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Adequacy of hemodialysis

The term adequacy comes from the Latin *ad-acquantum* which means "equal to" or "similar to". The concept adequate includes blood purification, maintenance of electrolyte fluid, and acid-base equilibrium. Dialysis can completely reverse the retention of some small molecules, electrolytes (K, Na, Mg), water and acid-base, and has no effect on anemia, hypertension, arteriosclerosis, cardiomyopathies, malnutrition bleeding or partial effect on Ca-P balances. Other therapeutic interventions are necessary to optimally treat the uremic syndromes.

Narrow, adequate to dialysis procedure should be taken into consideration. Substances that are responsible for uremic symptoms and thus are useful as markers of uremic status are presented in Table 1. None of them is the sole cause of uremic status (15). However, the absence of any reliable and universally acceptable marker has prevented the standardization of dialysis therapy until urea was elected as a marker of a patient outcome (13). This choice has been ratified by National Cooperative Dialysis Study (12). Urea kinetic modelling is probably the most objective way of measuring the

Table 1. Uremic toxins

Small water-soluble compounds	Large (middle) molecules	Protein-bound compounds
Guanidines	Advanced glycosylation products	Indoles (3-carboxyl-4-methyl-5-propyl-2-furano-propionic acid)
Asymmetric dimethylarginine	Oxidation products peptides	Hipuric acid
Creatinine	β_2 microglobulin	Homocysteine
Purines	Complement factor D	Indoxyl sulfate
Phosphorus	Parathyroid hormone	p-Cresol
Urea	Cystolin C, clara cell protein leptin	Polyamines

efficiency of dialysis but we must remember that there are numerous alterations in ESRD which cannot be measured by urea kinetic modelling.

Urea kinetic modelling during dialysis and interdialysis may be described by a single or double-pool model (Fig. 1) (5, 7, 12, 14).

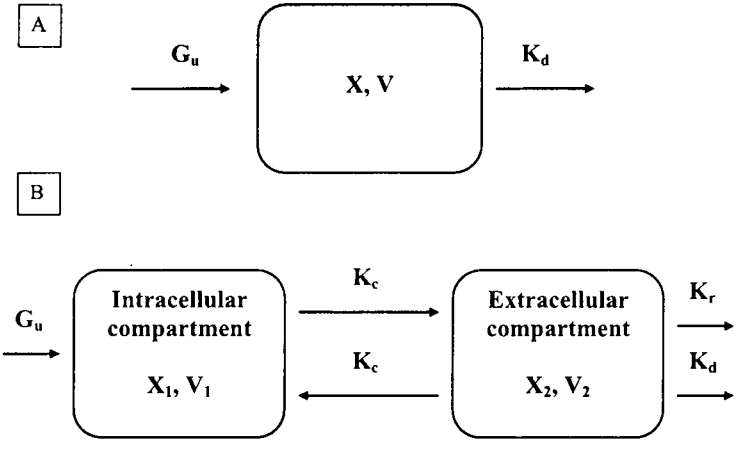

Fig. 1. Diagrammatic representation of single-pool (A) and double pool (B) models of urea kinetics. Abbreviations: G_u – urea production rate; X – urea body mass; V – urea diffusion volume; X_1 – intracellular urea compartment; V_1 – intracellular urea diffusion volume; X_2 – extracellular urea compartment; V_2 – extracellular urea diffusion volume; K_c – intercompartment urea transfer coefficient; K_d – dialyzer clearance; K_r – residual renal clearance

In the single-pool urea model, the amount of body urea is related to urea generation (G_u) and urea removal (K_d). In the single-pool model, the dynamic mass balance is expressed by the following equation:

$$\frac{dx}{dt} = \frac{K_d}{V} \text{ x } X + G_u$$

K_d summarizes two different values: the dialyzer clearance and the residual urea clearance in the interdialysis period, V – urea diffusion volume, X – body urea.

Furthermore, the single-pool concept may be even used to measure the fractional clearance of urea distribution volume. (K_d x X/V), thus providing a measure of the individualized dialysis dose.

The mathematical equations of the two-compartment model are as follows:

$$X_1 (t) = K_{eff}\, C_1 (t) + K_c [\, C_2 (t) - C_1 (t)] + G \quad \text{(Eq. 1)}$$

$$X_2 (t) = -K_c [\, C_2(t) - C_1(t)] \quad \text{(Eq. 2)}$$

Where, X_1 (t) and X_2 (t) are compartment masses of urea (mmol/L), C_1 (t) = X(t) V_1 (t) and C_2 (t) =X_2 (t) V_2 (t) represent urea concentration (mmol/L), K_c (ml/min) is the intercompartmental urea mass transfer coefficient, K_{eff} (ml/min) is the dialyser clearance.

The Kt/V is calculated by the formula:

$$Kt/V = -L_n (R - 0.008 \times t) + (4 - 3.5 \times R) \times UF/W$$

in which, L_n is the natural logarithm; R is the post-dialysis BUN ÷ pre-dialysis BUN; t is the dialysis session length in hours; UF is the ultrafiltration volume in liters: and W is the patient's post-dialysis weight in kilograms.

A practical alternative to Kt/V is the urea reduction ratio (URR) – the percentage of urea decline during single treatment. It is obtained by using the following equation:

$$URR = \frac{Co \quad Ct}{Co} \times 100\%$$

Co and Ct represent predialysis and postdialysis plasma urea nitrogen levels in mg/L, respectively.

In contrast to Kt/V for urea, it is a better measure of dialysis adequacy, the calculation of URR is simple (9, 11). URR does not take the effects of ultrafiltration and interdialytic urea generation (2, 4). More precise in the estimation of dialysis dose is modified URR (mURR), which corrects the effects of ultrafiltration and ultradialytic urea generation.

The equation of mURR is as follows:

$$mURR = [1 - (\frac{R}{1 \quad 2xUF/BW}) + 0.01 \times t] \times 100\%$$

R – postdialysis plasma urea nitrogen (PUN) to predialysis PUN, UF – ultrafiltration volume in liters, BW – postdialysis body weight in kilograms, t – dialysis session length in hours.

The URR has been used to assess mortality rate in a large database (10). It is a very inexpensive parameter to obtain, a maximum number of patients for whom some measure of dialysis dose is available.

Approximately 90% of waste catabolite nitrogen accumulating in body water in uremia is urea. Urea nitrogen generation rate can be readily calculated from urea kinetic modelling (8) and nitrogen balance studies have shown to be quantitatively related to the net rate of protein catabolized to waste nitrogen (1, 3, 6).

A useful approximation equation to estimate PCR is presented as follows:

$$PCR\ (g/d) = 6.49 \times UNA + 0.294 \times V$$

UNA – urea nitrogen appearance ("urea production"), UNA (g/dl) – urinary urea N + dialysate urea N + A body urea N

$$UNA\ (g/dl) = (V_d \times DUN + V_U \times UNN)/\ t$$

V_d – dialysate volume, V_u – urine volume, DUN – dialysate urea N (g/l), UUN – urine urea N (g/l).

PNA = PCR (g/d) + protein losses

PNA – protein equivalent of total nitrogen appearance, PNA (g/d) = 10.76 x (0.69 x UNA + 1.46).

The analysis with BUN, NPCR and Kt/V showed that all patients with Kt/V<0.8 had a high probability of failure, irrespective of BUN or NPCR (Fig. 2) (6). The patient's social and professional life may benefit from effective integration in the renal replacement therapy programs.

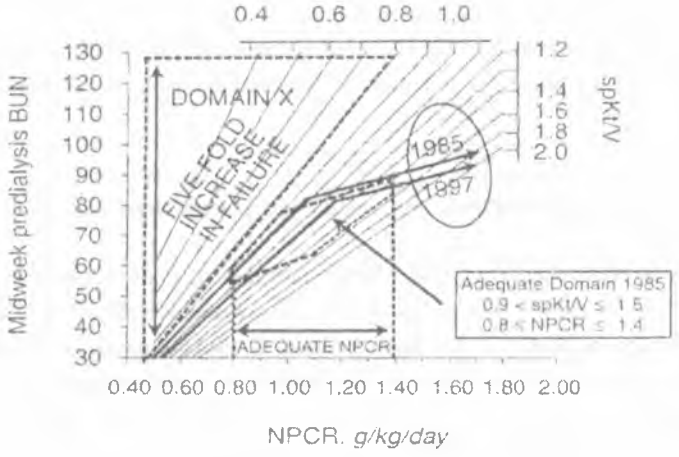

Fig. 2. Adequate dialysis defined by Kt/V and studied in the National Cooperative Dialysis Study (NCDS) ranges from 0.9 to 1.5 depending on the normalized protein catabolic rate (NPCR). [F. A. Gotch, Kidney Int., 76, S3-S18] 2000

In evaluation of the targets for therapy, the complete approach would require the assessment of three major points, as reported in Figure 3. The concentration of urea nitrogen will therefore be the reflection of protein breakdown and dialysis efficiency.

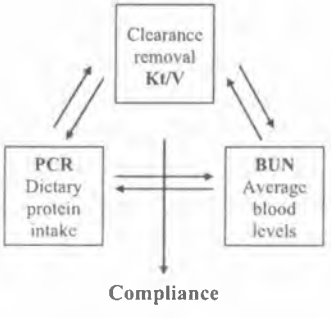

Fig. 3. Overall approach to treatment targets

Although some of the equations reviewed previously in this article serve a very useful purpose in both clinical therapy and research, sometimes, they violate a fundamental law of science that "everything should be made as simple as possible, but not simpler" (Albert Einstein, Readers Digest, October 1977).

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SUMMARY

The concept adequate includes blood purification, maintenance of electrolyte fluid, and acid-base equilibrium. Dialysis can completely reverse the retention of some small molecules, electrolytes (K, Na, Mg), water and acid-base, and has no effect on anemia, hypertension, arteriosclerosis, cardiomyopathies, malnutrition, bleeding, or partial effect on Ca-P balances. Other therapeutic interventions are necessary to optimally treat the uremic syndromes. Urea kinetic modelling is probably the most objective way of measuring the efficiency of dialysis but we must remember that there are numerous alterations in ESRD which cannot be measured by urea kinetic modelling.

Adekwatność hemodializy

Pojęcie adekwatności zawiera oczyszczanie krwi, utrzymanie równowagi elektrolitowej, wodnej i kwasowo-zasadowej. Dializa może całkowicie odwrócić retencję niektórych małych cząstek, elektrolitów, wody i zaburzeń kwasowo-zasadowych, lecz nie ma wpływu na niedokrwistość, nadciśnienie, miażdżycę, kardiomiopatię, niedożywienie oraz wywiera częściowy wpływ na gospodarkę Ca-P. Inne terapeutyczne postępowania są konieczne, aby optymalnie leczyć zespół mocznicowy. Modelowanie kinetyczne mocznika jest prawdopodobnie najbardziej obiektywnym sposobem pomiaru wydajności dializy, lecz musimy pamiętać, że istnieją liczne zmiany w schyłkowej niewydolności nerek, które nie mogą być mierzone za pomocą kinetyki mocznika.