The Effect of Iodinated Contrast Media on Technetium-99m Red Blood Cell Labeling

Wilhelm J. Mayer and Joan Berezowsky

South Saskatchewan Hospital Center, Regina, Saskatchewan

This paper investigates the effect of iodinated contrast media on labeling of red blood cells with [^{99m}Tc]pertechnetate. Although many factors, including presence of plasma, may reduce binding, iodinated contrast media do not appear to have this effect. Multiple drug therapy may explain some cases of reduced labeling.

The advent of new ^{99m}Tc red blood cell (RBC) labeling techniques has been important in the rapid growth of cardiovascular imaging over the past decade. Three labeling techniques commonly employed are in vitro (*1*), in vivo (*2*), and the modified in vivo or in vivo/vitro (*3*). The in vitro method produces high quality tagging, but is labor-intensive and involves an added risk to patients if samples are switched (*4*). The in vivo technique, while simple and safe, exhibits variable labeling. The third method, however, utilizes the advantages of both previous techniques, but binding efficiency may occasionally be erratic.

The inconvenience to patients and staff, as well as the additional costs resulting from inconsistent binding, prompted us to review the factors known to influence RBC labeling. Temperature, stannous ion concentration, hematocrit, RBC antibodies, and various drugs including heparin, methyldopa, hydralazine, digoxin, prazosin, and sulfonamides have been shown to affect the kinetics of labeling (*5–11*). Most of our patients exhibiting poor tagging were polypharmaceutical recipients with multiple medical problems. Drug effects were considered pertinent but poorly understood.

Tatum, et al. (*12*) have implicated iodinated contrast media (ICM) as a direct causative factor in poor quality labeling. A study was therefore undertaken to assess the effect of such media on RBC labeling with ^{99m}Tc.

MATERIALS AND METHODS

Thirty patients (22 male and 8 female; ages 27 to 74) undergoing cardiac catheterization consented to the taking of blood samples before and after the procedure. The amount of ICM* administered ranged from 56 to 304 ml.

In vitro ^{99m}Tc tagging was achieved with a modified Smith and Richards technique (*1*). Just before and immediately after cardiac catheterization, 16 ml of whole blood was drawn from each patient into ACD† anticoagulant (*13*). A portion of each sample was spun for 10 min at high speed in a centrifuge‡ at 1,500 G to allow the separation of plasma for later use.

Freshly prepared stannous pyrophosphate§ (PYP) was added to the remaining whole blood to produce a concentration of 0.15 μg stannous ion per milliliter of blood. Following 5 min of incubation at room temperature, the tube of blood was then spun upside down for 10 min at high speed. Packed tinned red cells were removed, washed with normal saline, and spun upright as before. The wash was discarded. Packed tinned red cells (0.5 ml) were added to tubes containing either 0.5 ml of previously prepared plasma or 0.5 ml of normal saline.

Following the addition of ~ 100 μCi (3.7 MBq) of [^{99m}Tc] pertechnetate, each tube was maintained at room temperature for 5 min. The reaction was halted by the addition of 50 μg of stannous ion as PYP and 5 ml of saline. The cells and supernatant were separated by centrifugation and assayed using a dose calibrator to determine percent binding using the following formula:

$$\%\text{binding} = (\text{RBC activity} \times 100) / \text{total activity}$$

All samples were done in duplicate. Statistical analysis was achieved using a paired t-test to determine the significance of the different labeling efficiencies. A chi-square test was used to determine relationships between variables. A p value of < 0.05 was considered significant.

RESULTS

In the presence of plasma, binding was 54 ± 15% (mean ± s.d.) with a range of 31–92% before contrast. After contrast, binding was 56 ± 11% with a range of 36–82%. When saline replaced plasma, binding increased to 76 ± 12% (range 57–99%) before contrast and 76 ± 11% (range 58–99%) after contrast. As shown in Table 1, RBC labeling was insignificant-

For reprints contact: W.J. Mayer, Nuclear Medicine Department, Pasqua Hospital, 4101 Dewdney Ave., Regina, Saskatchewan, Canada S4T 1A5.

ly altered following injection of ICM. Mean percent binding in pre- and postcardiac catheterization samples was nearly identical.

Labeling in the presence of plasma (as compared to that of normal saline) was significantly lower ($p < 0.001$) both before and after contrast. The binding efficiency was independent of sex, age, and the volume of contrast injected.

DISCUSSION

These results indicate that ICM are unlikely to adversely affect RBC labeling performed with the usual techniques. Tatum, et al. (*12*) reported three cases of poor quality images following ICM exposure and recommended that patients requiring ^{99m}Tc blood-pool studies be scheduled before the use of contrast. Our results suggest that this precaution seems unjustified.

Binding efficiencies found in this study were usually lower than those found in healthy volunteers taking no drugs. Drug interference is a plausible explanation for at least part of this discrepancy. Multiple drug therapy was identified in 27 of the 30 patients in this study.

The presence of plasma inhibited labeling. Whereas plasma proteins are known to bind [^{99m}Tc]pertechnetate (*14*), thereby reducing the amount available for uptake by protein in the red cell (*15*), it is unknown whether other plasma constituents play a role.

Red blood cell labeling is a complex process affected by numerous extrinsic and intrinsic factors. We feel that there is no need to consider exposure to iodinated contrast as a strong factor influencing scheduling of blood-pool studies. Drug therapy does seem to be important and more research in this area may help to reduce problems in the clinical setting.

TABLE 1. Percent Red Cell Binding

Patient No.	Volume of Contrast (ml)	Plasma Solution		Saline Solution	
		Pre-Contrast	Post-Contrast	Pre-Contrast	Post-Contrast
1	148	48	47	61	70
2	98	65	69	85	76
3	83	42	54	78	70
4	191	41	61	65	76
5	96	52	56	73	78
6	126	56	49	85	68
7	83	53	60	75	81
8	118	39	43	61	60
9	91	37	47	61	67
10	96	37	41	61	61
11	96	44	44	63	65
12	106	41	46	65	64
13	56	46	46	72	64
14	86	41	49	65	68
15	96	53	69	80	89
16	164	50	47	76	72
17	304	50	52	70	69
18	126	50	57	73	75
19	91	31	36	57	58
20	96	52	55	80	82
21	161	64	54	82	78
22	96	58	62	85	85
23	86	83	69	95	85
24	106	92	73	99	89
25	111	57	76	82	95
26	126	76	82	94	94
27	96	82	63	98	99
28	176	49	55	75	82
29	96	63	65	83	83
30	114	53	57	83	83
Mean ± s.d.	—	54 ± 15	56 ± 11	76 ± 12	76 ± 11

FOOTNOTES

*MD-76, Mallinckrodt Inc., St. Louis, MO.
†Special Formula, Frosst Radiopharmaceuticals, Kirkland, Quebec, Canada.
‡Clinical, International Equipment Co., Needham Hts., MA.
§Technescan PYP, Mallinckrodt Inc., St. Louis, MO.

REFERENCES

1. Smith TD, Richards P. A simple kit for the preparation of Tc-99m labeled red blood cells. *J Nucl Med* 1976;17:126–32.
2. Pavel DG, Zimmer AM, Patterson VN. In-vivo labeling of red blood cells with Tc-99m: A new approach to blood pool visualization. *J Nucl Med* 1977;18:305–8.
3. Callahan RJ, Froelich JW, McKusick KA, et al. A modified method for the in-vivo labeling of red blood cells with Tc-99m. *J Nucl Med* 1982;23:315–18.
4. Mollison PL. *Blood Transfusion In Clinical Medicine,* 5th Ed. Oxford, Blackwell Scientific Publications, 1972, pp 571–617.
5. Hegge FN, Hamilton GW, Larson SM, et al. Cardiac chamber imaging: A comparison of red blood cells labeled with Tc-99m in vitro and in vivo. *J Nucl Med* 1978;19:129–34.
6. Leitl GP, Drew HM, Kelly ME, et al. Interference with Tc-99m labeling of red blood cells (RBCs) by RBC antibodies. *J Nucl Med* 1980;21:P44.
7. Chervu LR, Castronuovo JJ, Huq SS, et al. Alterations in red cell tagging with sulfonamides. *J Nucl Med* 1981;22:P70.
8. Chervu LR, Huq SS, Joseph JA, et al. Medication induced changes in biodistribution of radiopharmaceuticals. *J Nucl Med* 1981;22:P72.
9. Callahan RJ, Froelich JW, McKusick KA, et al. Factors affecting the rate and extent of incorporation of Tc-99m into pre-tinned red blood cells. *J Nucl Med* 1982;23:P109.
10. Hladik WB, Nigg KK, Rhodes BA. Drug-induced changes in the biologic distribution of radiopharmaceuticals. *Semin Nucl Med* 1982;12:184–218.
11. Lee H, Wexler JP, Scharf SC, et al. Pharmacologic alterations in Tc-99m binding by red blood cells. *J Nucl Med* 1983;24:397–401.
12. Tatum JL, Burke TS, Hirsch JI, et al. Pitfall to modified in-vivo method of technetium-99m red blood cell labeling—iodinated contrast media. *Clin Nucl Med* 1983;8:585–87.
13. Porter WC, Dees SM, Freitas JE, et al. Acid-citrate-dextrose compared with heparin in the preparation of in-vivo/in-vitro technetium-99m red blood cells. *J Nucl Med* 1983;24:383–87.
14. Miller W. Technetium-99m biorouting. In *Textbook of Nuclear Medicine Technology,* 3rd ed, Early PJ, Razzak MA, Sodee BD, eds, St. Louis, CV Mosby, 1979, pp 544–70.
15. Dewanjee MK. Binding of Tc-99m ion to hemoglobin. *J Nucl Med* 1974;15:703–6.