Human Pancreas Scintigraphy Using Iodine-123-Labeled HIPDM and SPECT

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The pancreatic affinity of iodine-123-labeled HIPDM (N,N,N′-trimethyl-N′-(2-hydroxy-3-methyl-5-iodobenzyl)-1,3-propane diamine) ([^{123}I]HIPDM) was studied in 18 cases (5 normal volunteers, 7 cases with pancreas cancer, and 6 with chronic pancreatitis). In the normal cases, the pancreas was visualized in the planar images as early as 3 hr, and again at 20 hr postinjection. Single-photon emission computed tomography (SPECT) performed following 3-hr planar scintigraphy, provided excellent pancreas images without an overlap of activity in the liver or spleen. The mean pancreas-to-liver (P/L) ratio was 1.26 ± 0.22 in normal controls. With the exception of one case of massive calcification in the pancreas, the entire pancreas could be observed in the cases with chronic pancreatitis, but the P/L ratio was 0.74 ± 0.15, significantly lower than that of normal cases. Defective areas of the distal portion of the pancreas were clearly seen in those with cancer of the pancreas. The results of our study indicate that [^{123}I] HIPDM may have clinical potential as a human pancreas imaging agent.

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Currently selenium-75- (^{75}Se) selenomethionine is the only pancreas imaging agent routinely utilized in the clinic. Its clinical usefulness is limited however, because its long effective half-life limits the injectable dose, while its rather high-energy gamma rays are not suitable for the scinticamera.

HIPDM (N,N,N′-trimethyl-N′-(2-hydroxy-3-methyl -5-iodobenzyl)-1,3-propane diamine) was developed as a brain perfusion imaging agent (*1*). Iodine-123-labeled HIPDM ([^{123}I]HIPDM) has been clinically used for the evaluation of the regional cerebral blood flow (*2*) and also applied as a lung imaging agent (*3*). The high affinity of HIPDM for the pancreas in mice and rats has been previously reported (*4*). Accumulation of [^{123}I] HIPDM to the pancreas also has been observed in dog studies. The results of animal studies suggest the possibility that this compound might be used for human pancreas imaging. This study attempts to assess the clinical feasibility of pancreas scintigraphy using ^{123}I-labeled HIPDM.

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MATERIALS AND METHODS

Eighteen cases (14 males and 4 females, ages 31–78 yr), including 5 normal volunteers, 7 with pancreas cancer, and 6 cases of chronic pancreatitis were studied. All of the patients underwent ultrasonography, x-ray computed tomography (CT), and endoscopic retrograde cholangiopancreatography (ERCP) examinations.

All of the cases with pancreas cancer and one of chronic pancreatitis had surgical treatment; the diagnosis was confirmed histologically. Consent forms were signed by all patients.

Radioiodination of HIPDM was carried out according to the method developed by Kung and colleagues (*1*). A solution of unlabeled HIPDM and ^{123}I (Nihon Mediphysics Co., Takarazuka, Japan) in a sealed vial was heated in boiling water for 30 min. The labeling efficacy was ~95%. Further purification procedures were not performed. Iodine-123-labeled HIPDM was then diluted with saline and passed through a millipore-filter (0.22 μ) just before injection.

Patients were premedicated with potassium iodide per oss from one day prior to the study for five days.

Usually 3 mCi (111 MBq) of [^{123}I]HIPDM was injected through the antecubital vein. The planar images of the upper abdominal region were obtained at 1, 3, 5, and 20 hr postinjection. Single-photon emission computed tomography (SPECT) was performed using a rotating scinticamera (Maxicamera 400T, General Electric, Milwaukee, WI) with a medium-energy collimator following the 3-hr planar imaging. Projection data were recorded 30 sec per each step from 64 projections around the body. Approximately 35 min was required to obtain sufficient data for the reconstruction of transaxial images. In three cases, SPECT was also performed 5 hr postinjection.

RESULTS

Study results for the 13 patients are shown in Table 1. The planar scintigrams of a normal volunteer at 1, 3, and 20 hr after administration of [^{123}I]HIPDM are

TABLE 1
Results of Ultrasonography, X-ray CT, ERCP, and Scintigraphy of the Cases with Chronic Pancreatitis (Case 1–6) or Pancreas Cancer (Case 7–13)

Case	Age	Sex	Ultrasonography	X-ray CT	ERCP	Scintigraphy
1	58	F	Glandular enlargement, slightly dilated MPD	Diffuse swelling, but within normal limit	Minimal dilatation of MPD with wall rigidity	Entire pancreas was imaged P/L ratio: 0.90
2	67	M	Coarse, decreased echogenecity dilated MPD	Almost normal except MPD dilatation	Dilatation of MPD, mild ectasia of side branches	P/L ratio: 0.83
3	78	M	Decreased echogenecity dilated MPD (3 mm)	Slightly atrophic, irregular margin	Dilated and tortuous MPD	P/L ratio: 0.76
4	75	F	Cystic echo (5 mm) in the head portion	Small low-density mass with smooth margin	Cystic dilatation of duct was not obtained	P/L ratio: 0.71, defect was not detected
5	70	M	Dilated MPD and small spotty echoes	Small calcifications MPD dilatation	Mild beaded appearance of MPD	P/L ratio: 0.51
6	57	M	Multiple strong echoes with acoustic shadow	Massive calcifications in entire pancreas	MPD; multiple stenoses, dilatation. Calculi(++)	Pancreas was not imaged
7	76	F	CBD dilatation. Low echoic region in head	Dilated bile duct, swelling of the head	Encasement and post-stenotic dilatation of MPD	No visualization except a small part of the uncus
8	59	M	Hypoechoic mass in head CBD, MPD dilatation	Irregular low density mass, dilated bile duct	MPD; not imaged	No visualization
9	62	F	Hypoechoic mass in head bile duct dilatation	Low density mass with irregular margin	MPD; not imaged	No visualization
10	63	M	Dilatation of bile duct mass lesion; not apparent	Dilated CBD. Body and tail portion: atrophic	Obstruction of MPD near the papilla of Vater	No visualization
11	66	M	Irregular hypoechoic mass in the body	Large low-density mass distal portion; atrophic	Obstruction of MPD at the body portion	Only the head portion was visualized
12	53	M	Low echoic tumor in the body. Splenic vs. invasion	Irregular low-density tumor at the body	Obstruction of MPD at the body portion	Only the head portion was visualized
13	75	M	Large hypoechoic region at the body and tail	Low-density mass at the tail ~ splenic hilum	Displacement and obstruction of MPD	Tail portion of pancreas was not imaged

MPD = main pancreatic duct; CBD = common bile duct; and P/L ratio = pancreas-to-liver ratio.

shown in Figure 1. At 1 hr postinjection, a small amount of radioactivity was seen in the pancreatic region. The pancreas was visible on the 3-hr image, along with the liver and the spleen. At 20 hr, the radioactivity in the pancreas remained, while activity in the spleen had decreased.

SPECT images (Fig. 2) of another normal volunteer obtained 3 hr postinjection showed excellent images of

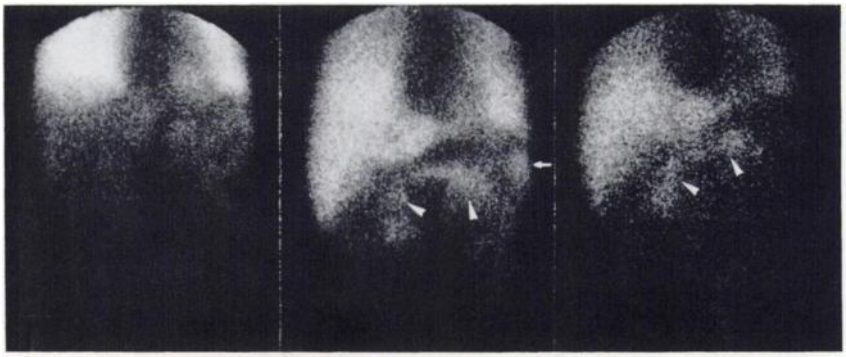

FIGURE 1
Planar images of a normal control (a 35-yr-old male) at 1 (left), 3 (middle), and 20 (right) hr postinjection of [^{123}I] HIPDM. The pancreas (arrow heads) is visible on the 3-hr image, along with the liver and spleen (arrow). At 20 hr, the pancreas (arrow heads) is clearly imaged, while activity in the spleen has decreased.

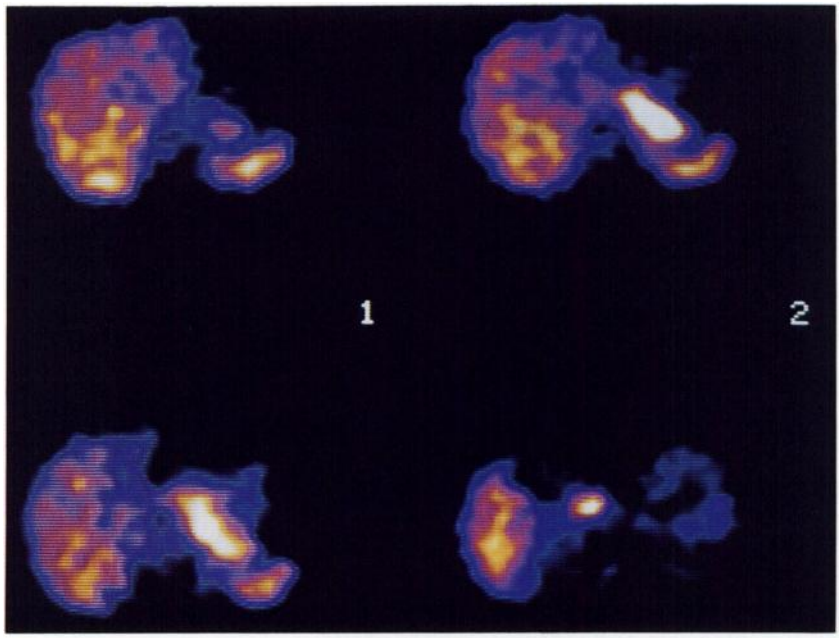

FIGURE 2
SPECT images of a normal case (a 31-yr-old male) obtained at 3 hr postinjection of [^{123}I]HIPDM. The pancreatic tail, body, and head are clearly imaged without the overlap of the radioactivity in the liver and spleen.

the pancreas' head, body, and tail without any overlap of the radioactivity in the liver and spleen. A small amount of radioactivity was observed in the intestinal tracts and the kidneys were not imaged. The pancreas-to-liver (P/L) ratio calculated from SPECT images was 1.32 in this case. The mean P/L ratio of five normal cases was 1.26 ± 0.22.

SPECT images of a 78-yr-old male with chronic pancreatitis are shown in Figure 3. Although the entire pancreas was imaged, radioactivity in the pancreas was lower than the normal cases. A relative increase of the radioactivity in the liver and the spleen was observed.

P/L ratio obtained from the SPECT image was 0.76 in this case. Several cases showed rather high radioactivity in the intestinal tracts. Another of the SPECT images, obtained at 5hr postinjection, was useful in distinguishing the activity in the pancreas from that in the intestinal tracts. In a 57-yr-old male with massive calcifications in the pancreas, as shown by x-ray CT (Fig. 4A), the pancreatic uptake was not recognized even in the SPECT images; the P/L ratio could not be calculated in this case. Relatively high radioactivity was seen in the liver and the spleen (Fig. 4B). The mean P/L ratio of five cases with chronic pancreatitis was 0.74

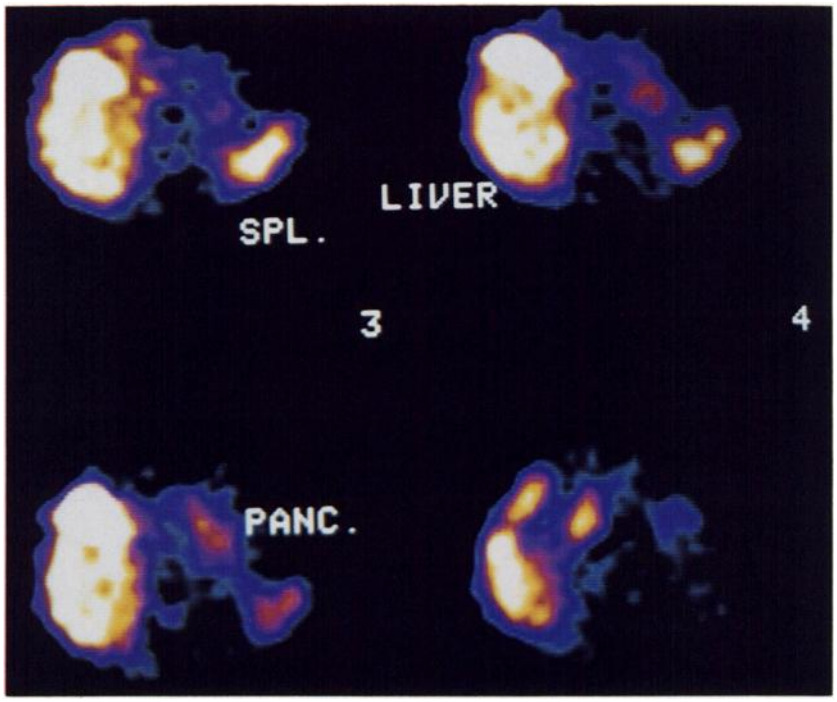

FIGURE 3
SPECT images of a 78-yr-old male with chronic pancreatitis (Case 3). The radioactivity in the pancreas is decreased in comparison with that of normal cases.

± 0.15, which is significantly lower than that of normal cases ($p < 0.05$).

Figure 5 depicts x-ray CT and SPECT images with [^{123}I]HIPDM of a 66-yr-old male with pancreas cancer. X-ray CT shows a low-density mass in the pancreatic body (Fig. 5A). The distal portion of the pancreas was atrophic, but abnormal findings were not detected in the pancreas head. In a SPECT image of the same case (Fig. 5B), the head portion of the pancreas showed an accumulation of [^{123}I]HIPDM, but the areas corresponding to the pancreatic cancer and the atrophic distal portion were defective.

In all the cases with pancreatic cancer, either the cancer or the regions with associated pancreatitis were not visualized with [^{123}I]HIPDM.

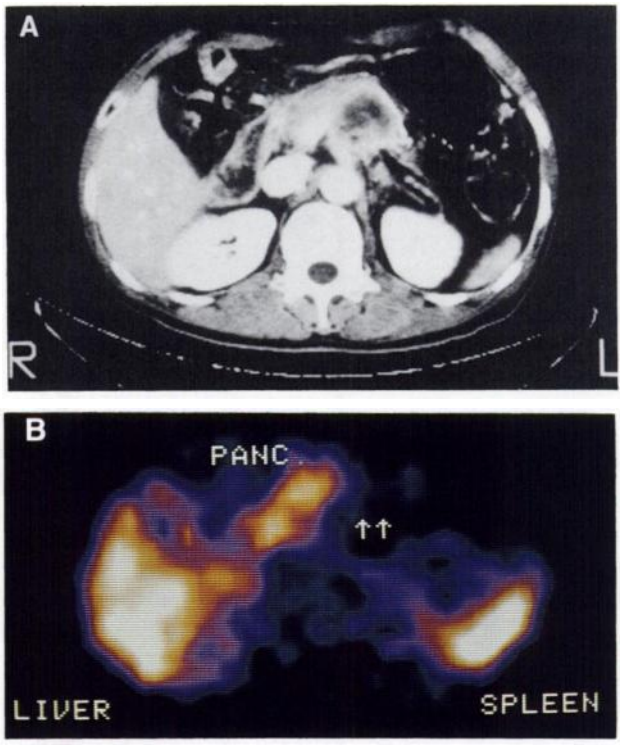

FIGURE 5
A 66-yr-old male with pancreas body cancer (Case 11). X-ray CT (A) depicts a low-density tumor in the pancreatic body, and the distal portion of the pancreas is atrophic. In a SPECT image (B), only the head portion of the pancreas shows accumulation of [^{123}I]HIPDM.

DISCUSSION

Cross-sectional imaging techniques, x-ray CT, and ultrasonography offer important anatomical informations about the pancreas. However, those examinations cannot clearly differentiate pancreas cancer from chronic pancreatitis in some cases and not rare cases of chronic pancreatitis that do not show significant abnormalities on x-ray CT and ultrasonography. The role of pancreas scintigraphy is considered still important in the evaluation of pancreatic diseases. Though various radiolabeled amino acid derivatives have been studied in the search for a pancreas imaging agent superior to ^{75}Se-selenomethionine (*5–7*), no ^{123}I-labeled compound had been considered for clinical application. This study suggests that ^{123}I-labeled HIPDM has an affinity for the human pancreas. In normal cases, the pancreas' image was obtained as early as 3 hr postinjection. Thirty-five minutes of data acquisition was sufficient for reconstruction of the SPECT images, which provided an excellent pancreas image without the overlap of radioactivity in the liver and the spleen. With the exception of one case with massive calcifications in the pancreas, the entire pancreas could be imaged in the cases with chronic pancreatitis, though the P/L ratio was significantly lower than that of normal cases.

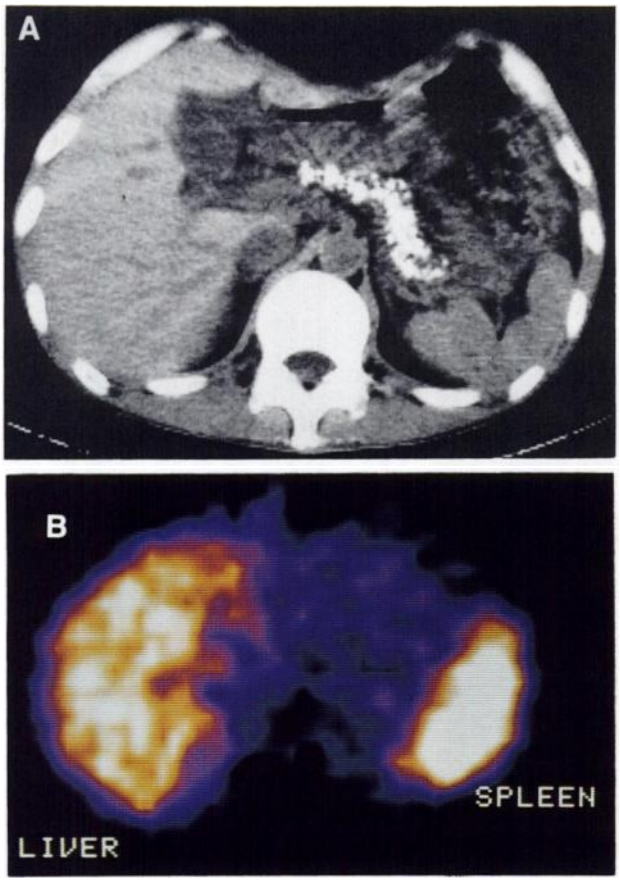

FIGURE 4
A 57-yr-old male with massive calcification in the pancreas (Case 6). In x-ray CT (A), multiple high-density spots are depicted in the pancreas. Pancreas is not visualized in SPECT (B).

HIPDM is a derivative of diamine and the accumulation mechanism of HIPDM to the pancreas is still unclear. As opposed to amino acids, pancreatic uptake of [^{123}I]HIPDM is admittedly rather slow, and radio-

activity remains in the pancreas for long time. Our animal experiments using rats determined that the decrease of pancreatic uptake of radioiodinated HIPDM correlated to the severity of pancreatic damage induced by dl-ethionine. In this clinical study, pancreatic uptake of [^{123}I]HIPDM was also lower in the cases of chronic pancreatitis than in normal controls and was not apparent in the lesions of pancreas cancer. These results suggested an accumulation of HIPDM to the pancreas might relate to pancreatic acinar cell functions. Iodine-123-labeled HIPDM might have clinical potential for pancreas scintigraphy. To verify its potential as a pancreas imaging agent, further research in the mechanism of pancreatic accumulation of HIPDM and the development new derivatives of HIPDM will be required.

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