# Assessment of the Different Methods to Predict Equilibrated Kt/V in Pediatric Hemodialysis

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***Objectives:*** *To determine the degree of urea rebound in children on hemodialysis and compare the different calculation models for Kt/V.*

***Material and Method:*** *The present study was performed in 50 hemodialysis sessions of 5 pediatric patients, 2 males and 3 females, aged 5-18 years, who had received hemodialysis for 7-48 months. Blood urea samples were obtained at the beginning, 70 minutes intradialysis, the end and every 10 minutes for 1 hour post- dialysis. The compared 6 different models of Kt/V were single pool, Daugirdas, equilibrated, rate equation, Maduell and Smye method.*

***Results:*** *Urea rebound was found to be completed at least 60 minutes post- dialysis and mean percentage value was 30.68 ± 9.663.Mean value of equilibrated Kt/V was 1.442 ± 0.259 while that of single-pool Kt/V calculated by lnC1/C2 was 1.705 ± 0.252 leading to overestimation of Kt/V by 0.265 ± 0.075. Mean value calculated by Daugirdas method was 2.083 ± 0.336. Mean values obtained by rate equation, Maduell and Smye methods were 1.485 ± 0.209, 1.442 ± 0.209 and 1.379 ± 0.343 which differed from equilibrated Kt/V by 0.086 ± 0.058 (p = 0.002), 0.069 ± 0.063 (p = 0.967) and 0.132 ± 0.132 (p = 0.015), respectively.*

***Conclusion:*** *Urea rebound in pediatric patients is completed at least 60 minutes after cessasion of hemodialysis. Kt/V calculated from single-pool is not suitable for children. The Maduell model gives the best correlation to equilibrated Kt/V when compared to rate equation and Smye models.*

***Keywords:*** *Hemodialysis, Pediatric, Kt/V, Urea rebound, Urea kinetic models, Adequacy*

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End stage renal disease (ESRD) is a critically important health care problem in pediatric patients. The care of children with ESRD has always been more challenging than that of adult patients[1]. The availability of renal transplantation has allowed pediatric patients to sustain full and active lives, various modes of dialysis serve most often as a bridge to care for these patients until they can be transplanted and hemodialysis is one of the treatment modalities[2]. Hemodialysis has been a safe and

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effective treatment for pediatric patients for more than 25 years[3,4]. The determination of adequacy of hemodialysis is a complex issue that remains controversial. Its prescription, based on patient's size, clinical parameter such as predialysis BUN or clinical assessment of well being, does not provide sufficient clinical accuracy[5]. At present the use of urea kinetic models (UKM) to assess the adequacy of hemodialysis is becoming popular. The adequacy of hemodialysis is defined as Kt/V which is calculated by product of dialyzer urea clearance (K) and time of treatment (t) divided by body urea volume of distribution (V)[6].

Due to the multiple pools nature of the human body and the mass transfer resistance of biological membranes, rapid removal of solute (including BUN) from extracellular fluid (ECF) during hemodialysis, while the rate of the fall of solute (including BUN) in intracellular fluid (ICF) is slightly slower than it is in the ECF, creates imbalance of intercompartment. Its result shows as increasing postdialysis BUN in logarithmic curve, termed urea rebound (UR)[7]. Urea rebound occurs until at least 30-60 minutes after hemodialysis is completely done[6-9].

The single pool urea kinetic models which is calculated by using the immediate postdialysis BUN sample is an overestimation because of the effects of recirculation and intercompartment tranfer. It leads to overestimation of Kt/V[10,11]. Ideally equilibrated Kt/V should be calculated by using a post-dialysis sample after the rebound is complete, at least 30-60 minutes post- dialysis which is impractical. For this reason, several models have been used to predict the equilibrated Kt/V.

Although urea kinetic models have been used extremely in adults, the data in pediatric patients is minimal[8-10].

## Objectives

The aims of the present study were to find the postdialysis time when urea rebound is completed and the suitable models for calculation of Kt/V in pediatric patients.

## Material and Method

The present study was performed in 50 hemodialysis sessions of 5 pediatric patients with stable ESRD, 2 males and 3 females, age 5-18 years, who have regularly been treated with hemodialysis for 7-48 months at Pediatric Nephrology Unit, Phramongkutklao Hospital, from July to August 2000. The causes of ESRD were neurogenic bladder[2], pauci-immune RPGN[1], birth asphyxsia[1] and unknown[1]. Dry weight was 17.2-49 kg and body mass index (BMI) was 12.8-19.1 kg/m$^2$. Vascular access were arteriovenous graft [2], arteriovenous fistula[2] and double lumen catheter [1]. Hemodialysis lasted 4-5 h. Blood flow was 120-350 ml/min while dialysate flow was 300-500 ml/min. All dialysis sessions during the study were performed with Baxter 550, Baxter 1550 and Fresenius medical care 4008E. Dialyzers were hollow fiber low-flux polysulfone (Fresenius F5, Fresenius F6), hollow fiber low-flux sureflux 150E and hollow fiber low-flux FB110A, with a surface membrane of 0.7-1.5 m$^2$.

Blood samples of BUN were drawn at the beginning (C1) after insertion of a needle into the vascular access. Intradialysis sampling (CS) was taken from the arterial line at 70 minutes when blood flow was slowed to 50 ml/min. At the end of hemodialysis (C2), blood sampling was obtained by the stopped pump method. Serial measurements of BUN were done every 10 minutes for 60 minutes post- dialysis. The double pool equilibrated sampling (CR) was calculated by using 1 hour BUN after stopping dialysis.

The compared 6 different models of Kt/V were single pool, Daugirdas, equilibrated, rate equation, Maduell and Smye method, all of which have been used in adults.

**Table 1.** Kt/V calculated by single pool (ln C1/C2) and double pool models

| Model | Kt/V | Comparisons with equilibrate Kt/V | | |
|---|---|---|---|---|
| | | Different Kt/V | *p* value | r |
| Single pool | 1.705 ± 0.252 | 0.265 ± 0.075 | <0.001 | 0.942 |
| Equilibrated | 1.442 ± 0.259 | | | |
| Rate equation | 1.485 ± 0.209 | 0.086 ± 0.058 | 0.002 | 0.941 |
| Maduell | 1.442 ± 0.209 | 0.069 ± 0.063 | 0.967 | 0.942 |
| Smye | 1.379 ± 0.343 | 0.132 ± 0.132 | 0.015 | 0.864 |

Daugirdas Kt/V = 2.083 ± 0.336

Different single pool = 0.38 ± 0.092

1. Single pool model (spKt/V)
   1.1 Single pool Kt/V = ln C1/C2[11]
   1.2 Daugirdas Kt/V = -ln (C2/C1-0.008xt) + (4-3.5xC2/C1) x UF/BW[12]
2. Double pool model
   2.1 Equilibrated Kt/V = ln C1/CR
   2.2 Rate equation Kt/V = spKt/V (1-0.6/t) + 0.03[13]
   2.3 Maduell Kt/V = 0.906xspKt/V - 0.26xK/V - 0.007[14]
   2.4 Smye Kt/V[15]
   Ceq = C1 x $e^{-kt}$
   k = 1/(t-s) x in CS/C2

## Statistical Analysis

The difference between equilibrated Kt/V and the other models was compared by paired *t*-test. Correlation coefficient *(r)* and linear regression were determined. A probability value *(P)* less than 0.05 was considered statistically significant.

## Results

Urea rebound in the present study was found to be completed at least 60 minutes post-dialysis and mean percentage value was 30.68 ± 9.663. There was little change of BUN level between 50 minutes (mean percentage value 28.87 ± 10.47) and 60 minutes (Fig. 1 and 2). A logarithmic equation for urea rebound was generated from measured BUN of all the patients as follows:

Mean percentage urea rebound (%UR) = 11.363 ln (t) - 16.163

Table 1 shows the mean value difference between single pool Kt/V calculated by ln C1/C2 and the other models. In the present study the mean value of single pool Kt/V was 1.705 ± 0.252 and equilibrated Kt/V was 1.442 ± 0.259, leading to overestimation of single-pool Kt/V by 0.265 ± 0.075 (Fig. 3). Correlation coefficient was 0.942 (Table 1). Mean values obtained by rate equation Kt/V, Maduell Kt/V and Smye Kt/V were 1.485 ± 0.209, 1.442 ± 0.209 and 1.379 ± 0.343. The difference between the equilibrated Kt/V compared to rate equation Kt/V, Maduell Kt/V and Smye Kt/V were 0.086 ± 0.058 (Fig. 4), 0.069 ± 0.063 (Fig. 5) and 0.132 ± 0.132 (Fig. 6) respectively. Correlation coefficients were 0.941, 0.942 and 0.864 ,respectively (Table 1). The mean value of single pool Kt/V by Daugirdas model was 2.083 ± 0.336 which differed from the mean value of single pool Kt/V (calculated by ln C1/C2) by 0.380 ± 0.092.

## Discussion

Since the first clinical report of hemodialysis in ESRD pediatric patients in 1966, the determination of adequacy in pediatric patients is still controversial. According to adult data, there is statistical significant correlation between delivered dose of dialysis and mortality risk. The mortality risk was lower by 7% with each 0.1 higher level of delivered Kt/V[16]. But the data in pediatric patients are minimal.

In the present study urea rebound was shown in logarithmic curve, the mean percentage value of postdialysis urea rebound at 50 minutes was 28.87 ± 10.47 and 30.68 ± 9.663 at 60 minutes. Because BUN level was not equilibrated between 50 minutes and 60 minutes, it showed that urea rebound tended to be completed at least 50-60 minutes postdialysis which was similar to the

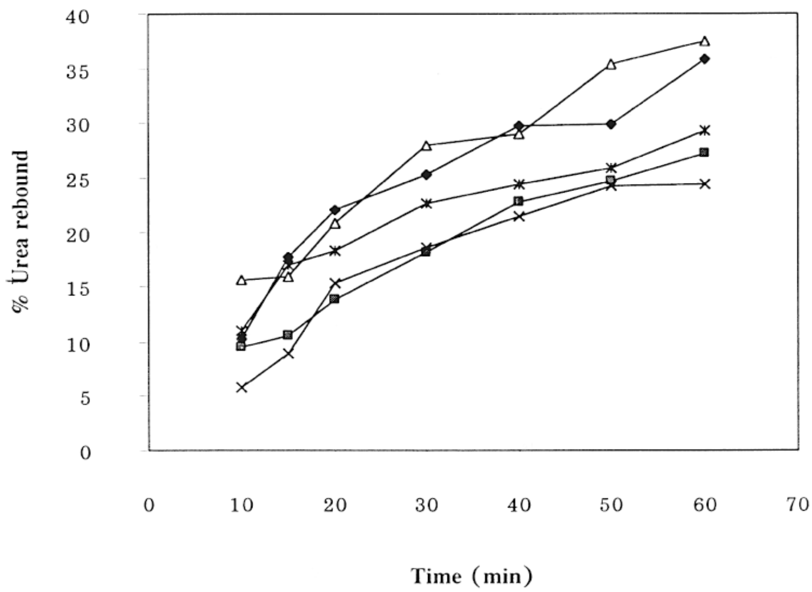


**Fig. 1** Mean percentage urea rebound postdialysis in each patient

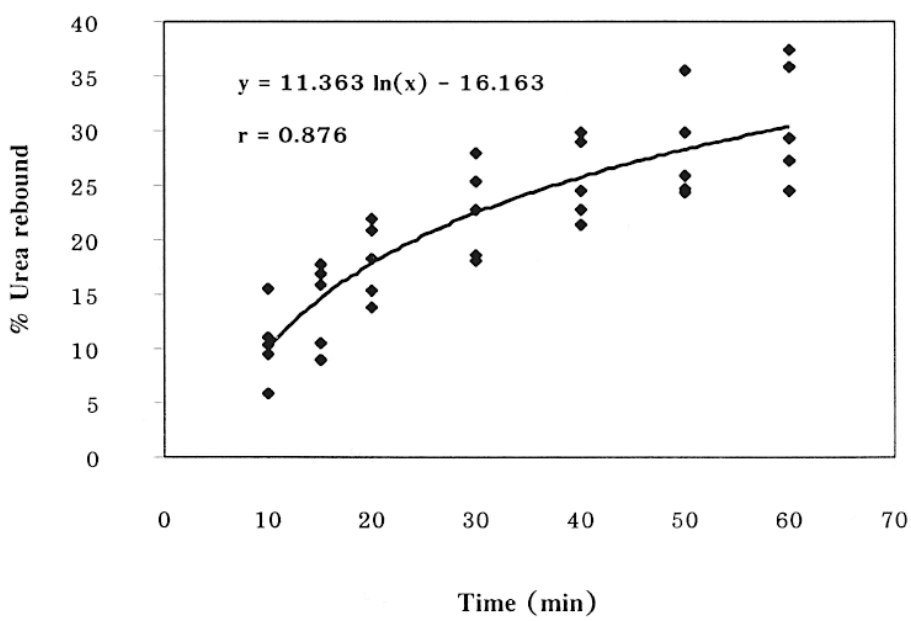


**Fig. 2** Mean percentage urea rebound postdialysis of entire patients

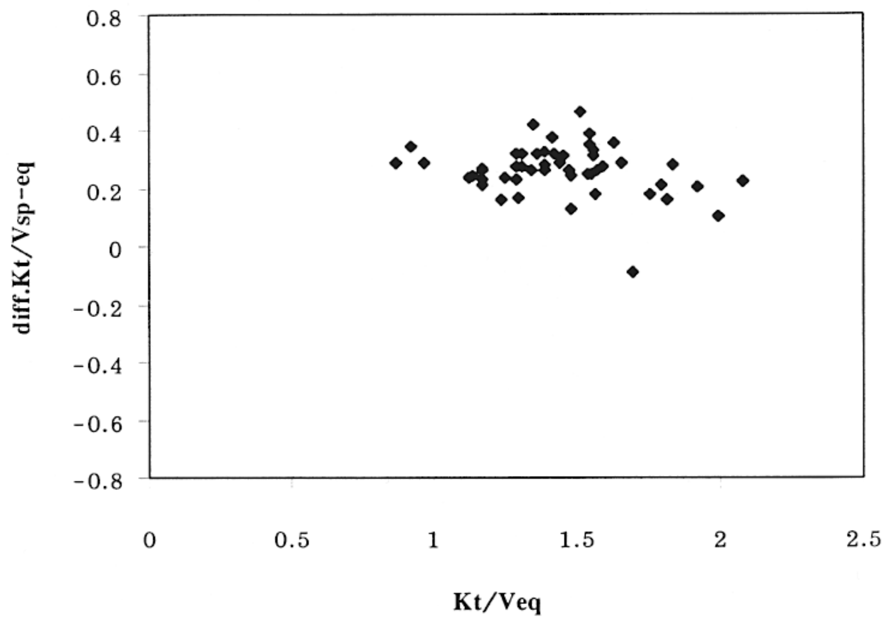


**Fig. 3** Mean value difference between single pool Kt/V and equilibrated Kt/V

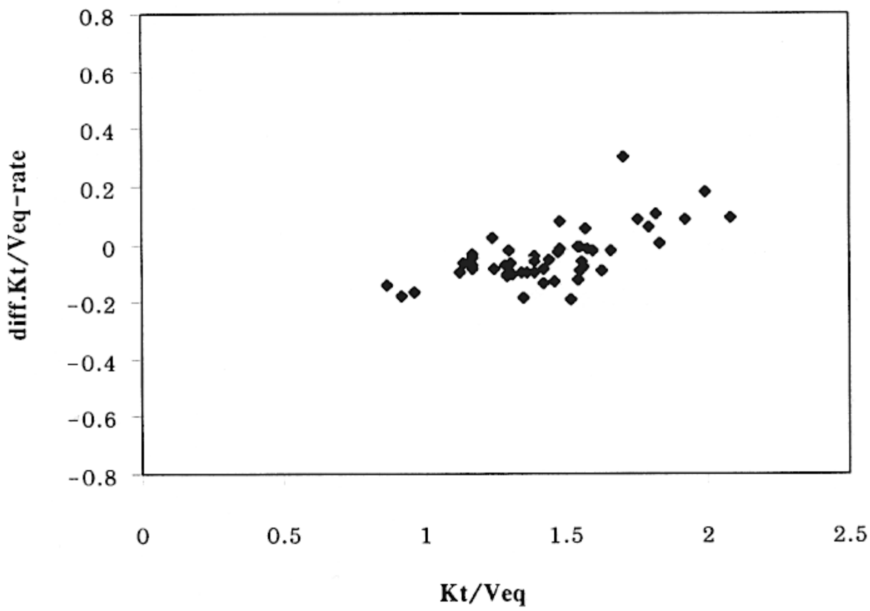


**Fig. 4** Mean value difference between equilibrated Kt/V and rate equation

previous reports in the pediatric patients[8,9]. But it was about 30-60 minutes in adult data.

The difference of equilibrated Kt/V by 0.265 $\pm$ 0.075 was similar to the previous reports in the pediatric and adults[8-10,14]. To measure the single pool Kt/V by Daugirdas model, its mean value was 2.083 $\pm$ 0.336. The difference of the mean value of single pool Kt/V calculated by Daugirdas model and ln C1/C2 was 0.380 $\pm$ 0.092. In the absence of pediatric data, current

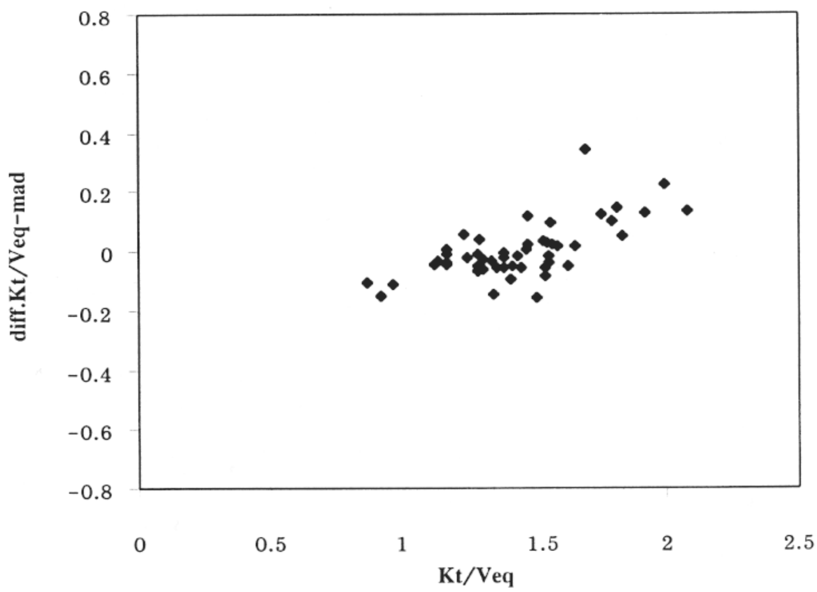


**Fig. 5** Mean value difference between equilibrated Kt/V and Maduell Kt/V

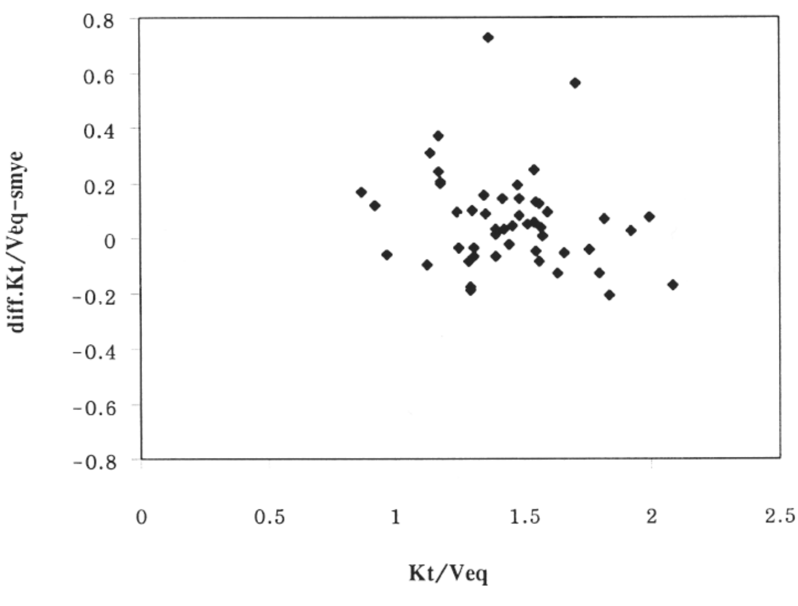


**Fig. 6** Mean value difference between equilibrated Kt/V and Smye Kt/V

recommendation of NKF-DOQI guideline for adequacy of hemodialysis is at least 1.2 by single pool Kt/V as reported in adult[17]. Not only the difference of single pool Kt/V calculated by Daugirdas model and ln C1/C2 but variable values of Kt/V calculated by several double pool models, led to a question that, which models of Kt/V were accurate for pediatric patients?

In the present study, the difference of equilibrated Kt/V and rate equation Kt/V was

$0.086 \pm 0.058$ ($p = 0.002$), Maduell Kt/V was $0.069 \pm 0.063$ ($p = 0.967$) and Smye Kt/V was $0.132 \pm 0.132$ ($p = 0.015$). Correlation coefficients were 0.941, 0.942 and 0.864, respectively. Based on these data, Maduell model was the best model to predict equilibrated Kt/V compared to rate equation and Smye model. This result was not be in agreement with the studies reported by others which showed that rate equation and Smye model were also accurate to predict equlibrated Kt/V[8-10,18,19]. This difference may be attributed to several factors such as 1. small sample size 2. having meal during hemodialysis session and 3.unsuitable models for pediatric patients.

## Conclusion

Urea rebound in pediatric patients is completed at least 60 minutes after cessasion of hemodialysis. Although NKF DOQI guideline recommends that adequacy of hemodialysis should be calculated by single pool[17,20], the present study demonstrates that Kt/V calculated from single-pool is not suitable for children. It results in overestimation of Kt/V. The Kt/V calculated by double pool model is accurate for assessing the adequacy of hemodialysis and Maduell model is the best model to predict equilibrated Kt/V when compared to rate equation and Smye models.

## References


1. Leichter HE, Kher KK. Management of end-stage renal failure-dialysis therapy. In: Kher KK, Makker SP, editors. Clinical Pediatric Nephrology. New York: Mc Graw-Hill, 1992; 559-97.
2. Evans ED, Greenbaum LA, Ettenger RB. Principles of renal replacement therapy in children. Pediatr Clin North Am 1995; 42: 1579-602.
3. Hutchings RH, Hideman R, Scribner BH. Chronic hemodialysis in a prealdolescent. Pediatrics 1966; 37: 68.
4. Bunchman TE. Pediatrics hemodialysis: Lessons from the past, ideas for the future. Kidney Int 1996; 49 (Suppl 53): s64-s67.
5. Harmon WE, Jabs KL. Hemodialysis. In: Barratt TM, Avner ED, Harmon WE, editors. Pediatric Nephrology.Baltimore: Williams & Wilkins, 1994: 1354-72.
6. Daugirdas JT. Second-generation logarithmic estimates of single-pool variable volume Kt/V: An analysis of error. J Am Soc Nephrol 1993; 4: 1205-13.
7. Daugirdas JT, Schneditz D. Overestimation of hemodialysis dose depends on dialysis efficiency by regional blood flow. ASAIO 1995; 41: 719-24.
8. Maduell F, Garcia -Valdecasas J, Garcia H, Hernandez - Jeras J, Siguenza F, Del Pozoc, et al. Validitation of different methods to calculate Kt/V considering postdialysis rebound. Nephrol Dial Transplant 1997; 12: 1923-33.
9. Smye SW, Dunderdale E, Brownridge G, Will E. Estimation of treatment dose in high-efficiency hemodialysis. Nephron 1994; 67: 24-9.
10. Held PJ, Port FK, Walfe RA, Stannard DC, Carroll CE, Daugirdas JT, et al. The dose of hemodialysis and patient mortality. Kidney Int 1996; 50: 550-6.
11. NKF-DOQI Clinical Practice Guidelines for Hemodialysis Adequacy. Am J Kidney Dis 1997; 30 (Suppl 2): s15-s57.
12. HEMO study group. Comparison of methods to predict equilibrated Kt/V in the HEMO Pilot Study. Kidney Int 1997; 52: 1395-405.
13. Tattersal JE, De Takats D, Chamney P, Greenwood RN, Farrington K. The post-hemodialysis rebound: Predicting and quantifying its effect on Kt/V. Kidney Int 1996; 50: 2094-102.

14. Von AB, Garcia-Valdecasas J, Barlee V. Solute rebound in highly efficient dialysis: Impact on quantification of therapy. J Am Soc Nephrol 1993; 4: 393 (abstr).
15. Depner TA. Assessing adequacy of hemodialysis: Urea modeling. Kidney Int 1994; 45: 1522-35.
16. Pedrini LA, Zereik S, Rasmy S. Causes, kinetics and clinical implications of post-hemodialysis urea rebound. Kidney Int 1988; 34: 817-24.
17. Evans JHC, Smye SW, Brocklebank JT. Mathematical modelling of hemodialysis in children. Pediatr Nephrol 1992; 6: 349-53.
18. Marsenic O, Peco-Antic A, Jovanovic O. Comparison of two methods for predicting equilibrated Kt/V (eKt/V) using true eKt/V value. Pediatr Nephrol 1999; 13: 418-22.
19. Goldstein SL, Sorof JM, Brewer ED. Evaluation and prediction of urea rebound and equilibrated Kt/V in pediatric hemodialysis population. Am J Kidney Dis 1999; 34: 49-54.
20. Gotch FA, Sargent JA. A mechanistic analysis of The National Cooperative Dialysis Study (NCDS). Kidney Int 1985; 28: 526-34.

## *การศึกษาเปรียบเทียบค่าคำนวณ Kt/V ในผู้ป่วยเด็กฟอกเลือด*

***ชูเกียรติ เกียรติขจรกุล, ประไพพิมพ์ ธีรคุปต์, ยุพาพิน จุลโมกข์, สาลี่ ใจโปร่ง, ศรันยา กิจพาณิชย์***

***วัตถุประสงค์:*** *เพื่อศึกษาว่าเวลาใดหลังการฟอกเลือดที่มีความสัมพันธ์กับภาวะ Urea rebound และ Kt/V จากการคำนวณด้วยแบบจำลองใดเหมาะสมกับผู้ป่วยเด็ก*

***วัสดุและวิธีการ:*** *ศึกษาจากการฟอกเลือด 50 ครั้ง ในผู้ป่วยเด็ก 5 ราย ประกอบด้วยเพศชาย 2 ราย เพศหญิง 3 ราย อายุ 5 - 18 ปี ที่ได้รับการฟอกเลือดเป็นเวลา 7 - 48 เดือน โดยการตรวจระดับยูเรียตั้งแต่ก่อนทำการฟอกเลือด, 70 นาที ขณะทำการฟอกเลือด, สิ้นสุดการฟอกเลือด และหลังจากนั้นทุก 10 นาที จนครบ 1 ชั่วโมง นำค่า Kt/V ที่คำนวณจากแบบจำลองต่างๆ 6 ชนิดมาเปรียบเทียบกัน ประกอบด้วยแบบจำลอง Single-pool, แบบจำลอง Daugirdas, แบบจำลองสมดุล, แบบจำลอง Rate equation, แบบจำลองของ Maduell และแบบจำลอง Smye*

***ผลการศึกษา:*** *ภาวะ Urea rebound ใช้เวลาอย่างน้อย 60 นาทีหลังการฟอกเลือดสิ้นสุด และพบว่าอัตราการเพิ่มของยูเรียเทียบร้อยละเท่ากับ $30.68 \pm 9.663$ ค่าคำนวณ Kt/V จากแบบจำลองสมดุลเท่ากับ $1.442 \pm 0.259$ พบว่าค่าคำนวณ Kt/V จากแบบจำลอง Single-pool เท่ากับ $1.705 \pm 0.252$ ซึ่งให้ค่าเกินจริง $0.265 \pm 0.075$ และค่า Kt/V จากแบบจำลองของ Daugirdas เท่ากับ $2.083 \pm 0.336$ ในขณะที่ค่าคำนวณ Kt/V จากแบบจำลอง Rate equation, Maduell และ Smye เท่ากับ $1.485 \pm 0.209$, $1.442 \pm 0.209$ และ $1.379 \pm 0.343$ ตามลำดับ แตกต่างจากค่าคำนวณ Kt/V ของแบบจำลองสมดุล เท่ากับ $0.086 \pm 0.058$ ($p = 0.002$), $0.069 \pm 0.063$ ($p = 0.967$) และ $0.132 \pm 0.132$ ($p = 0.015$)*

***สรุป:*** *ภาวะ Urea rebound ในประชากรกลุ่มศึกษาใช้เวลาอย่างน้อย 60 นาที จึงเข้าสู่ภาวะสมดุล และการใช้ค่าคำนวณ Kt/V จากการใช้แบบจำลอง Single-pool อย่างเดียวไม่เพียงพอ พบว่าค่าคำนวณ Kt/V จากแบบจำลองของ Maduell ให้ผลที่ใกล้เคียงกับค่าคำนวณ Kt/V ในภาวะสมดุลและเชื่อถือได้มากที่สุดเมื่อเทียบกับค่าคำนวณแบบจำลองของ Smye และ Rate equation*