Single-Sample Effective Renal Plasma Flow Determination with Technetium-99m-MAG3, Not Requiring a Standard

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Objective: There exists a variety of methodologies for the quantitation of effective renal plasma flow (ERPF) with ^{99m}Tc-MAG3, from very accurate in vitro techniques to less accurate, yet reliable and easy gamma camera methods. This study compares a new technique that uses a single blood sample but does not require the preparation of a standard, with the in vitro single sample ERPF determination (Tauxe).

Methods: Thirty ERPF determinations were made by both techniques. One strictly followed the Tauxe methodology. In the second technique, the Tauxe method was modified slightly by deleting the need for standards in the calculation of the theoretical volume of distribution (Vt). In this technique, the dose activity injected was measured in cpm, and the plasma activity concentration was determined in cpm/liter, from which Vt was calculated in order to determine the ERPF. Cesium-137 and ^{57}Co sealed sources were used for gamma well counter constancy checks.

Results: There was a significant correlation between the ERPF values from both modalities (r = 0.98, p = 0.012).

Conclusion: This simplified technique can be used to reliably determine ERPF, with the accuracy of a plasma sample technique, yet with the simplicity of not requiring standards for each patient.

Key Words: effective renal plasma flow; technetium-99m-MAG3; Tauxe method

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The use of exponential regression curves to arrive at a general formula derived from a single-injection/compartment analysis technique has greatly simplified the determination of effective renal plasma flow (ERPF). They are based on the orthoiodohippurate (OIH) concentration in a single plasma sample at a given time postinjection being inversely related to the total ERPF (*1*). With the introduction of ^{99m}Tc-mercaptoacetyltriglycine (MAG3, Mallinckrodt Medical, Inc., St. Louis, MO) as a replacement for OIH, these formulas have been modified by the application of a correction factor, which has varied greatly in the literature, in order to be used with the new pharmaceutical (*2–6*).

These in vitro techniques however, require meticulous attention, and because of the work involved, camera-based methods may become more popular although their accuracy has been questioned (*7–9*).

The aim was to determine if ERPF quantitation could be achieved with the accuracy of the single-sample technique, without the required preparation of standards for each patient as described in the literature (*10*). This study tests for agreement between the two methods.

MATERIALS AND METHODS

The study population consisted of 30 patients randomly selected from a previous Tauxe study (*6*), with already known MAG3 ERPF values.

The count rate per microcurie of the injected dose was determined for the well counter (NaI crystal Picker Nuclear well counter with a Picker spectroscaler 4R single channel analyzer, Crystal size 2″ × 2″, Picker International, Bedford, OH), using a National Institute of Standards and Technology (NIST) traceable ^{99m}Tc source and its constancy and efficiency were checked and followed with sealed ^{137}Cs and ^{57}Co sources.

The plasma activity was converted to net well counter readings per liter (cpm/liter), the net total activity injected was also converted to net well counter readings (cpm), from which Vt was calculated in order to determine the ERPF (*3,5*).

The actual sample calculations of ERPF are described in the Appendix. Data analysis consisted of using the Student's paired t-test, the Pearson correlation coefficient (r) and simple linear regression.

RESULTS

A plot of the estimated ERPFs is shown in Figure 1, along with the linear regression equation y = 0.99x + 15.66. The standard error of the estimate (s.e.e.) was 29.0 ml/min. Additional results of the statistical data analysis are listed in Table 1. The global ERPF values obtained with the new

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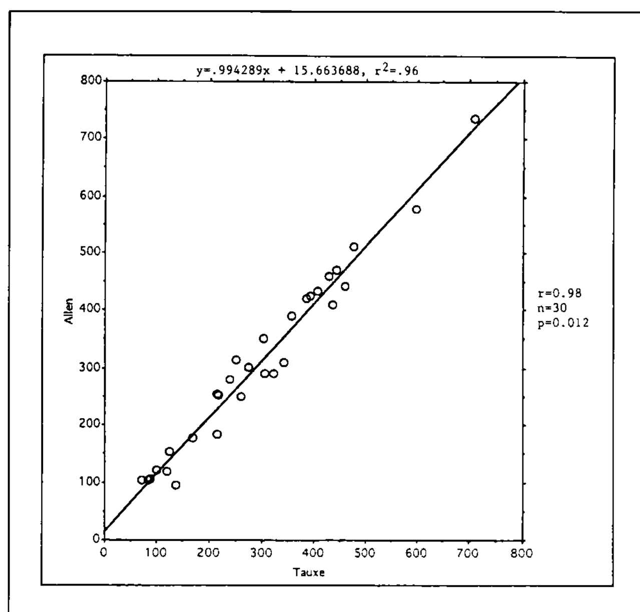

FIGURE 1. Correlation between the determined ERPF using both techniques.

technique were highly correlated with the Tauxe method, r = 0.98, p = 0.012. These values are listed in Table 2.

DISCUSSION

Renal procedures that require up to six or more samples to determine ERPF generally are not considered practical for routine clinical use, although these methods are certain to be the most accurate. The renal clearance of para-aminohippurate (PAH), using the classic constant infusion technique, serves as a "gold standard" for the nephrologist and the renal physiologist, with a s.e.e. of 30–34 ml/min (*3,13*).

Among the more practical clinical in vitro methods is the two-plasma sample technique, usually drawn at 12 and 94 min for MAG3, which has shown excellent correlation with PAH clearance, r = 0.90, p < 0.01 (*9,11,12*). Improvement in the formula by updated coefficients, have increased the correlation with PAH to r = 0.95, p < 0.01, and reduced the s.e.e. to 8 ml/min, although it seems to overestimate the ERPF by 10%–15% (*11,12*).

The single-plasma technique, although slightly less accurate, has also gained wide acceptance, with optimum sampling time at approximately 43 min, and a s.e.e. of 20–25 ml/min. The comparison correlations are r = 0.95 for PAH (*3,11,13*) and r = 0.98 for the two-plasma sample technique. The s.e.e. between the single-plasma and two-plasma sample technique is 42 ml/min (*9*). These two in vitro techniques have been adapted for MAG3, however they still require the proper preparation of standards (*5,7,11*).

Because of the labor involved in the preparation of standards and the meticulous care that goes along with it, many nuclear medicine departments do not perform quantitative renal analysis. When such analyses are done, most personnel rely on the in vivo camera methods. Although their accuracy has been questioned, in vivo methods are more popular than the in vitro techniques because they avoid the need of a delayed plasma sample and the rigorous in vitro preparations (*8,9*). These camera-based methods are also varied. They include the Schelegel method for OIH and modified for MAG3 (*6,14*), two-compartment analysis of the cardiac curve, deconvolution analysis of the left ventricle, clearances determined from the cardiac or renal curves and gamma variate fit to the ratio of counts in the initial bolus-to-the counts at 24 min over the aorta. These methods have correlation coefficients ranging from r = 0.76 to r = 0.93, and a s.e.e. ranging from 27 to 63.5 ml/min, when compared to

TABLE 1
Student's t-test Statistics for Paired Data

	Mean	s.d.	95% Confidence Interval
Tauxe (with standard)	297.13	157.22	[240.87, 353.40]
Allen (without standard)	311.10	158.90	[251.76, 370.44]
Difference	−13.97*	5.21	[−24.18, −3.76]

*2-tailed paired t-test p-value for the difference is p = 0.012.

TABLE 2
Global ERPF Values for MAG3 (ml/min)

Patient no.	In vitro single sample procedure: Tauxe method	Allen method
1	476	510
2	126	154
3	101	120
4	459	441
5	305	291
6	249	314
7	303	351
8	384	421
9	217	252
10	238	280
11	341	311
12	355	391
13	213	254
14	260	250
15	392	424
16	138	95
17	441	471
18	434	410
19	323	291
20	215	184
21	406	433
22	708	736
23	167	177
24	83	104
25	427	459
26	88	106
27	120	119
28	275	302
29	597	578
30	73	104

the in vitro technique (*15–18*). These curve analyses are done in attempts to improve the camera method, without relying on plasma or urine samples or corrections for photon attenuation, in order to arrive at more accurate ERPF values. Even with the excellent results from the newest camera method, which calculates the renal clearance and converts it to ERPF, many still doubt that in vivo camera methods can be as accurate as in vitro techniques (*6,9,19*).

Our study seeks to find if a compromise between the in vitro and the in vivo camera methods could be achieved. Although statistically the ERPF is different between the two techniques ($p = 0.012$), in the clinical setting that difference (-13.97 ± 5.21) is not substantial. The new technique (*10*) was used to calculate the ERPF on our data. The results showed good agreement with the values obtained with the single-plasma sample (Tauxe). If desired, selective kidney ERPF is determined by multiplying the global ERPF by the percent of kidney uptake derived from the renal curves.

CONCLUSION

In summary, the results of our initial work demonstrate the potential for this approach, and suggest that ERPF can be determined with the accuracy of the in vitro single-plasma technique. This new approach does not require standards for each patient, nor the necessary corrections for the sources of error associated with the camera method. However, additional studies need to be done to verify the validity of this technique and to try to optimize it. A prospective study is currently under way in our laboratory.

APPENDIX

Sample calculation for the in vitro techniques
Patient 1:

$$\text{Net } \mu\text{Ci injected} = 2031\ \mu\text{Ci}$$

$$\mu\text{Ci D-Std} = 910\ \mu\text{Ci}$$

$$\text{Net cpm P-Std} = 11{,}545\ \text{cpm}$$

$$\text{Net cpm/2 ml plasma} = 39{,}612 \times 0.67 = 26{,}540\ \text{cpm}$$

$$\text{Well counter count rate} = 553{,}444\ \text{cpm per } \mu\text{Ci of } ^{99m}\text{Tc}$$

Sample drawn at 45 min

Tauxe Technique

$$V_t = \frac{80(\mu\text{Ci injected})(\text{cpm P-Std})}{(\mu\text{Ci D-Std})(\text{plasma cpm})}$$

$$V_t = \frac{80(2031)(11545)}{(910)(26540)}$$

$$V_t = 77.67\ \text{liters}$$

$$\text{ERPF} = F_{max}[1 - e^{-\alpha(V_t - V_{lag})}]$$

$$\text{ERPF} = 1131.49[1 - e^{-0.0078(Vt - 7.68)}]$$

$$\text{ERPF} = 476\text{ml/min}$$

Allen Technique

$$V_t = \frac{(\mu\text{Ci injected})(\text{cpm per } \mu\text{Ci})}{(\text{plasma cpm per liter})}$$

$$V_t = \frac{(2031)(553)K}{(26540/0.002)}$$

$$V_t = 84.64\ \text{liters}$$

$$\text{ERPF} = F_{max}[1 - e^{-\alpha(V_t - V_{lag})}]$$

$$\text{ERPF} = 1131.49[1 - e^{-0.0078(Vt - 7.68)}]$$

$$\text{ERPF} = 510\text{ml/min}$$

The net microcuries injected was determined by assaying the full syringe in the dose calibrator immediately prior to, and right after injection and making the appropriate substraction.

We started with 2 ml (to approximate the volumes of the pharmaceutical injected, volume of the dose used to prepare the standard, volume of the patient standard, and the volume of the patient plasma sample, used in the Tauxe method) of solution with a known activity. And then proceeded to decay it to approximately $<1/4$ of a microcurie. Keeping all geometries constant, it was counted for 5 min in the well counter and then converted to cpm per microcurie.

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