UPTAKE OF ^{203}Hg-HYDROXY-MERCURY-FLUORESCEIN IN MYOCARDIAL INFARCTS

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Attempts have been made in the past to scan myocardium with various radiopharmaceuticals in order to visualize infarcts. Some, like radioisotopes of potassium (*1*), rubidium (*1*), cesium (*2*), and radioiodinated fatty acids (*3*), localize in the normal muscle and show the ischemic muscle as a "cold" area. On the other hand, ^{203}Hg-chlormerodrin (Neohydrin) has been reported to show an area of infarct as a region of "positive" uptake in the scan (*4*). Most of these radiopharmaceuticals were tried in experimental animals and the scans obtained with them were far from satisfactory. None of them therefore has been generally employed as a clinically useful diagnostic agent.

Recently it was observed by Malek et al (*5,6*) that ^{203}Hg-labeled hydroxy-mercury-fluorescein was taken up selectively by the infarct compared with normal muscle in dogs after an i.v. injection. Malek et al were successful in obtaining scans of infarcts in animals in vivo within a few hours of ligation of a branch of the coronary artery. Their results encouraged us to investigate the localization of this compound in infarcts.

METHODS

The ^{203}Hg-hydroxy-mercury-fluorescein was obtained from two sources: (A) Isotope Div., BARC, India, and (B) Squibb Radiopharmaceuticals (Mercurascan-203). The results obtained with both these preparations were identical, and they are presented together.

Myocardial ischemia was produced in dogs (weighing 12–16 kg) by temporarily ligating the descending branch of the left coronary artery. Fifty microcuries of ^{203}Hg-hydroxy-mercury-fluorescein was administered i.v. at various times before and after the release of ligature. In one set of experiments the ligation was done after the injection.

The duration of ligation varied in different experiments. The dogs were usually sacrificed either 4 or 24 hr after the administration of the radioactivity. In addition to the ratio of radioactivity in the normal and infarcted myocardium, the percent of the administered dose in liver, kidney cortex, kidney medulla, and blood were determined. The counting of aliquots of tissues was done in a well counter. The radioactivity in the blood was calculated for the expected blood volume in that dog based on 7% of the body weight. The kidney was assumed to be 50% cortex and 50% medulla.

RESULTS

Table 1 shows the distribution of the radiopharmaceutical in eight dogs in which the radioactivity was injected after the release of the coronary ligation. The varying duration of ligation and time of injection after the release of ligation are indicated in this table. The highest concentration in the infarct region was observed when the ligation was kept for 1 hr and the injection was made 1 hr after the release of the ligation.

Table 2 shows the distribution of the radiopharmaceutical in eight dogs injected before the ligation was released. In none of the dogs was the ratio of radioactivities in ischemic and normal myocardium higher than 2.7, whereas ratios above five were reached when the injection followed release of the ligation.

Table 3 shows similar poor uptakes in a series of six dogs where the ligation was carried out shortly after the injection of the radiopharmaceutical.

COMMENTS

Scanning of a myocardial infarct is a challenging problem, not only because there is no suitable radiopharmaceutical which has significant selective lo-

Received June 1, 1971; original accepted June 4, 1971.

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calization in either normal or infarcted myocardium but also because scanning a small lesion in the presence of high blood background and ever present movement of the heart would pose difficulties even if a radiopharmaceutical with desirable properties was available.

The series of studies reported here indicate that the ratio of radioactivity in diseased and normal myocardium was too low to permit scanning of a myocardial infarct. In any case, the uptake was far lower than that reported by Malek et al (*6*) in their original observations.

In the studies reported here three kinds of procedures were tried: injecting the radiopharmaceutical after releasing the ligation, before releasing the ligation, and lastly injecting it even before the ligation. It was hoped that in a case where the mechanism of localization is ill understood these variations would produce different results. The lack of significant change in the results was surprising to us. None of the procedural variations appeared to produce any dramatic degree of change in the distribution of the radiopharmaceutical. It was felt that the concentration in the infarct was often about twice that

TABLE 1. DISTRIBUTION OF ^{203}Hg-HYDROXY-MERCURY-FLUORESCEIN IN DOGS INJECTED AFTER RELEASE OF CORONARY LIGATION

No.	Duration of ligation (hr)	Time of inj. after release of ligation	Time of sacrifice after the inj. (hr)	% of administered dose				% administered dose/gm myocardium		Ischemic/ normal ratio
				Liver	Kidney cortex	Kidney medulla	Blood	Ischemic	Normal	
1	1	1 hr	4	15.4	27.3	13.6	5.8	0.0188	0.0032	5.87
2	1	1 hr	24	11.6	19.4	9.6	2.1	0.0083	0.0016	5.19
3	2	1 hr	4	21.6	27.8	14.3	10.3	0.0074	0.0034	2.18
4	2	1 hr	4	27.6	34.2	16.4	5.8	0.0104	0.0040	2.60
5	2	1 hr	24	17.2	21.4	10.6	2.9	0.0027	0.0020	1.35
6	2	1 hr	24	13.6	23.9	7.9	1.9	0.0026	0.0017	1.53
7	3	15 min	24	11.6	23.6	11.3	2.3	0.0055	0.0020	2.75
8	24	1 hr	4	17.6	29.9	13.3	6.9	0.0060	0.0042	1.43

TABLE 2. DISTRIBUTION OF ^{203}Hg-HYDROXY-MERCURY-FLUORESCEIN IN DOGS INJECTED WITH CORONARY LIGATION IN PLACE

No.	Duration of ligation before inj.	Time of sacrifice after inj. (hr)	% of administered dose				% administered dose/gm of myocardium		Ischemic/ normal ratio
			Liver	Kidney cortex	Kidney medulla	Blood	Ischemic	Normal	
1	1 hr	4	19.2	33.2	17.1	6.9	0.0150	0.0055	2.72
2	1 hr	4	24.8	31.6	16.3	7.1	0.0104	0.0042	2.48
3	1 hr	4	15.9	26.3	19.2	9.2	0.0105	0.0050	2.10
4	1 hr	24	14.3	19.2	8.9	3.2	0.0065	0.0026	2.50
5	24 hr	4	19.3	30.8	15.3	7.3	0.0054	0.0052	1.04
6	24 hr	4	23.3	29.6	11.8	6.3	0.0116	0.0042	2.76
7	7 days	4	22.3	33.6	17.2	11.2	0.0083	0.0039	2.13
8	10 days	4	15.3	33.6	12.9	6.1	0.0111	0.0055	2.02

TABLE 3. DISTRIBUTION OF ^{203}Hg-HYDROXY-MERCURY-FLUORESCEIN IN DOGS INJECTED 5 MIN BEFORE CORONARY LIGATION

No.	Duration of ligation	Time of sacrifice after inj. (hr)	% of administered dose				% administered dose/gm of myocardium		Ischemic/ normal ratio
			Liver	Kidney cortex	Kidney medulla	Blood	Ischemic	Normal	
1	2 min	4	29.8	27.8	14.1	6.2	0.0070	0.0036	1.94
2	15 min	4	27.3	31.3	13.6	7.1	0.0076	0.0042	1.81
3	1 hr	4	24.2	30.8	13.7	6.1	0.0080	0.0039	2.05
4	2 hr	4	20.8	29.2	12.8	5.9	0.0086	0.0043	2.00
5	15 min	24	12.8	17.5	9.9	2.3	0.0119	0.0055	2.16
6	1 hr	24	13.1	18.3	10.2	2.6	0.0096	0.0047	2.04

in the normal myocardium but was never sufficiently high in terms of fraction of the dose injected to permit effective scanning in vivo. Furthermore the distribution of the radiopharmaceutical was such that consideration of radiation dose to the liver and kidney would be worrisome.

SUMMARY

Distribution of ^{203}Hg-labeled hydroxy-mercury-fluorescein was studied in a series of 22 dogs in whom a myocardial infarct was produced by ligation of a branch of the coronary artery. Several procedural variations were tried, but they did not seem to alter the results significantly. The ratio of radioactivities in ischemic myocardium to normal myocardium varied from 5.89 to 1.04. The liver showed a maximum of 29.8% of the administered dose 4 hr after injection, while the kidney showed a maximum of 34.2% at the same time period. The results did not appear to indicate that this agent in its present form would be effective for in vivo scanning of myocardial infarcts.

ACKNOWLEDGMENTS

We are thankful to R. S. Mani and his associates at Isotope Division, BARC for preparing ^{203}Hg-hydroxy-mercury-fluorescein for this study and to Squibb Radiopharmaceuticals for supplying a batch of Mercurascan-203 for comparative studies.

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