Comparison of Four Commercial Tc-99m(Sn)DTPA Preparations Used for the Measurement of Glomerular Filtration Rate: Concise Communication

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To find a commercially available DTPA preparation that could be used for the measurement of glomerular filtration rate (GFR), the plasma clearances of four different Tc-99m(Sn)DTPA preparations were compared with that of Cr-51 EDTA using a single-injection technique. One preparation yielded results identical to those obtained with Cr-51 EDTA, whereas the others underestimated the GFR to a varying degree. It is concluded that Tc-99m DTPA can be used to estimate the GFR, but that the accuracy will depend on the commercial source.

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Chromium-51 EDTA has gained wide acceptance for routine determination of glomerular filtration rate (GFR) using a single-injection method (*1,2*). Cr-51 EDTA is cleared only by the kidneys and the plasma clearance is practically identical to that of inulin (*2–4*).

Commercial tin-reduced preparations for instant delivery of Tc-99m DTPA (diethylenetriamine pentaacetic acid) have been on the market for several years. Only a few reports have been published on the use of Tc-99m DTPA for the estimation of GFR, and in only two reports were commercially available DTPA preparations used (*5,6*).

In a pilot study, the DTPA preparation used so far in our department yielded inaccurate clearance values compared with Cr-51 EDTA. We therefore decided to investigate the clearance of Tc-99m DTPA as prepared from four different commercially available preparations, using the clearance of Cr-51 EDTA as reference.

MATERIAL AND METHODS

One hundred and two patients with various levels of kidney function, referred for routine determination of the GFR, participated in the study. None had edema. They were confined to bed during the investigation. Eating, drinking, and smoking were allowed. Informed consent was obtained.

The single-injection method described by Bröchner-Mortensen was used (*7*). A catheter was placed in an antecubital vein, and a blood sample was taken for estimation of blood background. Approximately 100 μCi Cr-51 EDTA* and 1–2 mCi Tc-99m DTPA were injected simultaneously, the injected volume being determined by weighing the syringes before and after the injection. Each Tc-99m DTPA was prepared according to the instructions from its manufacturer. Four preparations were tested (A–D)† and several batches of each were used. The contents of the preparations are given in Table 1. [^{99m}Tc]pertechnetate was obtained from a 300-mCi Mo-99 → Tc-99m generator.*

Starting 3 hr after the injection, five blood samples were taken at intervals of approximately 30 min (exact time after injection noted). Two milliliters of plasma were counted together with three sets of technetium standards. Twenty-four hours later the same plasma samples were counted together with Cr-51 standards. Cross-talk was insignificant.

The numbers of patients examined with each preparation are given in Fig. 1. Only one preparation was used on each patient. The studies with the different preparations were performed concurrently, and the patients and preparations were allocated in such a way as to ensure that all levels of kidney function were investigated with each preparation.

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TABLE 1. CONSTITUENTS OF FOUR COMMERCIAL DTPA PREPARATIONS (DATA FROM THE MANUFACTURERS)

Preparation*	Compound	DTPA μmol/vial	$SnCl_2$ μmol/vial	mol DTPA / mol $SnCl_2$
A	$CaNa_3$-DTPA	18.2	2.04	8.9
B	Na_5-DTPA	9.9	1.32	8.3
C	$CaNa_3$-DTPA	20.1	2.22	9.1
D	H_5-DTPA	61.0	16.8	3.6

* A: Cea Ire Sorin, Gif-sur-Yvette, France; B: Diagnostic Isotopes, Bloomfield, NJ; C: New England Nuclear, Boston, MA; D: Solco Nuclear, Basle, Switzerland.

Assuming a one-pool system, the clearance was calculated according to the equation

$$Cl = \frac{Q_0}{\int_0^\infty C_p(t)dt} = \frac{Q_0}{\int_0^\infty Y_0 \cdot e^{-\beta t}dt} = \frac{Q_0}{Y_0} \cdot \beta$$

where Q_0 is the total activity injected, $C_p(t)$ the plasma activity at time t, Y_0 is the intercept, and β the final plasma clearance rate constant. β and Y_0 were calculated by the method of least squares. Clearance values have not been corrected for overestimation due to the assumption of a one-pool system (*7*).

The clearance values obtained with the four DTPA preparations were plotted against the corresponding Cr-51 EDTA clearance values (Fig. 1) and the regression line for each set of observations was calculated by the method of least squares (Table 3).

Standard statistical methods were used (*8*). Differences were considered significant if $2P < 0.05$.

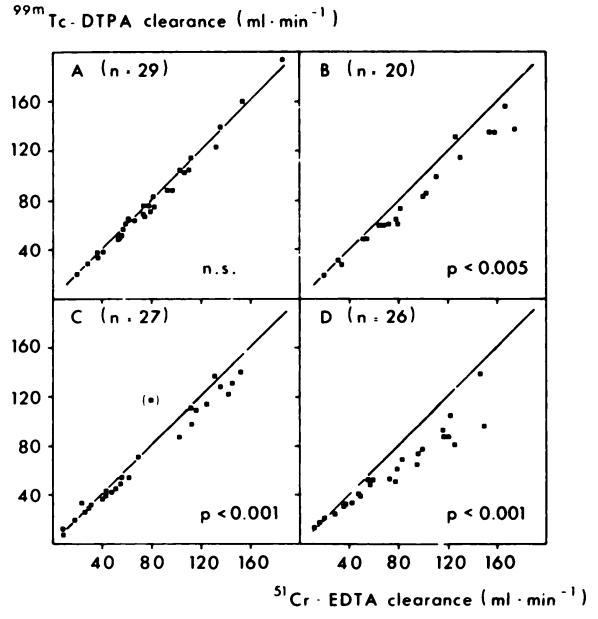

FIG. 1. Plasma clearances of Tc-99m DTPA (preparations A–D) plotted against plasma clearance of Cr-51 EDTA. Number of patients for each preparation is given. Each P value denotes level of statistical significance of difference between slope of regression line for each set of observations and line of identity (solid line).

RESULTS

Table 2 shows the mean plasma clearances of Tc-99m DTPA and Cr-51 EDTA in the four groups, and the standard deviation of the estimated mean plasma clearance value of Tc-99m DTPA. The mean plasma clearance of preparation A did not differ from that of Cr-51 EDTA ($P > 0.1$), whereas the mean clearances of the other preparations were significantly smaller than the corresponding Cr-51 EDTA value (Table 2).

Table 3 gives the linear regression equations and correlation coefficients for the sets of data plotted in Fig. 1. The regression line for preparation A has unity slope ($P > 0.1$), whereas the other slopes are significantly less than 1.

The variance around each regression line was calculated. Preparation A had the lowest variance, though it was not significantly different from that of preparation C. The variances for preparations B and D were significantly larger than that of preparation A.

Figure 2 shows the final rate constants for plasma clearance obtained with the four DTPA preparations, plotted against that for Cr-51 EDTA. Linear regression has not been performed since the points obviously do not fall on a straight line. At high values the points deviate from the line of identity, i.e. the final disappearance rate constants of Tc-99m DTPA are smaller than those of Cr-51 EDTA. This applies to all four DTPA preparations.

DISCUSSION

For a compound to be suitable for the measurement of GFR, it is necessary to show that the GFR measured with the new agent is the same as that measured simul-

TABLE 2. MEAN PLASMA CLEARANCES OF FOUR Tc-99m DTPA PREPARATIONS (WITH s.d. OF MEAN) AND OF Cr-51 EDTA

Preparation	Cl_{DTPA} (ml) min^{-1}	s.d.m.	$\overline{Cl}_{EDTA}$ (ml) min^{-1}	P*
A	78.9	0.83	80.1	n.s.
B	81.5	1.61	92.3	< 0.001
C	68.0	1.08	72.4	< 0.001
D	58.6	1.68	74.5	< 0.001

* P value denotes level of significance of the difference between the mean clearance of Tc-99m DTPA and Cr-51 EDTA.

TABLE 3. ESTIMATED PARAMETERS (± s.d.) FOR THE REGRESSION EQUATION $Cl_{DPTA} = a + b \times Cl_{EDTA}$ COMPARING CLEARANCES OF FOUR Tc-99m DTPA AGENTS WITH THAT OF CR-51 EDTA; WITH COEFFICIENTS OF CORRELATION

Preparation	b	a	Coefficient of correlation
A	1.04 ± 0.021	−4.1 ± 1.9	0.994
B	0.87 ± 0.035	1.4 ± 3.7	0.985
C	0.91 ± 0.023	2.2 ± 2.0	0.992
D	0.73 ± 0.041	4.2 ± 3.5	0.963

taneously with an accepted agent, using the same method. The method of Bröchner-Mortensen for estimation of the GFR is both precise and accurate (*9*). The assumption of a one-pool system is an oversimplification, but this does not matter when one is simply comparing two compounds.

For all preparations, Tc-99m DTPA plasma clearance was highly correlated with Cr-51 EDTA plasma clearance. Nevertheless, the accuracy varied, and correct clearance values for the whole range of kidney function were obtained only with preparation A. Furthermore, the variances of the results obtained with the four preparations differed. Preparation A was also superior in this respect. As the method applied was the same for all preparations, the difference in variance is most likely ascribable to differences in the homogeneity of the products.

Klopper et al. (*10*) found that Tc-99m DTPA underestimated the GFR by about 8% as compared with I-125 iothalamate, but their DTPA was not a commercially available preparation. Hilson et al. (*5*) have compared the plasma clearance of Tc-99m DTPA (preparation B) with that of Cr-51 EDTA. In order to obtain identical results they had to use a correction factor of 0.964 for DTPA and 0.87 for EDTA, and consequently the clearance of Tc-99m DTPA must have been about 11% lower than that for Cr-51 EDTA. This agrees with our finding of approximately 13% for preparation B. Rossing et al. (*6*) compared the clearance of Tc-99m DTPA (preparation C) with that of Cr-51 EDTA, using exactly the same technique as ours, and found the clearances to be identical. Their data were corrected for the overestimation of GFR due to the assumption of a one-pool system, and only two clearance values above 100 ml/min were obtained. If we correct our data in the same way, we have six clearance values above 100 ml/min, and this may explain the difference between their data and ours. For clearance values below 100 ml/min, we find that preparation C is just as good as preparation A in estimating the GFR, whereas for values above 100 ml/min, preparation C runs 7% below the

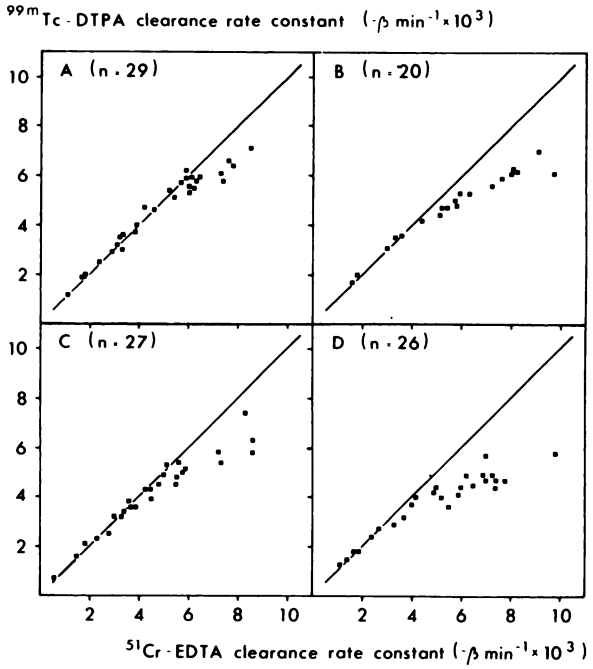

FIG. 2. Comparison of final rate constants for plasma clearances of Tc-99m DTPA (preparations A–D) and Cr-51 EDTA. Number of patients for each preparation is given. Solid line is line of identity.

corresponding Cr-51 EDTA clearance. This does not apply to preparation A.

Three batches of preparations A and C have been investigated for in vitro protein binding, and 0.4%, and 1.8%, respectively, were found. This may account for the difference seen, since the influence of protein binding increases at high clearance values. On the other hand, factors such as generator-kit compatibility and batch-to-batch variation may also be of importance.

In vitro radiochemical analyses of the different preparations fail to explain the differences seen in vivo. The DTPA ligands in the preparations are not identical. Preparations A and C contain $CaNa_3$-DTPA; preparation B Na_5-DTPA; and preparation D, the acid form of DTPA. All the preparations have a labeling yield over 99%. The analysis gives no clue as to why the disappearance rate constants are smaller for Tc-99m DTPA than for Cr-51 EDTA at high values. The most likely explanation is protein binding.

From our results we have concluded that Tc-99m DTPA can be used to estimate the GFR, but that the source of the preparation affects the accuracy of the result.

FOOTNOTE

* Amersham

† A: Cea Ire Sorin, Gif-sur-Yvette, France; B: Diagnostic Isotopes, Bloomfield, NJ; C: New England Nuclear, Boston, MA; D: Solco Nuclear, Basle, Switzerland.

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