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Kt/V A MEASURE FOR QUALITY CONTROL OF HAEMODIALYSIS THERAPY: HOW VALID IS IT?

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A b s t r a c t: Since the beginning of maintenance haemodialysis many attempts have been made to quantify this kind of renal replacement therapy. The most widely used methods are urea kinetic models and simple approximation formulae based on measured data of the individual patients. The most common term of dialysis dose is Kt/V. The errors of data put into the calculations are transferred to the result. Analysis of the error of the calculated result depending on the errors of the primary data using Gauss' law of progression of errors reveals errors of the calculated Kt/V between 7.7% and 18%. It is concluded that comparison of different groups of dialysis patients by means of Kt/V should only be done using one method with the least error.

Key words: maintenance haemodialysis, quality, renal replacement therapy, Kt/V.

Since the beginning of extracorporeal dialysis therapy it has been a problem to evaluate how much of this kind of therapy is necessary to keep an individual patient in acceptable health. On the other hand this time-consuming treatment should be as short as possible and patients are always asking if artificial kidney therapy could not be shortened.

During the 1960s dialysis therapy was quantified almost empirically by the time and frequency of treatment, the available blood flow, and by laboratory data indicating a decrease of those substances which are normally excreted by the kidneys such as urea, creatinine, potassium and phosphate. These substances have been denominated as uraemic toxins [12].

But already at this time it was clear that the patients tolerated well elevated levels of urea and creatinine even if they could not be reduced to

normal values at the end of one treatment. Moreover it could be observed that patients with higher levels of creatinine were in a better clinical condition than patients with low levels of creatinine. In contrast to the pre-dialysis stadium of chronic renal failure creatinine concentration was no more a measure of uraemic intoxication of dialysis patients [3]. Therefore many physicians were watching for other parameters of adequate dialysis therapy [2].

Since 1970 many attempts have been made to quantify dialysis therapy in a more individual way independent of actual laboratory data. It was Kopp who in 1971 proposed the litre/kilogramme concept, which meant that as many litres of blood should be cleansed during one dialysis session as correspond to the body weight of the patient [7]. This concept took into account that patients with higher body weight needed a higher dose of treatment than patients with low body weight. It also indicated that adequate therapy is not related to a certain serum concentration of a uraemic toxin but to a definite amount of fluid per treatment, which has to be cleared (litres/session).

Also in 1971 Babb proposed the square-metre/hour hypothesis [1] when looking to the clearance of small uraemic toxins and higher molecular weight uraemic toxins in different kinds of dialyzer membranes. He observed that patients were in a better clinical condition when clearance of higher molecular weight substances, so-called "middle-molecules", was increased. Clearance of these substances was more dependent on the membrane area (square metres) and the duration (hours) of treatment than on the blood flow through the dialyzer. In this concept adequate dialysis was defined as the relation between the estimated weekly volume of middle-molecules cleared by dialysis and glomerular filtration rate versus the estimated weekly volume cleared to prevent uraemic neuropathy. This dialysis index for the first time defined adequate dialysis as clearance of some kind of a uraemic toxin in relation to the individual need for such clearance. At that time high-flux membranes for better removal of so-called middle-molecules were not yet available.

Clearance in nephrology is used as a term to measure glomerular filtration rate in terms of inulin clearance or creatinine clearance. In general, clearance describes the amount of fluid which is completely cleared from a certain substance within a definite period of time. When cleaning fluids like blood, it means removing a certain amount of dirty fluid (ultrafiltrate) and adding the same amount of clean fluid within a definite period of time. That is why clearance is mathematically termed ml/min. In haemofiltration, clearance of a solute is dependent on the amount of filtrate replaced by substitution fluid within a certain period of time. In haemodialysis, where mass exchange is driven by differences of concentration, clearance indicates that minor part of

blood flow which is completely cleared from a solute. Clearance is independent of the blood concentration of a uraemic toxin. It only describes the part of the blood flow that is cleaned of uraemic toxins.

When looking at the metabolism of urea in 1983, Lowrie and co-workers found that dialysis adequacy is related to Kt/V, which is the exponent of the non-linear curve describing the decrease of urea concentration during one dialysis session [8].

In this term K is the urea clearance which has been given to the patient, t is duration of one dialysis session and V is the urea distribution volume of the individual patient. In this term urea clearance (K) is the quantity of blood cleansing which has to be applied for a certain time (t) and is related to the volume where urea is distributed in the body. Consequently Kt/V was called the dose of dialysis therapy. Although it is well known that urea, even in high concentration, has almost no specific toxic effects on the tissue, this compound has several advantages over all the other uremic toxins: urea is evenly distributed in body water, it is chemically inert, not bound to other substances, highly permeable, and the end product of protein metabolism. Thus it is representative of what is done in dialysis therapy: removing water-soluble substances from blood by means of clearance, and it can be easily described numerically using mathematical models. Unfortunately, urea clearance is only representative of low molecular weight uraemic toxins.

Determination of Kt/V was primarily done using one or two kinetic compartment models in which urea concentration in the fluid compartments, mainly the extracellular and the intracellular fluid compartment, urea generation and dialytic and non-dialytic urea removal is calculated.

There are two kinds of urea models: the mid-week dialysis cycle model [5] comprising the time from mid-week onset of dialysis where blood urea concentration has to be measured at the beginning of the mid-week dialysis session, at the end of this dialysis session and at the beginning of the next dialysis (Gotch); the other model comprises the weekly cycle [11] where blood samples may be taken at the beginning and at the end of any dialysis session during the week and optionally at any other dialysis session. (Stiller/Mann). The Gotch model is only valid for a three times per week dialysis regimen. The Stiller/Mann model is applicable for any duration and frequency of dialysis therapy during one week. It also includes residual renal function (residual urea clearance of the patients' kidneys).

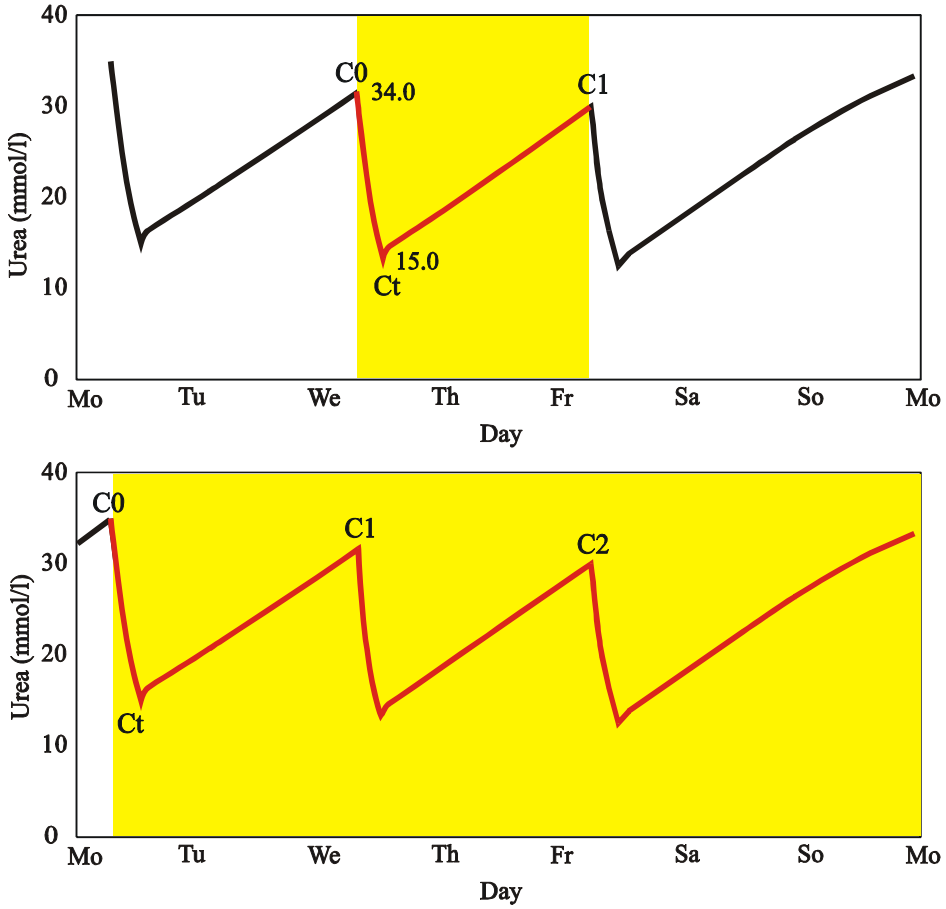

Figure 1 – The two mathematical models for urea kinetics. Upper curve the mid-week model (Gotch), lower curve the weekly model (Stiller/Mann)

Слика 1 – Два математички модели на кинетиката на уреата. Горната крива одговара на полунеделниот модел (на Gotch), а долната крива на неделниот модел (на Stiller/Mann)

Because model calculation needs some mathematical effort, since 1989 several simplified approximation formulae have been established for clinical practice in order to calculate Kt/V from pre- and post-dialysis urea concentration, duration of treatment and urea distribution volume [4]. The most widely used formula is that of Daugirdas. This formula was modified in 1993 and 1995.

Daugirdas I: (1989)

$$Kt/V = - \ln (R - 0.008 * t) - f * UF/V)$$

Daugirdas II single pool: (1993)

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

Daugirdas III equilibrated: (1995)

$$eKt/V = spKt/V - 0.6 * spKt/V / t + 0.03$$

Where

R = the relation of pre (Co)- post (Ct) urea concentration Ct/Co

UF = the amount of ultrafiltrate

V = urea distribution volume

W = body weight

t = duration of one dialysis session

During the last 20 years of measuring the dose of haemodialysis by means of Kt/V there has been a never-ending discussion about the target value of Kt/V which has to be obtained. Whereas initially a Kt/V of 1.0 was recommended, most guidelines today recommend a Kt/V value of 1.2 – 1.4. Additionally there are considerable differences in the result when Kt/V is calculated by different models or approximation formulae [6, 10].

The main problems of measuring Kt/V are the sampling of blood in a way that is independent from blood recirculation and the day of dialysis during one week. Another problem is valuable data of time (t) and urea distribution volume (V).

A recent progress for measurement of K is on-line clearance measurement during dialysis using intermittent measurement of sodium clearance [9]. There is still a considerable problem of measurement of V. There are many different approximation formulae for estimating V depending on body-weight, age, gender and fat content. Bio-impedance methods are also used. But all these methods used today do not provide a sufficiently accurate urea distribution volume to calculate Kt/V [13].

When Kt/V is generally accepted as a valuable tool for quality control of dialysis therapy we should also be aware of the accuracy or the error of this kind of index. Since Kt/V is composed of different parameters which have to be measured separately, such as urea concentration, time, body-weight, urea distribution volume and clearance, it must be taken into consideration that the errors of the components which Kt/V is based on may accumulate. The error in the result of the calculation is possibly much greater than the error in each component.

In order to evaluate the standard error of Kt/V, different methods of calculation have been examined on the basis of Gauss's law of progression of errors. In this analysis only the errors of laboratory data are considered. Errors in wrong sampling of blood and wrong data have not been taken into consideration.

The following equations for the calculation of Kt/V have been compared:

- Simple formula Kt/V with K from the dialyzer data sheet, t as indicated by the physician and V with the formula body-weight × 0.58
- Approximation formula of Daugirdas II
- Formal urea kinetics (Stiller/Mann)
- On-line clearance measurement

The following figures show the results of this calculation.

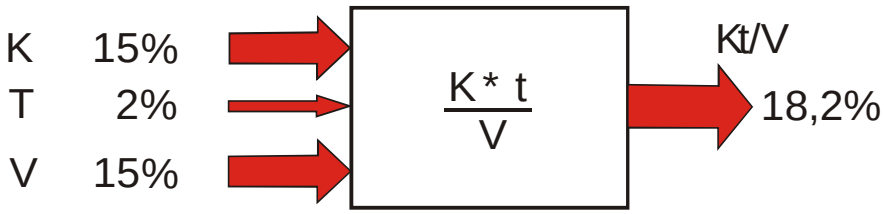

Figure 2 – Errors in the simple calculation: K = dialyzer clearance, t = prescribed time, V = body weight × 0.58

Слика 2 – Грешки во пресметувањето: K = клиренс на мембраната, т = препишаното време, B = телесната тежина × 0.58

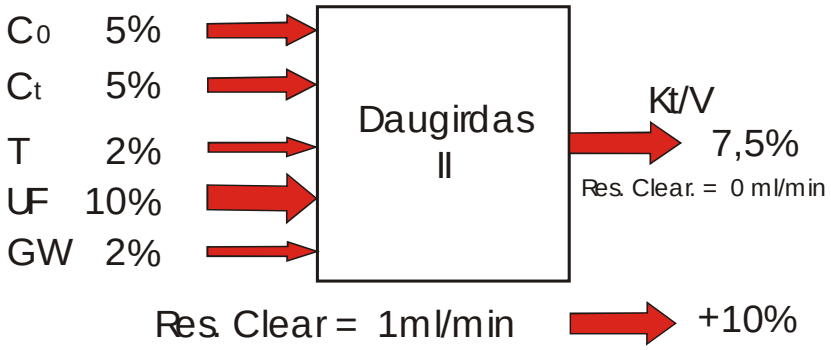

Figure 3 – Errors in Daugirdas II formula

Слика 3 – Грешки во формулата на Daugirdas II

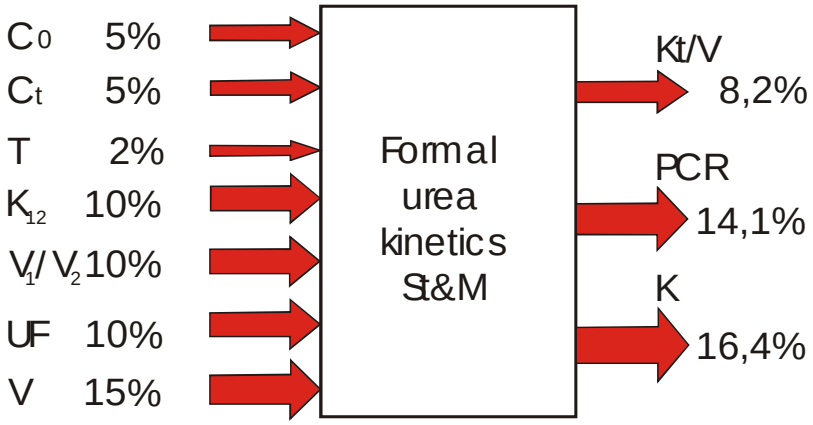

Figure 4 – Errors in the Stiller/Mann model. Errors of input are mainly transmitted to PCR and delivered clearance K

Слика 4 – Грешки во Stiller/Mann моделот. Грешките на влезот главно се пренесуваат при одредувањето на PCR и клиренсот на K

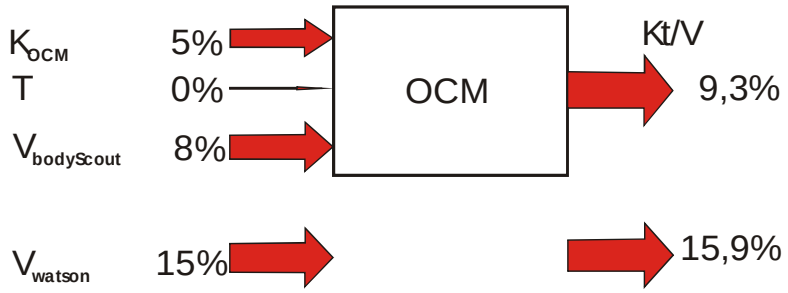

Figure 5 – Errors in online-clearance measurement. Error of Kt/V mainly depends on measurement of V (Bioimpedance or Watson-formula

Слика 5 – Грешки во мерењето на online-клиренсот. Грешките во Кт/В главно зависат од мерењето на В (Биоимпенданса или формулата на Watson)

On the left side of the figures there are the errors going into the calculation, on the right side there is the error in the result. As can be seen, the error of the different methods ranges between 7.5% (Daugirdas) and 18.3% (prescribed clearance). When the residual kidney function of the patient is neglected it should be mentioned that each ml/min of

residual kidney function increases the error by about 10%. Only in the kinetic model is residual kidney function included.

Discussion and conclusion

For quality control of extracorporeal artificial kidney therapy, a parameter for measuring the dose of dialysis is needed.

Theoretically Kt/V is a reasonable method to evaluate the dose of dialysis given to an individual patient. There are many methods of measuring Kt/V depending on different data put into the calculation. The errors of these in-put data are transmitted to the result of the calculation.

As evaluated using the law of error progression, the error of calculation of Kt/V, using different methods, has to be considered to be at least +/- 7.5% and up to +/- 18% depending on the method of calculation used.

In order to minimize the errors in calculating Kt/V from these findings it can be concluded that in comparing different groups of patients, only one method with known standard error should be used.

According to our results formal urea kinetics with online-clearance and standardized measurement of V including residual kidney function is the best method to obtain valuable data on urea metabolism.

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Р е з и м е

МЕРЕЊЕ НА Кт/В ЗА ОДРЕДУВАЊЕ НА КВАЛИТЕТОТ НА ХЕМОДИЈАЛИЗНАТА ТЕРАПИЈА: КОЛКАВА Е НЕГОВАТА ВАЛИДНОСТ

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Од стартот на хроничната хемодијализна програма, направени се повеќе обиди со цел да се квантифицира овој вид на бубрежно заместителна терапија. Најчесто употребувани методи се моделите на кинетика на уреата и одредување на параметрите за секоја индивидуа посебно. Најчесто употребуван термин за дозата на дијализа е Кт/В. Вредностите на параметрите користени во формулата имаат влијание на резултатот. Анализата на грешките при калкулирање со помош на формулата на Кт/В, пресметано со Гау-

совиот закон за прогресија на грешките, изнесува од 7.7% до 18%. Споредувањето на различни групи на пациенти на дијализа според средните вредности на Kt/B, треба да биде спроведено со формулата со најмалку грешки.

Клучни зборови: одржувачка хемодијализа, квалитет, бубрежна заместителна терапија, Kt/V.

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