Prospective Validation of a Single Sample Technique To Determine Technetium-99m-MAG3 Clearance

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METHODS

The study population consisted of 34 consecutive patients in whom technically satisfactory multiple sample $^{99mTc}$-MAG3 clearances were obtained. None of the patients had ascites or marked edema. The $^{99mTc}$-MAG3 studies were approved by the Institutional Review Board.

Sixteen patients were studied using an HPLC-purified preparation of $^{99mTc}$-MAG3 and 18 patients were studied using a commercial preparation (1,2,8). Radiochemical purity of the kit formulation was determined by miniaturized-column chromatography (Sep-Pak, Waters Associates) and averaged 99.4% ± 0.5%; unpublished results in our laboratory indicate that Sep-Pak chromatography overestimates radiochemical purity as compared to high-performance liquid chromatography (HPLC). In all patients, 6-11 plasma samples were obtained from 9 to 60 min postinjection; in 28 patients, an early sample was obtained 4-5 min postinjection. Clearances were calculated based on a single injection, two-compartment model (14). The clearance was also calculated using the published regression equation based on a single plasma sample obtained approximately 43 min postinjection.

RESULTS

One patient had a multiple sample clearance of approximately 600 ml/min compared to a single sample clearance of 351 ml/min. However, since none of the multiple-sample $^{99mTc}$-MAG3 clearances exceeded 450 ml/min in the group of patients used to derive the regression equation (11), this patient was excluded from further analysis. In the remaining 33 patients, there was excellent correlation between the two measurements ($r = 0.976$; slope = 1.01) with a standard error of the estimate of 24 ml/min. Figure 1 shows the single sample $^{99mTc}$-MAG3 clearance plotted against the multiple sample clearance; the solid line is the line of identity.

To determine if there were any differences between the HPLC-purified $^{99mTc}$-MAG3 and kit formulation, we analyzed each data set separately. There was no significant difference in the correlation coefficients (0.976 versus

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To determine if there were any differences between the HPLC-purified $^{99mTc}$-MAG3 and kit formulation, we analyzed each data set separately. There was no significant difference in the correlation coefficients (0.976 versus
0.981) or the slopes (0.97 versus 1.01) for the HPLC or kit formulations respectively.

The published regression equation was derived with the first sample beginning at approximately 10 min postinjection (11); other studies have obtained the first plasma sample approximately 4 min postinjection (2,7,8). To determine the effect of the early sample, we compared the 4–60 min multiple sample clearances with the 9–60 min multiple sample clearances and found no significant difference in the results (Fig. 2). The correlation coefficient was 0.99 and the standard error of the estimate was 12.8 ml/min.

DISCUSSION

The single-sample procedure is technically straightforward, but it does require meticulous attention to detail to obtain accurate results. An image should be obtained over the injection site to exclude infiltration because infiltration of the dose can invalidate the results. Pipetting, dilutions and preparation of standards must be performed with care. Well counters can be easily overloaded by levels of radioactivity used for imaging techniques; overloading the well counter will lead to deadtime losses and erroneous results. The plasma sample should not be drawn form the same catheter used to administer the $^{99m}$Tc-MAG3. Furthermore, plasma samples should be obtained as close to 43 min as possible and the time should be accurately recorded.

The optimal sample time for single-sample clearance methods depends on the level of renal function. When renal function is good, the plasma sample can be obtained closer to the time of injection. When renal function is poor, or when clearances are slow as they are for $^{99m}$Tc-DTPA, longer sample times are needed (11–13,15). As previously described, the optimal time of 43 min was derived mathematically from the original sample population and is a good value to use when function is not known in advance (11). A more accurate two-sample method to determine $^{99m}$Tc-MAG3 clearance is available, but it requires plasma samples at 12 and 94 min postinjection and essentially doubles the time the patient needs to remain in the department (11).

The accuracy of the single-sample method for determining the $^{99m}$Tc-MAG3 clearance is quite similar to the accuracy of the $^{99m}$Tc-DTPA and the $[^{31}]$IOH single-sample methods (13,15,16). By using 125 ml/min as the normal GFR, 600 ml/min as the normal ERPF and 370 ml/min as the normal $^{99m}$Tc-MAG3 clearance, the percentage errors for the three single-sample techniques are 5.5% for $^{99m}$Tc-MAG3, 6.5% for $^{99m}$Tc-DTPA and 8.0% for $[^{31}]$IOH (11). In summary, with the exception of patients with unusually high $^{99m}$Tc-MAG3 clearances, the single-sample estimate closely approximates the multiple-sample clearance and this technique can be used in the clinical setting with an accuracy comparable to the single-sample techniques for OIH and $^{99m}$Tc-DTPA.

APPENDIX

Sample Calculation for Single-Sample Method

A plasma sample obtained at 44 min postinjection had $1.49 \times 10^6$ cpm/liter. The dose injected was $6.07 \times 10^7$ cpm. By using the published formula (below), the following values can be calculated using a hand calculator (11):

$$\text{MAG3 clearance (ml/min)} = F_{\text{max}}(1 - \exp(-\alpha(1/c - V_{\text{lag}})))$$

where

- $c$ = fraction of dose per liter of plasma, liter$^{-1}$
- $t$ = time between injection and withdrawing of sample in minutes
- $F_{\text{max}} = 0.04 t^2 - 8.2 t + 915$ ml/min
- $\alpha = 6.5 \times 10^{-6} t^2 - 8.6 \times 10^{-4} t + 3.91 \times 10^{-2}$ liter$^{-1}$
- $V_{\text{lag}} = -0.0015 t^2 + 0.01 t + 8.79$ liter.
The calculated clearance is in ml/min. The optimal sample time is 43 min. The plasma sample must be obtained between 35 and 55 min. A sample calculation is also provided in (11).

\[
c = 0.0246 \text{ liter}^{-1}
\]

\[
F_{\text{max}} = 631.6 \text{ ml/min}
\]

\[
\alpha = 1.258 \times 10^{-2} - 3.784 \times 10^{-2} + 3.91 \times 10^{-2} = 0.0138 \text{ liter}^{-1}
\]

\[
V_{\text{inf}} = -2.904 + 0.44 + 8.79 = 6.33 \text{ liter}
\]

\[
e^{-\alpha t + \sqrt{\alpha^2 V_{\text{inf}}}} = e^{-0.138(40.71-6.33)} = 0.622
\]

MAG3 clearance = 239 ml/min.

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REFERENCES


