Prospective Validation of Single Plasma Sample ^{99m}Tc-Ethylenedicysteine Clearance in Adults

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^{99m}Tc-L,L-ethylene, L, dicysteine (EC) clearance shows strong correlation with orthoiodohippurate clearance, and it is possible to estimate effective renal plasma flow from ^{99m}Tc-EC clearance. In routine clinical studies, it is practical to use the one or two plasma sample method instead of multiple plasma samples for clearance determination. A single-sample technique was developed for ^{99m}Tc-EC, and a regression formula was generated. A prospective study tested the validity of this regression formula. **Methods:** The study population was composed of 26 patients with a wide range of renal function. Multiple plasma sample ^{99m}Tc-EC clearances were calculated from all patients using the open two-compartment model. Single plasma sample clearances were also determined from the 54-min plasma sample using the regression formula published previously. **Results:** The multiple-sample plasma clearance of ^{99m}Tc-EC ranged from 46 to 668 mL/min with a mean of 300.76 ± 150.73 mL/min. The clearances obtained from the 54-min plasma sample ranged from 49 to 699 mL/min, with a mean of 297.39 ± 152.23 mL/min. There was an excellent correlation between the clearances obtained by the two techniques (r = 0.99, slope = 0.9911). The standard error of estimation was found to be 25.9 mL/min. **Conclusion:** This study suggests that ^{99m}Tc-EC clearance can be estimated from 54-min plasma samples with an acceptable error of estimation for most routine clinical studies.

Key Words: ^{99m}Tc-L,L-ethylene, L, dicysteine; radionuclide renography; effective renal plasma flow; renal function

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Technetium-99m-L,L-ethylene, L, dicysteine (EC) is a new technetium-labeled renal tubular tracer developed as an alternative to ^{99m}Tc-mercaptoacetyltriglycine (MAG3) (*1*). ^{99m}Tc-EC is a metabolite of the brain perfusion agent ethylensisteinedimer (*1–3*). Initial studies with ^{99m}Tc-EC gave promising results, and significant clinical experience has already been obtained (*4–13*). Studies in volunteers and patients have demonstrated that ^{99m}Tc-EC is a suitable replacement for orthoiodohippurate (OIH) and provides high-quality images and a low radiation dose to the patient. The labeling procedure is easy, radiochemical purity is high and the complex is stable for a long time. It is also suitable for clearance determinations. The strong correlation with OIH clearance allows estimation of effective renal plasma flow (ERPF) from ^{99m}Tc-EC clearance (*4,9–13*).

The renal function quantitation with renal radiolabeled agents is widely used. However, the multiple-sample method is not practical for quantitative routine renal function determination. To overcome this limitation, one- or two-plasma sample methods have been used as simple procedures sufficiently accurate for routine clinical use (*14,15*). A similar single-sample technique was also developed for ^{99m}Tc-EC, for which the optimal sampling time was found to be 54 min postinjection. A regression formula to estimate ^{99m}Tc-EC clearance from the 54-min plasma sample was also generated and published previously (*16*). This study investigates the validity of this theoretically derived regression formula.

MATERIALS AND METHODS

The study group was composed of 26 patients with a wide range of renal function (15 males, 11 females; age range 17–59 y). The study protocol was approved by the Medical Faculty Ethical Committee.

Subjects were injected with 25–100 MBq ^{99m}Tc-EC (Institute of Isotopes, Bucharest, Hungary). Injection was made through a three-way stopcock connected to an intravenous catheter and flushed with saline. Subsequently, seven blood samples were obtained from each patient, including a 54-min sample, over a period of 60 min. Blood samples were centrifuged, 0.2-mL plasma samples were weighted and plasma radioactivity (C) was determined by counting the samples in a well scintillation gamma counter. The injected dose (ID) was estimated from the weight difference of syringes before and after the injection and that of a standard activity prepared at the time of injection and diluted in 100–250 mL saline. The data were plotted against time and rate constants (α and β), and the intercepts (A and B) for slow and fast components were calculated using the biexponential curve fit analysis. An open two-compartment model suggested by Sapirstein et al. (*17*) was used for plasma clearance (Cl) determination:

$$Cl = \frac{ID \times \alpha \times \beta}{(A \times \beta) + (B \times \alpha)}. \quad \text{Eq. 1}$$

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Clearances from 54-min plasma samples were also calculated using the regression equation published previously (16):

$$Cl_{EC} = 1454.21 \times [1^{-(-0.00457\,((ID/C_{54}) - 3.55))}]. \quad \text{Eq. 2}$$

From the same data, clearances from 60-min plasma samples were also calculated, and these may be preferred for practical purposes, since the standard error of estimation was not significantly different (SEE = 33.70 mL/min) (16).

Statistical analysis was performed by Student t test and conventional regression analysis ($P < 0.05$, 95% confidence intervals).

RESULTS

The multiple-sample plasma clearance of ^{99m}Tc-EC ranged from 46 to 668 mL/min with a mean of 300.76 ± 150.73 mL/min. The clearances obtained from the 54-min plasma samples ranged from 49 to 699 mL/min, with a mean of 297.39 ± 152.23 mL/min (Table 1). There was an excellent correlation between the clearances obtained by the two techniques (r = 0.99, slope = 0.9911). The SEE was found to be 25.9 mL/min (Fig. 1). The clearances calculated from the 60-min plasma samples ranged from 48 to 672 mL/min (mean, 295.10 ± 152.47 mL/min) (Table 1). When we compared the 60-min clearances with multiple-sample clearances, there was again an excellent correlation (r = 0.99, slope = 0.9887). However, this time the SEE was slightly higher (29.2 mL/min) (Fig. 1).

TABLE 1
Multiple-Sample ^{99m}Tc-Ethylenedicysteine Clearances (Cl_{MS}) and Single-Sample ^{99m}Tc-EC Clearances Obtained from 54-Minute (Cl_{54}) and 60-Minute (Cl_{60}) Plasma Samples

Patient no.	Cl_{MS} (mL/min)	Cl_{54} (mL/min)	Cl_{60} (mL/min)
1	447	439	486
2	359	385	367
3	544	560	534
4	148	122	122
5	515	493	493
6	396	443	479
7	668	699	632
8	80	96	92
9	435	470	440
10	350	302	284
11	370	359	363
12	687	617	672
13	46	49	48
14	70	76	60
15	81	81	72
16	51	55	59
17	367	359	325
18	310	292	305
19	193	175	181
20	404	418	410
21	318	287	272
22	290	301	313
23	213	197	190
24	259	246	272
25	145	139	131
26	74	73	70
Average	300.76	297.39	295.10
SD	150.73	152.23	152.47

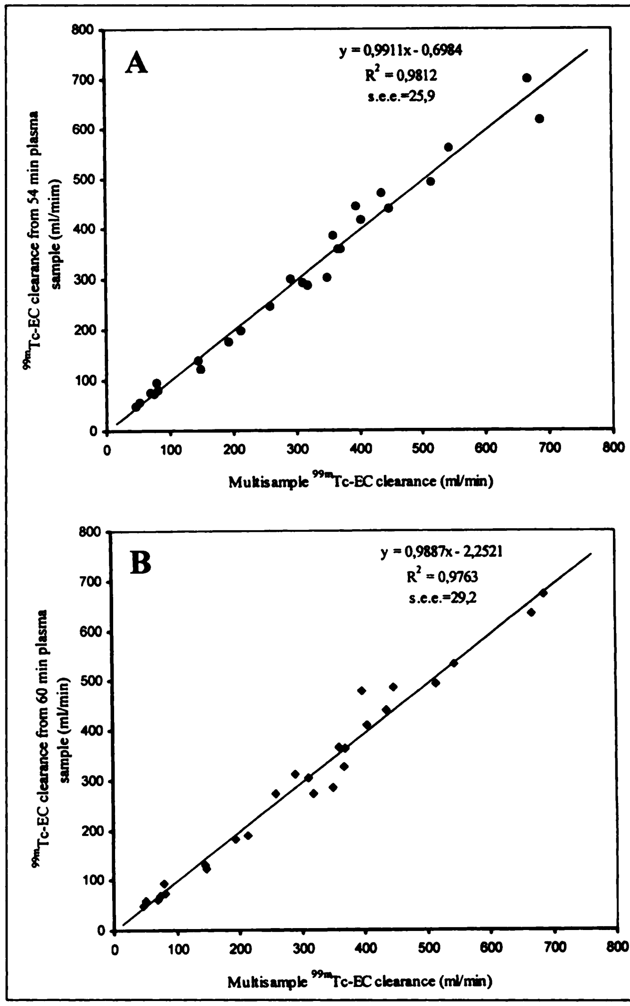

FIGURE 1. Correlation between multiple-sample and single-sample clearance determination techniques of ^{99m}Tc-EC. (A) 54-min plasma sample; (B) 60-min plasma sample.

DISCUSSION

Pharmacokinetic studies have demonstrated that ^{99m}Tc-EC more closely resembles OIH than does ^{99m}Tc-MAG3 (1–4,8–12). ^{99m}Tc-EC has biological behavior similar to OIH in both normal and depressed renal function. Almost similar ratios of ^{99m}Tc-EC with respect to OIH clearance values in healthy volunteers and in patients with renal disorders were reported (4,9–12,18). The plasma clearance of ^{99m}Tc-EC was found to be systematically higher than that of ^{99m}Tc-MAG3, by a value of 30%, and ^{99m}Tc-EC showed a strict correlation with OIH (1–4,9,18). The existence of a very strict correlation between ^{99m}Tc-EC and OIH clearances makes it possible to estimate ERPF from ^{99m}Tc-EC clearance (1–4,9–13,18).

However, the multiple plasma sample method for clearance determination is not practical. In adults, several algorithms are available that allow estimation of the renal clearances of ^{99m}Tc-MAG3 and OIH by means of one plasma samples obtained at 43 and 44 min after injection (*14,15*). Similarly, a regression formula was published previously for estimation of ^{99m}Tc-EC plasma clearance from a single plasma sample (*16*). The regression formula, mathematically derived from theoretical volume distributions, has shown that the optimal sampling time for least SEE is 54 min postinjection (SEE 32.7 mL/min). To test the formula, multiple-sample plasma clearances were compared with 54-min plasma clearances. The results of this prospective study show that the ^{99m}Tc-EC clearance calculated from 54-min samples closely approximates the multiple-sample clearance. Clearances obtained by the two methods show an excellent correlation. Furthermore, the SEE of the 54-min plasma sample clearance was lower than that of theoretical calculations (32.7 versus 25.9 mL/min).

CONCLUSION

This study suggests that ^{99m}Tc-EC clearance can be estimated from a single plasma sample with an acceptable error of estimation for most routine clinical studies (SEE 25.9 mL/min). Single-sample clearance determinations are sufficiently accurate and simple methods for routine clinical studies. However, accurate results depend on strict attention to the general guidelines for standard preparation, injection and blood sampling (*19*).

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