DYNAMIC STUDY OF EXOCRINE FUNCTION OF THE PANCREAS IN DIABETES MELLITUS WITH SCINTIGRAPHY USING ^{75}SE-SELENOMETHIONINE

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A dynamic study of scintigraphy of the pancreas using ^{75}Se-selenomethionine in diabetic patients was performed. Patients were selected who complained of abdominal pain or diarrhea or both and whose pancreatic exocrine functions were thought to be disturbed. Selenium-75-selenomethionine (3 μCi/kg body weight) was injected intravenously and radioactivity (cpm) was recorded by a scinticamera for 10 min successively up to 120 min. After 20–30 min the increase of radioactivity in the selected area of the displayed pancreas usually reached a plateau. Pancreozymin (1 Harper unit/kg) and secretin (1 Harper unit/kg) were administered intravenously and decrease of radioactivity in the same area was followed for 60 min to examine pancreatic exocrine function. After ^{75}Se-selenomethionine injection, the angle of the initial increase of radioactivity, the height of the plateau, and the reactive decrease of radioactivity after pancreozymin and secretin were analyzed in each case. Radioactivity recorded on data tape was reproduced for each 10-min period on a cathode-ray tube display. Areas of interest were selected for dynamic analyses. To supplement the diagnosis by visual image of a scintigram of the pancreas, the scintigram was quantified in the present study and the dynamic curves of radioactivity in the selected area of the displayed pancreas were studied for a total of 3 hr. Application of the dynamic study of the pancreas scintigraphy and the additional data analyses seemed useful for the early detection of pancreatic exocrine dysfunction in diabetic patients in whom the ordinary laboratory pancreatic exocrine function tests gave uncertain results.

Ordinary scintigraphy of the exocrine pancreas has seldom been used to study abnormalities in diabetic patients although there are some recent reports (*1,2*) that many diabetics, particularly those of the young, insulin-dependent type, show a relatively low pancreatic uptake of ^{75}Se-selenomethionine.

The authors have studied radioactive isotope data analysis using an Anger scintillation camera combined with a minicomputer on line to facilitate evaluation of pancreatic scintigraphy of diabetic patients with additional intravenous injection of pancreozymin and secretin during scintigraphy for early detection of pancreatic exocrine dysfunction.

MATERIALS AND METHODS

Patients with diabetes mellitus were limited to cases in which the complaints included abdominal pain or diarrhea or both. Alcoholic history, family history of diabetes mellitus, obesity index, and treatment of diabetes are listed in Table 1. For the imaging of the pancreas, the axis of the collimator (5,400 holes) of an Anger scintillation camera (Hitachi Ltd. Co.) was set from the perpendicular line to a 15-deg angle to the right side of the patient and to 5 deg caudally to avoid overlap of liver and pancreas scintigrams and as close as possible to the abdomen of the patient. Window width of the pulse-height analyzer was set at the spectrum peak of 270 keV ±20%.

Immediately after the intravenous injection of 3 μCi/kg ^{75}Se-selenomethionine [Radiochemical Centre, Amersham, England (30–40 mCi/mg specific radioactivity and >96% radiochemical purity)], cumulative amounts of the radioactivity in the pancreatic area were recorded with a minicomputer system (Fig. 1) on magnetic tape for every 10 min in a 64 × 64 matrix. Radioactivity usually reached a

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TABLE 1. CLINICAL DIAGNOSIS, HISTORY, AND TREATMENT OF DIABETES MELLITUS IN PATIENTS STUDIED WITH PANCREAS SCINTIGRAPHY

Patient	Age, Sex	Clinical diagnosis	Alcoholic history	Family history of diabetes mellitus	Obesity index (%)	Treatment for diabetes mellitus
NN	47, M	Gastric ulcer	+	—	98	None
KS	21, F	Chronic thyroiditis	—	—	108	None
SM	55, F	Irritable colon	—	—	110	None
SE	57, M	Diabetes mellitus	+	—	109	Diet
UM	65, M	Diabetes mellitus	+	—	110	Diet
TT	36, M	Diabetes mellitus	+	—	96	Diet
AN	66, M	Diabetes mellitus	+	—	90	SU and BG
IM	55, M	Diabetes mellitus	+	—	110	SU
TK	43, F	Diabetes mellitus; chronic pancreatitis suspected	—	—	101	Diet
YS	65, F	Diabetes mellitus; chronic pancreatitis suspected	—	—	114	Diet
ST	30, M	Diabetes mellitus; chronic pancreatitis suspected	+	—	110	Diet
HO	52, M	Diabetes mellitus; gallstones	+	—	120	Diet
MS	23, F	Diabetes mellitus; pancreas stone	—	—	89	Diet
TM	57, F	Diabetes mellitus; pancreas stone	—	—	104	SU
RA	62, M	Diabetes mellitus; cancer in pancreas head	+	+	70	Insulin
IO	60, F	Diabetes mellitus; cancer in pancreas head	—	—	80	Insulin

Obesity index: (weight (kg)/[height (cm) — 100] × 0.9) × 100 (%).

plateau level within 20–30 min after the start of the injection. At 120 min 1 unit/kg pancreozymin (Harper units, Boots Pure Drug Co. Ltd., Nottingham, England) and 1 unit/kg (Harper units, Boots) secretin were injected intravenously through the brachial vein of the opposite side. The consequent decrease of radioactivity in the area of interest in the pancreas image was followed further for 60 min.

For the data analyses, radioactivity (cpm) recorded on magnetic tape was reproduced and displayed on the cathode ray tube (CRT) display (Fig. 1). The area of interest ($8 \times 6 = 48$ elements; size 32×24 mm) was selected in the scintigram of the pancreas head (Fig. 2) and the recorded radioac-

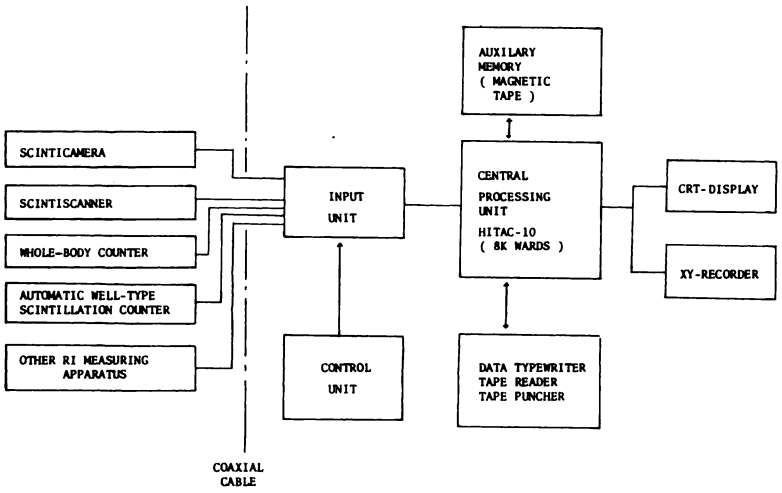

FIG. 1. Block diagram of radioactive isotope data-processing system.

FIG. 2. Area of interest selected in pancreas scintigram for dynamic study of radioactivity after ^{75}Se-selenomethionine, pancreozymin, and secretin.

tivity for this area was then typed out for the dynamic study of exocrine function. For the separation of liver and pancreas scintigrams, ^{198}Au-colloid (150 μCi) was injected intravenously after the pancreas scintigraphy with ^{75}Se-selenomethionine before the patient's position was changed. Subtraction of the liver scintigram, if necessary, was performed using the ^{75}Se-to-^{198}Au ratio 20 min after injection of ^{198}Au-colloid studied at the pulse height of 410 keV ±20%. No special pretreatment was given to patients before the pancreas scintigraphy. The precise method for the subtraction was reported previously (*3*).

RESULTS

For the dynamic study, the initial increase of radioactivity for the first 20–30 min, the plateau height of radioactivity, and the reactive decrease of radioactivity following intravenous injection of pancreozymin and secretin were studied.

The initial increase of radioactivity for the first 20–30 min. The angle of initial increase of radioactivity after the intravenous injection of ^{75}Se-selenomethionine was studied in nondiabetic patients and in patients with diabetes mellitus, some of whom also had cancer of the pancreas or chronic pancreatitis with calculi that were visible on the abdominal x-ray film (Table 1).

Within 20–30 min after injection, diabetic patients reached a plateau of radioactivity, and it was not necessarily different in patients who were suspected of having parenchymal pancreatic damage such as calculi or cancer of the pancreas (Fig. 3).

The plateau height of radioactivity. Diabetic patients achieving the plateau height of radioactivity more than 20 min after intravenous injection of ^{75}Se-selenomethionine (Fig. 3) were divided into two groups. Patients with good uptake, i.e., more than 400 cpm, were similar to nondiabetic patients with other diseases (Table 1). Patients whose uptake was at a level around 200 cpm had about the same level of radioactivity as patients with pancreatic calculi or cancer.

Reactive radioactivity decrease following intravenous injection of pancreozymin and secretin. As the radioactivity level in the area selected for dynamic studies reached the plateau, pancreozymin and secretin were injected for the enhancement of pancreatic exocrine functions at 60 min to examine reactive decrease of radioactivity in the selected area. Radioactivity decreased from the plateau level for about 20–30 min and then increased gradually to the former level (Fig. 4).

When pancreozymin and secretin were injected at 120 min after the ^{75}Se-selenomethionine injection, radioactivity decreased continuously thereafter, at least for the subsequent 60 min studied. Following these procedures, patients with high plateaus showed good reactive decreases; however, patients with low plateaus had low responses. In general, for the low plateau group of patients it was not always easy to judge visually the radioactivity responsiveness after injections of pancreozymin and secretin (Fig. 3).

Radioactivity changes in blood after injection of ^{75}Se-selenomethionine. Radioactivity in blood was studied successively at 5, 10, 15, 30, 45, 60, 120, and 240 min (Fig. 5) after the injection of ^{75}Se-selenomethionine. Counts were converted to percentages of radioactivity in the specimen taken at 2 min after the ^{75}Se-selenomethionine injection. Radioactivity percentages in blood (expressed as total counts in Fig. 5) decreased to about 30% at 30 min and returned to 50–60% gradually. In the same specimen, radioactivity found in the supernatant frac-

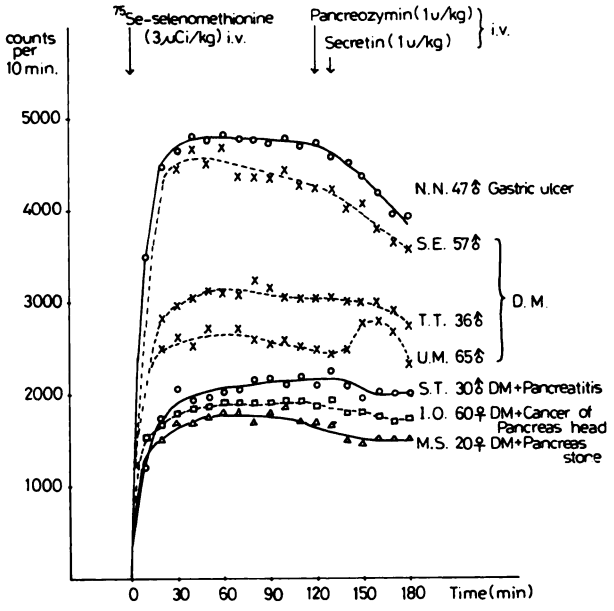

FIG. 3. Typical examples of dynamic studies of radioactivity in selected area of pancreas scintigrams after ^{75}Se-selenomethionine, pancreozymin, and secretin administration.

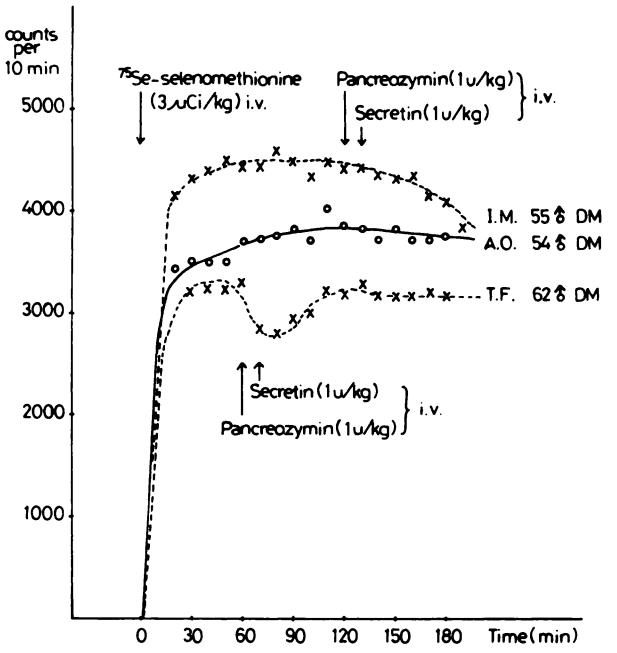

FIG. 4. Comparative studies of reactive decrease of radioactivity in area of interest of pancreas scintigram after pancreozymin and secretin injections. (AO, without pancreozymin and secretin. TF, pancreozymin and secretin were given at 60 min. IM, pancreozymin and secretin were given at 120 min.)

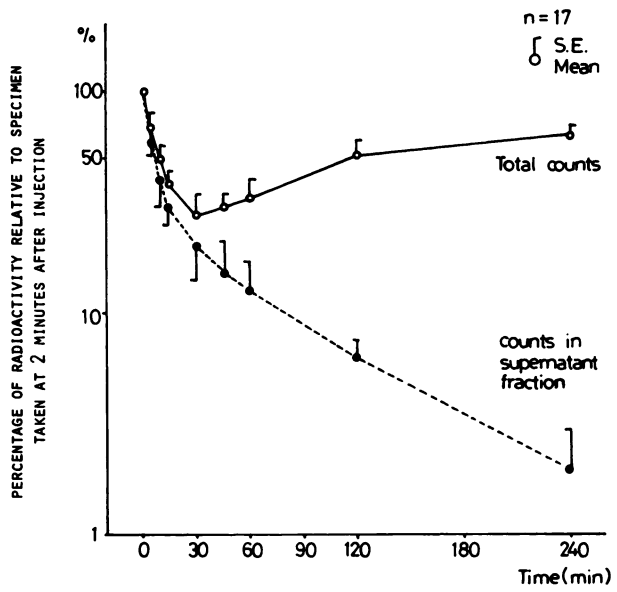

FIG. 5. Changes of radioactivity in blood after injection of ^{75}Se-selenomethionine.

tion of blood treated with 5% trichloroacetic acid (TCA) decreased continuously to 13% at 60 min and 6–7% at 120 min.

DISCUSSION

For the diagnosis of pancreatic dysfunction with scintigraphy, qualitative impressions of visual images have generally been major determining factors (*1,2,4,5*). The authors have attempted to convert these visual and subjective impressions to objective data. For this purpose, radioactivity in a selected area of the pancreatic image in the cathode ray tube display was followed successively every 10 min from the beginning of intravenous injection of ^{75}Se-selenomethionine to 120 min and then another 60 min after the pancreozymin and secretin injections.

For examination of the exocrine function of the pancreas the time for intravenous injections of pancreozymin and secretin appears to be 120 rather than 60 min after injection of ^{75}Se-selenomethionine. It could be speculated that transient radioactivity decrease in the selected pancreas area upon injection of enzymes 60 min after the ^{75}Se-selenomethionine injection was followed by increased uptake of radioactivity from blood (*4–7*) (probably from the supernatant fraction after precipitation with 5% TCA), which raised the radioactivity in the selected area. However, decrease of radioactivity after pancreozymin and secretin injections at 120 min was not replaced by the radioactivity in blood because radioactivity in the supernatant fraction had by this time decreased to roughly 6–7% of the administered radioactivity and remaining radioactivity in blood, which could be precipitated with 5% TCA, resisted uptake by the pancreas.

Elimination of radioactivity into examined gastric, duodenal, and pancreatic juices and bile has been found to be low compared with the radioactivity taken up by liver and pancreas before 180 min (*8,9*). Radioactivity in the extrapancreatic and extrahepatic area on the CRT display increased gradually to 180 min after the ^{75}Se-selenomethionine injection; therefore followup of pancreatic radioactivity was stopped at 180 min in the present studies.

Results of pancreas scintigraphy analyses coincided well with those from other methods such as pancreozymin–secretin test* and plasma trypsin (*10*) and amylase (*11*) activities as responses* to pancreozymin and secretin (Table 2). For those patients in whom abnormalities were found in any of the first three function tests in Table 2, the plateau level and/or the reactive decrease of radioactivity in pancreatic scintigraphy was also abnormal. In four patients (NN, KS, SE, and AN) who were normal in the pancreozymin and secretin tests and plasma pan-

* In the pancreozymin–secretin test, duodenal juice was collected for 80 min after injection of pancreozymin and secretin at intervals of 20 min. Normal ranges of trypsin and amylase in this test were 13.0–46.8 μM/kg body weight/80 min, and 880–7,400 Somogyi units/kg body weight/80 min, respectively. Plasma enzyme responses (trypsin and amylase) were also measured every 20 min, and normal ranges of these enzymes were less than 0.05 μM/ml/min, and less than 32 Somogyi units/dl, respectively (*6,7*).

TABLE 2. COMPARATIVE STUDIES OF PANCREAS SCINTIGRAPHY WITH PANCREOZYMIN–SECRETIN TEST AND PLASMA PANCREATIC ENZYME RESPONSES TO PANCREOZYMIN AND SECRETIN

Patient	Pancreozymin and secretin test	Plasma pancreatic enzyme responses to pancreozymin and secretin		Pancreas scintigraphy	
		Trypsin	Amylase	Plateau level	Reactive decrease
NN	•	—	—	•	•
KS	•	—	—	•	•
SM	↓	—	—	↓	↓
SE	•	—	—	•	•
UM	↓	—	—	↓	↓
TT	•	+	—	↓	•
AN	•	—	—	•	•
IM	•	—	—	•	•
TK	•	+	—	↓	↓
YS	↓	+	+	↓↓	↓
ST	↓	+	+	↓	↓
HO	•	+	—	↓	↓
MS	↓↓↓	++	—	↓	↓
TM	•	+	+	↓↓	↓
RA	•	++	+	↓	↓
IO	•	+	—	↓	↓

• Within normal range, ↓ slightly decreased response, ↓↓ moderately decreased response, and ↓↓↓ markedly decreased response.
Presence (+) or absence (—) of abnormal plasma enzyme responses to pancreozymin and secretin.

creatic enzyme responses to pancreozymin and secretin, pancreatic scintigraphy was also normal in the present analyses.

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