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EXPERIMENTAL SUPPRESSION OF HEPATIC UPTAKE OF ^{75}Se-SELENOMETHIONINE

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Preliminary infusion of unlabeled methionine into the proper hepatic artery, the distal splenic artery, or the superior mesenteric artery does not enhance the ratio of pancreatic to hepatic uptake of ^{75}Se-selenomethionine. No threshold dose rate of methionine could be found below which the liver cleared methionine entirely from the blood during one passage.

Intra-arterial administration of ^{75}Se-selenomethionine into the celiac artery increases the specific activity in the pancreas but may be associated with substantial variation in activity along the length of the pancreas.

In 1961 Blau and Manske (*1*) prepared ^{75}Se-selenomethionine. Since then imaging of the pancreas has been obtained by scanning after intravenous administration of ^{75}Se-selenomethionine (*2–6*). However, the pancreatic scan is frequently of nondiagnostic quality and the head of the pancreas is often obscured by the activity of the adjacent liver. This experimental study was undertaken in an attempt to improve the clarity of the pancreatic scan by suppressing hepatic uptake of the radionuclide by preliminary infusion of unlabeled methionine into the liver. Methionine was administered as an aqueous solution in saline.

MATERIALS AND METHODS

Unconditioned, nonfasted mongrel dogs weighing between 11 and 33 kg were used. Each animal was anesthetized by intravenous administration of sodium pentobarbital (25 mg/kg body wt). Six experimental series were performed. Unless otherwise noted, a total dose of 3 μCi/kg body wt of ^{75}Se-selenomethionine was given in each experiment regardless of the route of administration. Group 1 (four dogs) received an intravenous injection of ^{75}Se-selenomethionine. No other procedures were performed on these dogs which served as controls. In Group 2 (seven dogs) ^{75}Se-selenomethionine was infused over 10 min through an intra-arterial catheter with its tip positioned in the celiac artery. In Group 3 (four dogs) 6 gm of unlabeled methionine in saline were infused over 30 min (0.2 gm/min) through a catheter with its tip positioned in the proper hepatic artery distal to the origin of the gastroduodenal artery. Selenium-75-selenomethionine was then injected intravenously. In Group 4 (three dogs) 4 gm of methionine in saline were infused over 30 min (0.13 gm/min) into the distal splenic artery. The catheter tip was positioned as far distally in the artery as possible. Selenium-75-selenomethionine was then injected intravenously. In Group 5 (five dogs) 4 gm of unlabeled methionine in saline were infused over 30 min (0.13 gm/min) into the superior mesenteric artery. The catheter tip was distal to the origin of the inferior pancreaticoduodenal artery.

In Group 6 (three dogs) a solution of unlabeled methionine (1 gm) mixed with 10 μCi of ^{75}Se-selenomethionine was infused into the proper hepatic artery in one dog and into the superior mesenteric artery in two dogs. A catheter was positioned in the right atrium and samples were taken during the infusion. The infusion rate was varied from 1 ml/min to 5 ml/min.

All animals were sacrificed by barbiturate overdosage 30 min after the dose of ^{75}Se-selenomethionine and the abdomen opened. The pancreas was removed and cut into 10–12 roughly equal sections, section 1 being the proximal pancreatic head and section 12 the most distal portion of the tail.

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After taking precautions to prevent cross-contamination of the liver by pancreatic activity, three sections were removed from the liver, one from the right lobe, one from the region of the porta hepatis, and one from the left lobe. Each sample was weighed and counted in a well counter. The results were expressed as counts per minute per gram of each tissue (specific activity). The ratio of specific activities (number of counts per minute per gram of tissue) of pancreas and liver was calculated for each experimental group. This ratio is hereafter referred to as the P/L ratio.

RESULTS

In Group 1 (control group) the pancreas had a specific activity about three times that of the liver. In Group 2 (radionuclide infused into the celiac artery) the specific activity of both liver and pancreas was increased over that of the control group. However, the P/L ratio was decreased. A striking variation of specific activity was observed in this group from one section of the pancreas to the next (Fig. 1).

Groups 3, 4, and 5 (preliminary dose of unlabeled methionine administered by various intra-arterial routes) showed an adverse effect of unlabeled methionine on the P/L ratio. The P/L ratio was never as high in any of these groups as that achieved with simple intravenous administration of the radionuclide alone.

The experiments of Group 6 demonstrated that even with infusion of ^{75}Se-selenomethionine-tagged methionine into the proper hepatic artery or the distal superior mesenteric artery at rates as low as 20 mg/min, the liver failed to clear the activity from the blood. That is, no threshold of administration of methionine could be found below which the liver entirely cleared methionine during one passage.

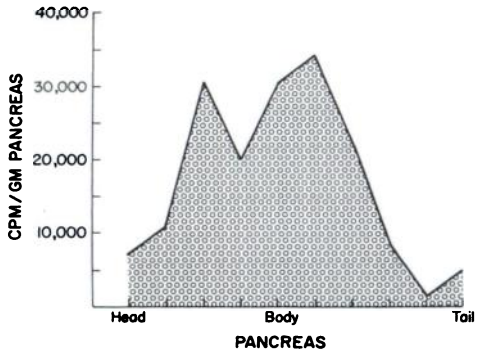

FIG. 1. Distribution of ^{75}Se-selenomethionine through pancreas following infusion into celiac artery in one dog. Uptake is uneven. Similar effect was observed in three other dogs.

The results of these experiments are summarized in Table 1.

DISCUSSION

Interference by activity in the liver is an important cause of inadequate pancreatic scans. Many attempts to improve the quality of pancreatic scanning by overcoming this interference have been described (*7–9*).

Oral administration of large doses of unlabeled methionine prior to the pancreatic scan does not suppress the hepatic uptake of ^{75}Se-selenomethionine (*10*). Enhancement of pancreatic uptake, with better definition of the pancreatic scan, has been reported by intra-arterial injection of radionuclide (*11–14*). The use of pancreatic stimulants has also been suggested (*13*). A recent report (*15*) suggests that preliminary injection of both urecholine and pancreazymin-CCK enhances the pancreatic concentration of ^{75}Se-selenomethionine.

TABLE 1. SUMMARY OF PANCREATIC AND HEPATIC SPECIFIC ACTIVITIES OF ^{75}Se-SELENOMETHIONINE AND P/L RATIO (CPM/GM PANCREAS/CPM/GM LIVER) FOR EACH METHOD OF ADMINISTRATION

Method of administration of tracer and methionine	Mean pancreatic specific activity cpm/gm tissue (range)	Mean hepatic specific activity cpm/gm tissue (range)	Average P/L ratio (range)
Intravenous ^{75}Se-selenomethionine	20,209 (13,446–25,008)	7,114 (4,665–8,910)	2.84 (2.36–3.49)
Celiac ^{75}Se-selenomethionine into artery	21,685 (8,422–58,841)	11,353 (4,361–28,002)	2.0 (1.14–3.27)
Methionine through proper hepatic artery plus i.v. ^{75}Se-selenomethionine	1,853 (1,244–2,404)	1,767 (1,367–2,041)	1.1 (0.9–1.3)
Methionine through deep splenic artery plus i.v. ^{75}Se-selenomethionine	3,651 (1,889–6,882)	4,426 (2,845–5,702)	0.82 (0.4–1.21)
Methionine through superior mesenteric artery plus i.v. ^{75}Se-selenomethionine	5,950 (1,895–11,652)	7,076 (1,156–13,346)	0.84 (0.52–1.64)

This study confirms that intra-arterial injection of tracer increases the absolute amount of radionuclide taken up by the pancreas for a given dose of radionuclide. However, the uptake is in some cases very uneven so that counts fluctuate markedly from point to point along the pancreas. This phenomenon has also been reported with intravenous administration at the junction of the pancreatic head and body (*16*). This may give rise to falsely cold areas in the scan.

These experiments show that infusion of methionine into the liver, by any of the routes attempted, adversely affects the P/L ratio and is therefore likely to decrease the quality of the pancreatic scan. No threshold was found below which infused methionine was completely cleared by the liver. Therefore, it is unlikely that modification of the dosage or infusion rate of the infused methionine would produce better results.

The specific activity of the pancreas resulting from a simple intravenous injection of ^{75}Se-selenomethionine in the dog is about three times that of liver. This agrees with the results of Kupic and Kasanter (*13*) but is lower than the results reported by Blau and Manske (*1*).

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