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ORIGINAL ARTICLE

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Measured versus estimated glomerular filtration rate in the Calvert equation: influence on carboplatin dosing

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Abstract *Purpose:* Carboplatin is frequently dosed to achieve a desired area under the plasma concentration-time curve (AUC) by using the Calvert or Chatelut equations to estimate carboplatin clearance. Accurate determination of glomerular filtration rate (GFR) is necessary to correctly calculate carboplatin clearance using the Calvert equation. In clinical practice, the Cockcroft-Gault formula is frequently used to estimate GFR, but this practice has been reported to under- and overestimate carboplatin clearance. The purpose of this trial was to compare determinations of carboplatin clearance using the Chatelut equation and four separate GFR determinations, including ^{99m}Tc-DTPA, the Cockcroft-Gault formula, a 24-h urine collection and a 2-h urine collection. *Methods:* Carboplatin clearance was estimated in 21 previously untreated extensive-stage small-cell lung cancer patients. GFR was determined using ^{99m}Tc-DTPA, the Cockcroft-Gault formula, 24-h urine collection and 2-h urine collection. Serum and urine creatinine concentrations were measured using enzymatic assays. The carboplatin clearance was then calculated by individually adding 25 to the four GFR determinations based on the Calvert equation, which states that carboplatin clearance equals GFR + 25 (nonrenal clearance). The carboplatin clearance was also estimated using the Chatelut equation. The five determinations of carboplatin clearance were compared using Friedman's test and post-hoc Wilcoxon signed rank tests. Precision and bias for each carboplatin clearance determination were calculated assuming that ^{99m}Tc-DTPA provided the most accurate measure of GFR. *Results:* A statistically significant difference was found between the five methods of estimating carboplatin clearance ($P < 0.001$). No difference was found between carboplatin clearance calculated using ^{99m}Tc-DTPA and the Chatelut equation, the Cockcroft-Gault formula or the 2-h urine collection. The Chatelut equation provided more precision and less bias than the 2-h urine collection (median precision 20% and 30%, median bias –1% and –18%, respectively). *Conclusion:* Compared to ^{99m}Tc-DTPA, the Chatelut equation more accurately estimates carboplatin clearance than the Cockcroft-Gault formula, the 2-h urine collection and the 24-h urine collection. The greater negative bias found for the latter three estimates of carboplatin clearance could result in underdosing of carboplatin.

Key words Carboplatin · Glomerular filtration rate · Creatinine clearance · Antineoplastic agents · Dosing

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Introduction

Carboplatin is a frequently used antineoplastic agent with documented activity against a broad range of tumors [4, 14, 17, 29, 32, 38]. Carboplatin is dosed to achieve a targeted area under the concentration time curve (AUC) more commonly than the traditional dosing strategy based on body surface area [14]. This approach is supported by the relationship between carboplatin AUC and toxicity, specifically thrombocytopenia and neutropenia [5, 15, 16, 19, 24, 26, 34, 39]. In ovarian cancer patients, increased response rates are noted with increasing carboplatin AUC up to a plateau of 5–7 mg·min/ml [21]. In addition, treatment failures occur more frequently in patients with nonseminomatous germ cell tumors who have a carboplatin AUC less than 5 mg·min/ml [11, 20, 31]. These facts, combined with considerable interindividual variability in carbopl-

atin clearance, have led to the standard practice of dosing carboplatin based on the desired AUC.

Since the carboplatin dose is calculated by multiplying the target AUC by carboplatin clearance (carboplatin dose = AUC\times carboplatin clearance), an accurate estimate of carboplatin clearance is essential. Glomerular filtration rate (GFR), measured in terms of ^{51}chromium edathamil (^{51}Cr-EDTA) clearance, correlates well with carboplatin clearance ($r^2 = 0.79$–0.81), since carboplatin is mostly (50–70%) excreted unchanged into the urine [9, 15, 39, 40, 44, 46]. Carboplatin clearance can be estimated using methods developed by Egorin et al., Calvert et al. and Chatelut et al., which incorporate GFR estimations and other covariates [5, 9, 16]. In clinical practice, carboplatin clearance is commonly calculated by adding the patient's GFR to 25 (nonrenal clearance based on the Calvert equation (carboplatin dose = AUC\times (GFR + 25)) [5]. The Calvert equation has been validated using ^{51}Cr-EDTA clearance to measure GFR, since ^{51}Cr-EDTA is highly correlated ($r^2 = 0.78$) with carboplatin clearance [5]. Technetium-99m diethylene triamine pentaacetic acid (^{99m}Tc-DTPA) clearance can also provide an unbiased estimate of carboplatin clearance when it is used to measure GFR [27].

The use of these accurate radionucleotide methods is unfortunately limited by their inconvenience and expense. In clinical practice, GFR is often estimated by calculating creatinine clearance (CrCl) using the Cockcroft-Gault formula [13]. Available data show that using the Cockroft-Gault formula to estimate GFR can lead to either an underestimate [6, 7, 8, 9, 10, 23] or an overestimate [1, 18, 28, 30] of carboplatin clearance. Therefore, the use of this estimate may lead to inaccuracy in dosing of carboplatin.

The objectives of this trial were to (1) compare three estimates of CrCl determined using a 2-h urine collection, a 24-h urine collection and the Cockroft-Gault formula with ^{99m}Tc-DTPA, and (2) compare carboplatin clearance calculated using the Chatelut equation [9], and the four GFR determinations (i.e. ^{99m}Tc-DTPA, 2-h urine collection, 24-h urine collection and the Cockroft-Gault formula).

Patients and methods

Patient characteristics and chemotherapy regimen

The demographic characteristics of the study population are shown in Table 1. Enrolled into a phase I study evaluating carboplatin, topotecan and etoposide were 21 patients with previously untreated extensive-stage small-cell lung cancer. The protocol was approved by the Institutional Review Board at the University of North Carolina and written informed consent was obtained for each patient prior to study conduct. The patients were admitted to the General Clinical Research Center (GCRC) at University of North Carolina (UNC) Hospitals to receive their first cycle of chemotherapy. Inclusion criteria included an ECOG performance status of 0 to 2, serum creatinine <1.6 g/dl or CrCl >40 ml/min (based on the Cockroft-Gault formula), and liver function tests less than three times the upper limit of normal. Patients were excluded if they had received prior chemotherapy or radiation therapy or had had a concurrent or previous malignancy within the previous 5 years. None of the patients had preexisting kidney disease or renal metastases. A standard diet was maintained throughout the study and none of the patients received medications known to inhibit renal tubular secretion (e.g. trimethoprim, cimetidine) or to cause nephrotoxicity (e.g. aminoglycosides).

Table 1 Patient characteristics*

No. of patients	21
Men	12
Age (years)	
Median	66
Range	44–77
Body weight, actual (kg)	
Median	67
Range	45–104
Body weight, as percent of ideal	
Median	109
Range	83–169
Body surface area (m^2)	
Median	1.7
Range	1.4–2.3
Serum creatinine (mg/dl)	
Median	0.8
Range	0.4–1.4
CrCl – Cockcroft-Gault (ml/min)	
Median	90
Range	41–172
Carboplatin dose (mg)	
Median	575
Range	328–985

All patients received combination chemotherapy with carboplatin, topotecan and etoposide. Carboplatin was dosed to a target AUC of 5 mg·min/ml and administered as a 30-min intravenous (i.v.) infusion. The actual administered carboplatin dose (in milligrams) was calculated using the Calvert equation as $5 \times (GFR + 25)$. The Cockcroft-Gault formula was used to estimate the GFR.

The first cohort ($n = 6$) received carboplatin on day 1 of the chemotherapy cycle. The remaining patients ($n = 15$) received carboplatin on the last day of i.v. chemotherapy, because patients in the first cohort developed dose-limiting toxicities. The first 15 patients received an 8-day regimen: carboplatin; topotecan i.v. targeted to a lactone AUC of 15, 30 or 45 ng·h/ml over 30 min, days 1–5; and oral etoposide 100 mg/m^2 per day, days 6–8. Subsequent patients received the same chemotherapy regimen with the duration of topotecan reduced to 3 days.

Estimates of GFR and carboplatin clearance

GFR was determined during the first chemotherapy cycle using four different methods (^{99m}Tc-DTPA, the Cockcroft-Gault, 2-h urine collection, and 24-h urine collection).

^{99m}Tc-DTPA clearance On day 2 of cycle one, patients received 3 mCi ^{99m}Tc-DTPA i.v. and blood samples were obtained at 1 and 3 h after administration [35, 36]. ^{99m}Tc-DTPA is the radioisotope routinely used to measure GFR at this hospital. The blood samples were centrifuged in Amicon Centrifree filters and the radioactivity was counted. The data were fitted to a validated two-compartment model and the plasma clearance of ^{99m}Tc-DTPA was calculated according to previously published methods [35, 36]. ^{99m}Tc-DTPA plasma clearance is highly correlated ($r = 0.97$) with ^{51}Cr-EDTA clearance, which has been shown to be correlated with carboplatin clearance in a number of clinical trials [5, 9, 27, 39]. Carboplatin clearance was estimated by adding the ^{99m}Tc-DTPA plasma clearance to 25 (nonrenal clearance) based on the Calvert equation.

Cockcroft and Gault calculated CrCl ($CrCl_{C/G}$). The CrCl was calculated by the following equation: CrCl = [(140 − age)× actual body weight (kg)] × [serum creatinine (mg/dl) × 72]. The resulting value was multiplied by 85% for women [13]. Serum creatinine concentrations were obtained before the first cycle of chemotherapy and within 48 h of measuring ^{99m}Tc-DTPA clearance. Carboplatin clearance was calculated by adding the $CrCl_{C/G}$ to 25 (nonrenal clearance) based on the Calvert equation.

2-h ($CrCl_{2h}$) and 24-h ($CrCl_{24h}$) measured CrCl. Urine collections were done during the first cycle of chemotherapy and within 24–72 h of measuring ^{99m}Tc-DTPA clearance. The urinary CrCl estimates were determined from two separate urine collections. To maximize the potential for an accurate urine collection, the patients were given frequent reminders to collect all of their urine and a urine collection container was left in the patient's personal bathroom during the collection periods. The 24-h collection was started immediately before chemotherapy administration and the 2-h urine collection was completed the evening before carboplatin administration. The 2-h urine collection was not obtained in two patients. CrCl was calculated from both of these two separate urinary collections using the following formula:

$$CrCl = U_{vol} \times U_{cr}/S_{cr} \times t$$

where U_{vol} is volume in milliliters of urine collected over the time period, U_{cr} is the urine creatinine concentration in milligrams per deciliter, S_{cr} is the serum creatinine concentration in milligrams per deciliter (same S_{cr} used to calculate $CrCl_{C/G}$) and t is the duration of the urine collection in minutes. Carboplatin clearance was calculated by adding the $CrCl_{2h}$ and $CrCl_{24h}$ to 25 (nonrenal clearance) based on the Calvert equation.

Chatelut equation. The Chatelut equation [8] was also used to calculate the carboplatin clearance for each patient: carboplatin clearance = 0.134 × weight (kg) + {218 × weight (kg) × [1-0.00457 × age (years)] × [1-0.0314 × sex (male 0, female 1)]}/serum creatinine (μM). The serum creatinine value and actual body weight were obtained immediately before chemotherapy administration.

Creatinine analysis

The serum and urine creatinine concentrations were assayed using previously published enzymatic methods [41]. Urine (10 µl) was added to a slide containing gel layers. As creatinine diffuses through the layers, it is hydrolyzed to creatine. The creatine formed is converted to sarcosine and urea by creatine amidinohydrolase. The sarcosine is subsequently oxidized to glycine, formaldehyde, and hydrogen peroxide. Finally, peroxidase oxidizes an indicator dye to produce a colored product. The slide is incubated at 37°C for 5 min. Rate determinations are made at 3.85 and 5 min. The rate of change between the two readings is proportional to the creatinine concentration in the urine sample. This analytical method is a standard laboratory method used to determine serum and urine creatinine. The coefficients of variation in the quality controls were $<4\%$ for serum creatinine and $<3\%$ for urine creatinine.

Data analysis

Statistical analyses were conducted using SPSS 9.0 software. The data were not normally distributed based on tests of skewness and kurtosis. Friedman's test was used to compare the five estimates of carboplatin clearance (the Chatelut equation, the Cockroft-Gault formula, 2-h urine collection, 24-h urine collection, and ^{99m}Tc-DTPA) with statistical significance set at $\alpha = 0.05$. Post-hoc Wilcoxon signed rank tests were also completed with Bonferroni correction (statistical significance at $\alpha = 0.0125$) for multiple comparisons.

The predictive performance of each estimate of carboplatin clearance was determined using the carboplatin clearance calculated from ^{99m}Tc-DTPA as the gold standard [30]. The carboplatin clearance calculated using each method was used to assess precision and bias. Precision was quantitated using absolute percent error [(|CrCl–^{99m}Tc-DTPA|/ ^{99m}Tc-DTPA) × 100)] [37] and bias was quantitated using the actual percent error [(CrCl–^{99m}Tc-DTPA/^{99m}Tc-DTPA) × 100] [37]. The carboplatin clearance estimates that fell within 25% of the carboplatin clearance calculated using ^{99m}Tc-DTPA were also calculated [i.e. (Chatelut equation/carboplatin clearance per ^{99m}Tc-DTPA) × 100].

Results

Of the 21 patients, 12 (57%) were men. The median age was 66 years (range 44–77 years). The median $CrCl_{C/G}$ was 90 (range 41 to 172 ml/min). Figure 1 shows the GFRs determined by ^{99m}Tc-DTPA compared with those determined by the Cockroft-Gault formula for all 21 patients. The median ^{99m}Tc-DTPA clearance was 96 ml/min (62–239 ml/min). The median GFR estimate for the 2-h urine collection was 79 ml/min (23–219 ml/min) and the 24-h urine collection was 48 ml/min (18–140 ml/min) (Table 2). The interindividual variability (measured by coefficient of variation) for GFR was greater for the 2-h urine collection (59%) and the 24-h urine collection (61%) than for the Cockroft-Gault formula (43%) and ^{99m}Tc-DTPA clearance (42%).

Impact on carboplatin clearance

Carboplatin clearance is the key determinant needed to calculate its dose when targeting a specific AUC (dose = target AUC × carboplatin clearance). A statistically significant difference was found between the five esti-

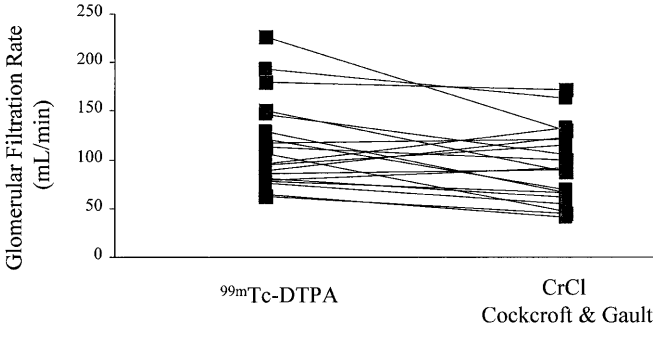

Fig. 1 Comparison of ^{99m}Tc-DTPA and CrCl calculated by the Cockcroft and Gault method

Table 2 Results of GFR methods*

Method	GFR (ml/min)		Coefficient of variation (%)
	Median	Range	
^{99m}Tc-DTPA plasma clearance	96	62–239	42
$CrCl_{C/G}$	90	41–172	43
$CrCl_{2h}$	79	23–219	59
$CrCl_{24h}$	48	18–140	61%

mates of carboplatin clearance ($P < 0.001$). Post-hoc analysis revealed that the carboplatin clearance calculated using ^{99m}Tc-DTPA did not differ from the carboplatin clearance calculated using the Cockroft-Gault formula ($P = 0.021$), the 2-h urine collection ($P = 0.198$), or the Chatelut equation ($P = 0.434$). Post-hoc power analysis was performed using the carboplatin clearance calculated from ^{99m}Tc-DTPA and the Chatelut equation ($\beta = 0.8$ and $\alpha = 0.05$). A normal distribution was assumed to complete the power analysis. It would be necessary to have 208 patients to detect a statistically significant difference between the means of the carboplatin clearance calculated from ^{99m}Tc-DTPA (138 ml/min) and the Chatelut equation (147 ml/min). Figure 2 shows the carboplatin clearance calculated using ^{99m}Tc-DTPA, the Chatelut equation, the Cockroft-Gault formula and the 2-h urine collection. The carboplatin clearance calculated using the 24-h urine collection was deleted from Fig. 2 because it significantly differed from the carboplatin clearance calculated using ^{99m}Tc-DTPA and it had the poorest precision and bias.

The carboplatin clearances calculated using $CrCl_{C/G}$, $CrCl_{2h}$, and $CrCl_{24h}$ were within 25% of the median carboplatin clearance calculated from ^{99m}Tc-DTPA in 62%, 42% and 19% of the patients, respectively (Table 3). The Chatelut equation had a similar performance to the Cockroft-Gault formula: 62% of patients were within 25% of the median carboplatin clearance calculated from ^{99m}Tc-DTPA. The precisions for the carboplatin clearance calculated from the Cockroft-Gault and the Chatelut equations were similar (19% and 20%, respectively). The precisions for carboplatin clearance calculated using the urine collections were higher (2-h urine 30%, 24-h urine 42%). The Chatelut equation provided the lowest bias (median –1%) compared with the bias determined for the Cockroft-Gault formula (–18%), the 2-h urine collection (–17%) and the 24-h urine collection (–42%).

Previous studies have shown a good correlation ($r = 0.93$ and 0.73) between $CrCl_{C/G}$ and GFR in patients with a GFR <100 ml/min [12, 27]. Additionally, Calvert et al. have reported that the Cockroft-Gault formula cannot accurately estimate the GFR as the GFR increases [6]. Therefore, the precision and bias were compared for patients with a ^{99m}Tc-DTPA clearance ≤100 ml/min versus >100 ml/min. The median (range) precision and bias for the carboplatin clearance calculated using the Cockroft-Gault formula were 31% (3% to 55%) and –31% (–55% to 3%) for patients with a ^{99m}Tc-DTPA clearance >100 ml/min and 27% (5% to 39%) and –15% (–37% to 39%) for patients with a ^{99m}Tc-DTPA clearance <100 ml/min.

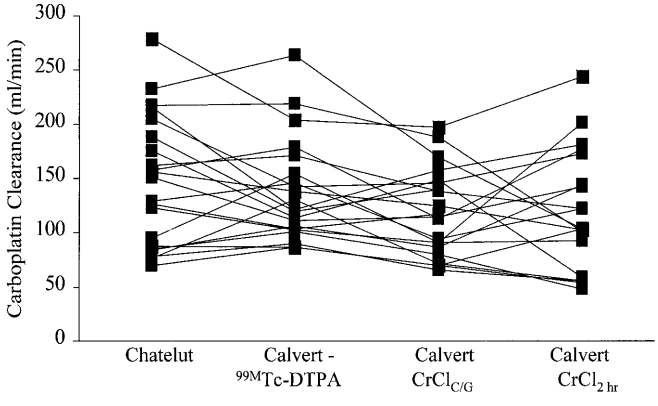

Fig. 2 Comparison of calculated carboplatin clearance

Discussion

$CrCl_{C/G}$ is commonly used in clinical practice to estimate GFR, despite its known limitations, because of its ease of use and low cost. Our results indicate that using $CrCl_{C/G}$ could underestimate carboplatin clearance. Available data suggest the Cockroft-Gault formula can both underestimate [6, 7, 8, 9, 10, 23, 42] and overestimate [1, 18, 28, 30] carboplatin clearance. This could lead to uncertainty concerning the dose intensity of carboplatin in reported studies. The discrepancies between the various studies evaluating the ability of $CrCl_{C/G}$ to estimate carboplatin clearance could be secondary to: (1) assumptions made in deriving the Calvert equation; (2) assumptions made in using the Cockroft-Gault formula to estimate GFR; (3) the different analytical techniques use to measure creatinine; and (4) different baseline GFR in the study populations.

The Calvert equation was derived from regression analysis of pretreatment GFR to clearance of free platinum in 31 cancer patients (27 women) with a ^{51}CrEDTA clearance range of 33 to 135 ml/min [5]. One of the assumptions made in creating this dosing formula was that the nonrenal clearance of carboplatin was consistent between patients. This assumption was based on a retrospective study that showed that the nonrenal clearance of free platinum varied between 25 and

Table 3 Differences in estimated carboplatin clearance

Method used	Calculated carboplatin clearance (ml/min)	Within 25% of ^{99m}Tc-DTPA (%)	Precision (%)	Bias (%)
Calvert equation – ^{99m}Tc-DTPA plasma clearance	121 (87 to 264)	100	NA	NA
Calvert equation – $CrCl_{C/G}$	115 (66 to 197)	62	19 (3 to 45)	–18 (–45 to 31)
Calvert equation – $CrCl_{2h}$	104 (48 to 244)	42	30 (1 to 61)	–17 (–61 to 50)
Calvert equation – $CrCl_{24h}$	73 (43 to 165)	19	42 (5 to 75)	–42 (–75 to 35)
Chatelut equation	151 (70 to 279)	62	20 (0 to 79)	–1 (–41 to 79)

50 ml/min except in one patient whose nonrenal clearance was 85 ml/min. This twofold variability in the nonrenal clearance could affect the relationship between carboplatin's renal clearance and total clearance.

The assumptions made in using the Cockcroft-Gault formula to estimate GFR could also explain the discrepancies. Creatinine is generated in the muscle from the conversion of phosphocreatine and creatine and it is eliminated through glomerular filtration and renal tubular secretion. Therefore, $CrCl_{C/G}$ exceeds GFR by the amount of creatinine that is cleared by tubular secretion. Tubular secretion of creatinine is enhanced in patients with reduced GFR, but creatinine shows considerable interpatient variability in the fraction that undergoes tubular secretion [25]. For example, 0 to 40% of excreted creatinine undergoes tubular secretion in patients with a GFR between 100 and 120 ml/min and 20 to 50% undergoes tubular secretion in patients with a GFR between 30 and 100 ml/min [25].

The relative influence of tubular secretion can be minimized when alkaline picrate assays (e.g. Jaffe) are used to measure creatinine [2]. Alkaline picrate methods can detect both creatinine and noncreatinine chromogens. These methods can overestimate serum creatinine by up to 20% [33], which can lower the estimate for CrCl calculated using the Cockroft-Gault formula. However, the $CrCl_{C/G}$ will minimally deviate from the GFR in patients with normal renal function, because creatinine undergoes variable tubular secretion. Numerous enzymatic methods (Ektachem and PAP) have been developed to circumvent interferences from the alkaline picrate reactions. These newer assays are more specific than the alkaline picrate reactions and they provide lower serum creatinine values than the alkaline picrate methods. These assays should yield a calculated $CrCl_{C/G}$ higher than the actual GFR. Ando et al. have suggested adding 0.2 to the serum creatinine concentrations determined with these enzymatic assays to compensate for the high estimates determined for CrCl with this method [1]. However, the type of enzyme should be noted, because the Ektachem method gives higher creatinine values than the PAP method at low serum creatinine concentrations [43]. Although our study used an enzymatic assay to measure creatinine, our results cannot be compared with the published results derived from the Ektachem and PAP enzymatic assays due to lack of published data comparing these methods.

In addition, the variable study populations may have contributed to the different outcomes reported concerning the use of the Cockroft-Gault formula to estimate carboplatin clearance. The overall range of renal function was similar between the studies, but stratifying patients based on renal function could provide further insight. Previous studies have shown that $CrCl_{C/G}$ is only correlated ($r = 0.93$ and 0.73) with ^{51}Cr-EDTA in patients with a GFR < 100 ml/min [12, 27]. Stratifying our results revealed a reduced bias between GFR estimations calculated using the Cockroft-Gault formula and ^{99m}Tc-DTPA in patients whose ^{99m}Tc-DTPA was < 100 ml/min.

This trial is the first study to use a 2-h urine collection to estimate carboplatin clearance for use in the Calvert equation. The 2-h urine was collected to assess its accuracy in estimating GFR, since the carboplatin clearance calculated from the 2-h urine could also be used clinically. Although the carboplatin clearance calculated from the 2-h urine did not significantly differ from the carboplatin clearance calculated from ^{99m}Tc-DTPA, the estimate from the 2-h urine collection produced less precision and more bias than the Chatelut equation. Few (42%) calculated carboplatin clearances determined using the 2-h urine were within 25% of the median carboplatin clearance calculated from ^{99m}Tc-DTPA, suggesting that using the 2-h urine would result in inaccurate dosing in a significant number of patients.

A 24-h urine collection has also been used to estimate GFR in the Calvert equation. Measured $CrCl_{24h}$ underestimated GFR by an average of 66% in this trial, which agrees with previous data [3, 22]. In addition, the GFR calculated from the 24-h urine collections showed greater variability than the GFR calculated using the Cockroft-Gault formula (Tables 2 and 3). However, other authors have shown that 24-h urine can overestimate carboplatin clearance [1, 30, 42, 45]. Inaccurate urine collections may have contributed to the disparity in the findings, although the urine was collected in a hospital environment [22].

The Egorin or Chatelut equations may provide more accurate estimates of carboplatin clearance than the Calvert equation, when the Cockroft-Gault formula or urine collections are used to estimate GFR [9, 16]. The Egorin equation uses the GFR and the degree of thrombocytopenia experienced with prior courses of carboplatin [16]. It could not be evaluated in this trial because patients concomitantly received topotecan and etoposide. Chatelut et al. used Bayesian techniques (NONMEM) to develop an equation incorporating weight, serum creatinine, gender, and age to calculate carboplatin clearance [9]. The Chatelut equation accurately predicted carboplatin clearance when it was compared with the carboplatin clearance calculated using ^{99m}Tc-DTPA in this study (Fig. 2). The Chatelut equation has also accurately predicted the carboplatin clearance for cancer patients with $CrCl_{C/G}$ ranging from 49 to 149 ml/min in a previous validation trial [9]. However, Okamoto et al. have found that the Chatelut equation does not accurately predict carboplatin clearance [30].

In conclusion, the Chatelut equation and the Cockroft-Gault formula both provide good estimates of carboplatin clearance compared with the carboplatin clearance calculated using ^{99m}Tc-DTPA. CrCl calculated with the Cockcroft-Gault formula had more precision and less bias in patients with a ^{99m}Tc-DTPA < 100 ml/min relative to patients with a ^{99m}Tc-DTPA > 100 ml/min. Measured urinary CrCl (2-h or 24-h collections) did not provide a more precise estimate of GFR than carboplatin clearance equations utilizing serum creatinine determinations, and these estimates showed greater

variability compared with the estimates determined using the Cockcroft-Gault formula. Further research is needed to construct methods to accurately and simply predict GFR and carboplatin clearance in the hope of improving the precision of carboplatin dosing.

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