nm/CONCISE COMMUNICATION

COMPARATIVE MYOCARDIAL UPTAKE AND CLEARANCE CHARACTERISTICS OF POTASSIUM AND CESIUM

Norman D. Poe

Center for Health Sciences, and Laboratory of Nuclear Medicine and Radiation Biology, University of California, Los Angeles, California

Myocardial scanning is potentially an important clinical tool for localization and quantitation of damaged cardiac tissue. Early attempts at scanning with potassium analogs, while encouraging, did not prove satisfactory because of the unsuitable gamma energies of available radionuclides (*1,2*). Recently, two new radionuclides have become accessible: ^{43}K and ^{129}Cs (*3,4*). Both have relatively short half-lives and dominant gamma emissions in the ^{131}I range. Because these two nuclides can be produced by the newly installed UCLA Biomedical Cyclotron, laboratory investigations in dogs were undertaken to compare the uptake and clearance characteristics of potassium and cesium after intravenous and coronary arterial injection. Observations were made with the prospect of using one or both of these agents for quantitative measurements of regional myocardial blood flow and function.

MATERIALS AND METHODS

Experiments were performed using ^{42}K and ^{131}Cs. When both radionuclides were to be compared, they were mixed and administered as a single solution. In vivo clearance data were obtained in medium-sized mongrel dogs under 30-mg/kg pentobarbital anesthesia. Recordings were made with the animals in the right lateral decubitus position with well-shielded probes placed over the head and precordium. Each probe was connected to a dual spectrometer-recorder system. For the intravenous experiments, quantitative injections were made through in-dwelling jugular vein catheters. Blood samples were drawn from an in-dwelling catheter in the opposite jugular. Continuous urine samples were collected from an in-dwelling bladder catheter. For the intracoronary injections, the left chest was opened and a 27-gage needle with fine polyethylene tubing attached was inserted into the anterior descending coronary artery. The tubing was preloaded with tracer in a 0.1-cc volume and kept outside the detector field. At the appropriate time, a bolus injection was made by flushing the tubing with saline. All observations in dogs were made with 50–100 μCi of the two radionuclides.

In vitro clearance studies were made in rats (approximately 300 gm) which were anesthetized with intraperitoneal pentobarbital. A femoral vein was exposed and then 15-μCi doses of radionuclides were quantitatively injected. Hearts were removed at selected intervals and counted in a well counter.

RESULTS

Intravenous, myocardium. A definite time differential is found between maximum uptake of potas-

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For reprints contact: Norman D. Poe, Div. of Nuclear Medicine, UCLA Medical Center, Los Angeles, Calif. 90024.

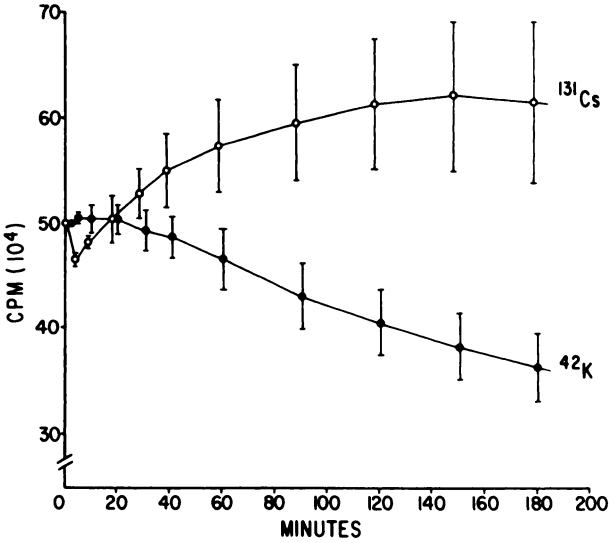

FIG. 1. After intravenous injection, different precordial uptake curves are observed for potassium and cesium in dogs. Potassium reaches peak concentration between 5 and 20 min. Cesium concentration is lowest at 5 min, then gradually rises to peak between 120 and 180 min. Values are means for three animals ±s.d. and represent total activity in myocardium, heart blood pool, and overlying muscle.

TABLE 1. PERCENT MYOCARDIAL UPTAKE IN RATS FOLLOWING INTRAVENOUS INJECTION: MEAN (RANGE) n = 3

	5 min	15 min	30 min	60 min
^{131}Cs	1.45 (1.34–1.51)	2.13 (1.82–2.31)	1.99 (1.79–2.25)	2.02 (1.90–2.25)
^{42}K	2.54 (2.49–2.59)	2.39 (2.30–2.49)	1.86 (1.76–1.97)	1.04 (0.95–1.10)

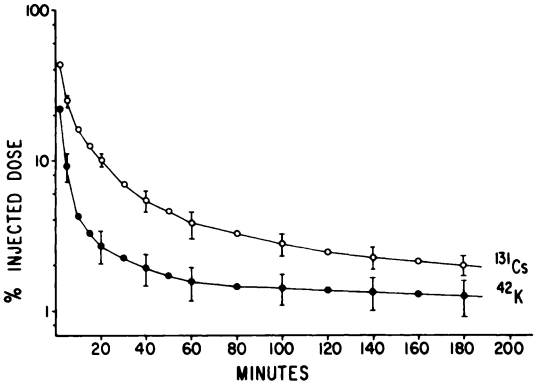

FIG. 2. Comparative canine blood clearance curves demonstrate more rapid and efficient removal of potassium from vascular space and earlier intracellular equilibration. Slower cesium clearance and consequent higher blood levels correlate with delayed precordial cesium peak seen in Fig. 1. Values expressed as means ±s.d.

sium and cesium (Fig. 1). Potassium reaches a plateau in the heart (with slight chest-wall contribution) within 5–20 min, then decreases during the next 90 min. A more gradual negative phase follows. The $T_{1/2}$ based on this latter curve in three animals ranges between 5.6 and 7.7 hr (average 6.5 hr). In contrast, cesium initially decreases, reaching a nadir at 5 min, then peaks between 120 and 180 min before a very gradual clearance phase develops. Although the three animals were followed for 5 hr, a clear-cut $T_{1/2}$ could not be identified. Further measurements were obtained at 24 hr. Based on this data, the $T_{1/2}$ ranges from 16.5 to 43.0 hr (average 27.3 hr). One animal followed for a week still retained 10% of the peak level.

Intravenous, head. Concentration increases over the head for the first 10 min with both tracers. Then a steady level of uptake is maintained for the following 180 min. The head represents a combination of both skeletal muscle and blood pools.

Intravenous, blood. A marked difference in blood clearance is seen between potassium and cesium (Fig. 2). At 2 min 42% of the cesium remains in the blood but only 22% of the potassium remains. At 1 hr these values drop to 3.8 and 1.6%, respectively. The disappearance curves are multiphasic, probably containing three basic components representing ion exchange in the intravascular, interstitial, and intracellular compartments.

Intravenous, urine. Cesium clearance only was measured. In three animals 3.5–5% of the injected dose was excreted in 5 hr.

Intravenous, in vitro. The data in 12 rats are summarized in Table 1. These values confirm the myocardial uptake pattern described in dogs above. In the rat the heart represents only 0.35% of the body weight in contrast to 0.9% in the dog.

Intra-arterial. The dichotomy between potassium and cesium is further exemplified in three animals after bolus injection of the two radionuclides into the anterior descending coronary artery (Fig. 3). Potassium is highly extracted with almost three times the efficiency of cesium (average 71% compared with 22%) on the first circulation through the coronary capillary bed. Likewise, potassium is cleared more rapidly from the heart. Based on the slope of the curve from 10–60 min, the $T_{1/2}$ for potassium is 78 min and for cesium 390 min.

DISCUSSION

The above observations show distinct differences in the myocardial concentration and blood clearance patterns between ^{42}K and ^{131}Cs. These findings are in accord with reports by previous investigators (*2,3,5,6*). Potassium is rapidly cleared from the blood and concentrated by the myocardium. Its high extraction on a single circulation through the vascular bed makes it a suitable indicator for coronary blood-flow measurements. Conversely, the blood clearance and myocardial uptake of cesium are slower and the intracellular retention much longer even though the maximum myocardial concentration of the two analogs is approximately the same. The differences in rate probably can be attributed to the inability of the cell membrane transport mechanism to handle the cesium ion with the efficiency of the potassium ion. Although the early reports of Carr and others (*2,7*) leave little doubt that radiocesium is perfectly adequate for qualitatively localizing sites of established myocardial infarcts, the behavior of this ion during acute and evolving infarction is not established. It has been demonstrated that the egress of potassium from ischemic myocardium is dependent both on the magnitude and duration of the ischemia (*8,9*). Presumably cesium will behave similarly, but until the effects of ischemia on the kinetics of this

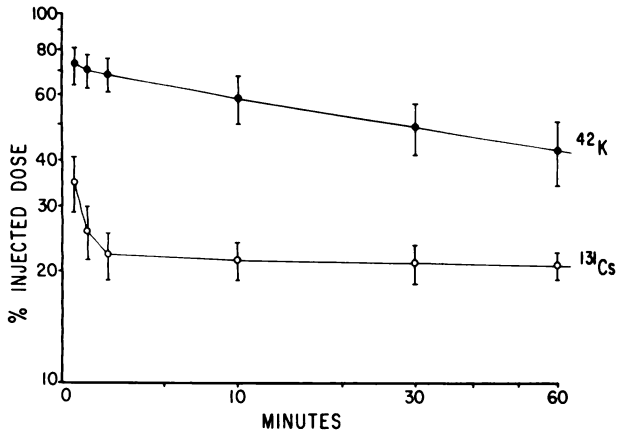

FIG. 3. Myocardial extraction of potassium in dogs after bolus injection directly into coronary artery is approximately three times that of cesium. Difference indicates much larger percentage of cesium is free to recirculate to other regions of myocardium (mean ±s.d.).

ion have been established, quantitative measurements with cesium during the developing stages of infarction are not justified.

The less efficient extraction of cesium following intracoronary arterial injection is a definite disadvantage in quantitative studies when the radionuclide is administered by this route. At least 75% of the injected dose will be free to recirculate throughout the body and return to the myocardium in proportion to coronary blood flow. Although the myocardium receives only about 5% on the cardiac output, the amount of cesium finally reaching the heart by recirculation could exceed 15% of the amount extracted on the initial injection. Comparative scans made after intracoronary injection of ^{131}Cs and ^{99m}Tc-labeled particles which have no recirculation do demonstrate substantial and readily detectable concentrations of cesium throughout the myocardium (*10*). This is not a problem with potassium because the percent available for recirculation is inconsequential.

The whole principle of the use of radiopotassium and related substances for regional flow measurements in damaged myocardium is open to question. Cellular extraction of these ions is not only a function of flow but also of cell membrane integrity. The capability of cells to concentrate potassium can remain nearly unimpaired with flow reductions up to 50% of normal (*9*). After ischemia has been produced, maintenance or recovery of function is related to the extent and duration of the hypoxia. During the acute and evolving stages of a myocardial infarction, significant inequalities between flow and cell damage very likely coexist. Under these circumstances erroneously low perfusion deficits could conceivably be obtained in the presence of normal perfusion.

After the intravenous administration of potassium, scanning can commence immediately as maximum counts are reached by 5 min. For cesium a delay of 1–1½ hr is required to attain maximum counting rates. The rapid clearance of potassium after intracoronary injection necessitates almost immediate scanning, preferably performed rapidly. Cesium clearance by this route is slow, making scanning possible any time within the first several hours after injection. For myocardial dosimetry calculations with intravenous potassium, the calculated 6.5-hr $T_{1/2}$ should be sufficiently accurate. However, the cesium data were less precise, and it is suggested that the 32-hr physical $T_{1/2}$ be used.

SUMMARY

Potassium-43 and its analog, ^{129}Cs, have recently been suggested as suitable radiopharmaceuticals for myocardial scanning. Studies with ^{42}K and ^{131}Cs were undertaken in dogs to determine the myocardial turnover characteristics of these two ions. After simultaneous intravenous injection, potassium clears rapidly from the blood, reaches a plateau in the myocardium within 5–20 min, and then clears with a $T_{1/2}$ of 6.5 hr. Initial cesium clearance is slower. A peak is reached gradually in the myocardium within 1–3 hr, and the clearance $T_{1/2}$ is 27.3 hr. Following intracoronary injection, potassium is extracted with 71% efficiency on a single circulation, but cesium is extracted with only 22% efficiency. It is concluded that cesium should be used with caution as a substitute for potassium in quantitative myocardial blood flow and function measurements, but that comparable results can be obtained with either radionuclide in localizing ischemic myocardium.

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