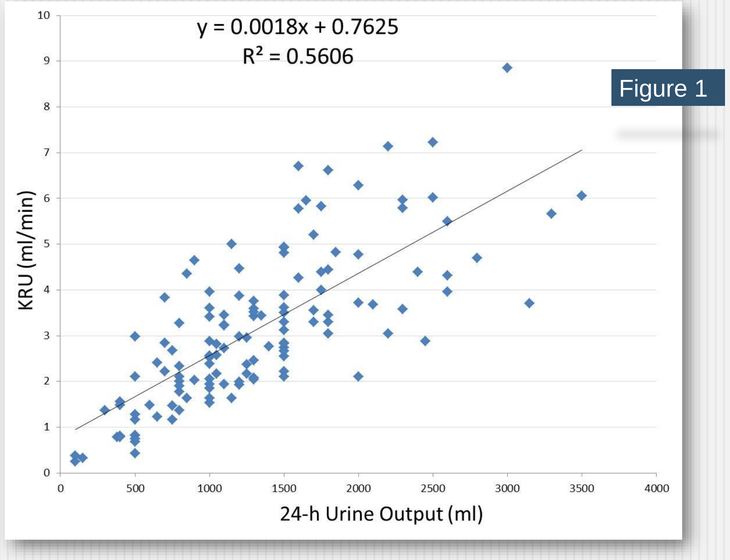

Figure 1

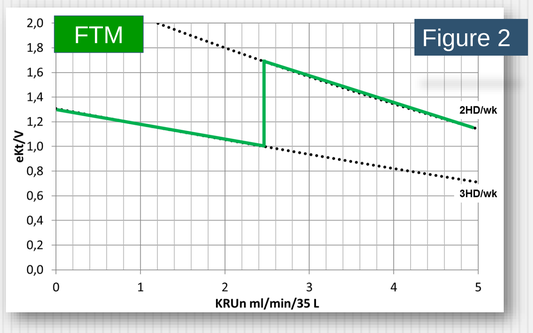

Figure 2

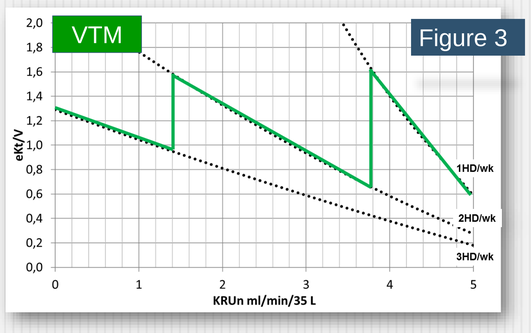

Figure 3

Table 1	Target EKRU = 12	Target stdKt/V = 2.3	Target EKRU = 12 - KRU
3HD/wk	$y = 0.0018x^2 - 0.1244x + 1.2979$ ($0 \le KRU \le 5.0$)	$y = 0.0145x^2 - 0.2549x + 1.2496$ ($0 \le KRU \le 5.0$)	$y = 0.0068x^2 - 0.2514x + 1.2979$ ($0 \le KRU \le 5.0$)
2HD/wk	$y = 0.0073x^2 - 0.2665x + 2.31$ ($1.5 \le KRU \le 5.0$)	$y = 0.0776x^2 - 0.9091x + 3.157$ ($1.5 \le KRU \le 5.0$)	$y = 0.0221x^2 - 0.4979x + 2.24$ ($1.0 \le KRU \le 5.0$)
1HD/wk	$y = 0.2739x^2 - 4.9239x + 23.473$ ($7.5 \le KRU \le 8.0$)	$y = 0.1755x^2 - 2.7563x + 10.999$ ($5.0 \le KRU \le 7.0$)	$y = 0.1532x^2 - 2.2250x + 7.9006$ ($4.0 \le KRU \le 5.5$)

A Paradigm Shift In Incremental HD Prescription

A recent paper by Casino and Basile suggested a variable target model (VTM), which gives more clinical weight to the RKF and allows less frequent HD treatments at lower RKF as opposed to the FTM, based on the wrong concept of the clinical equivalence between KRU and Kd (2).
In contrast to the FTM, they proposed that the total EKR target varies as an inverse function of KRU, from a maximum value in anuria to a minimum value at KRU levels not yet requiring dialysis.

variable target model (VTM): total EKR = 12 - KRU

By using the "Solute-Solver" software, Casino and Basile computed eKt/V values to be prescribed to attain either the fixed or the variable target total EKR for KRU varying from 0 to 5.0 ml/min/1.73 m2, and for 1, 2, and 3 HD sessions per week **(Figures 2 and 3 and Table 1)**.
The new criteria suggest that, at least in relatively healthy patients, HD can be started at KRU~ 5 ml/min/35 L on a 1HD/w schedule, that can be maintained until KRU falls below 4 ml/min/35 L, when it should be replaced by a 2HD/w schedule, that, in turn, could be maintained until KRU falls below 2 ml/min/35 L, when the 3HD/w schedule becomes really necessary (2).

Application Of Urea Kinetic Modelling To Incremental HD

The 3HD/wk regimen has been assumed, until recently, almost as a dogma in the dialysis community. Incredibly, the 3HD/wk schedule has been widely accepted worldwide without ever undergoing any randomized controlled trial (RCT) to examine whether less frequent HD treatments would be inadequate or harmful.
The general principle for calculating the amount of dialysis required to compensate for RKF reduction is based on the constancy of a given target value for the total (dialytic + renal) equivalent continuous clearance (total EKR) over a week period: i.e. at any point in time the sum of renal urea clearance (KRU) and the component of the equivalent continuous clearance provided by the intermittent dialysis clearance (EKRd), should achieve the fixed total EKR target.
The current guidelines advise to achieve a total EKR (EKRd + KRU) at least equal to the adequacy value corresponding to an equilibrated Kt/V (eKt/V) of 1.2 x 3 times a week = 12 ml/min/35 L.

fixed target model (FTM): total EKR = EKRd + KRU = 12 ml/min/35 L

However, fixing the total EKR necessarily implies perfect equivalence of its renal (KRU) and dialytic (EKRd) components. This assumption is wrong because KRU has a much greater clinical weight than dialytic clearance (Kd). The equivalence between KRU and EKRd, correctly assumed by the urea kinetic models (UKM), only means that each ml/min of EKRd clears the urea from the blood just as one ml/min of KRU does. By no means should such kinetic equivalence imply that 1 ml/min of Kd is clinically equivalent to 1 ml/min of KRU provided by the native kidneys. The latter, in addition to a wider spectrum of solutes cleared, exert clinically important endocrinological and metabolic effects.

Conclusions

A paradigm shift from FTM to VTM in the prescription of incremental HD is proposed: actually, VTM would allow less frequent treatments at lower KRU, with important clinical and economic implications. This approach is very probably safe, being in agreement with many observational literature data, as well as with the recent K/DOQI endorsement of the addition of KRU at 100% to the dialysis stdKt/V (2). However, it needs to be confirmed by RCTs. The UKM is the keystone for conducting such studies.

References

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