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Assessment of ^{18}F-FDG-Leukocyte Imaging to Monitor Rejection After Pancreatic Islet Transplantation

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ABSTRACT

Aim. We sought to investigate the feasibility of ^{18}F-FDG-leukocyte imaging to detect islet rejection.

Methods. Two thousand Sprague-Dawley (SD, syngeneic group) or Lewis (allogeneic group) islet equivalents were intraportally injected into SD rat recipients. Four and 7 days after transplantation, 10^8 ^{18}F-FDG–labeled splenocytes were injected into the jugular vein. Splenocytes were harvested from naïve or sensitized (12 days after intraportal transplantation of 2000 Lewis IEQ) SD rats. Positron emission tomography (PET) imaging was started 5 minutes after splenocyte infusion and performed hourly for 4 hours.

Results. One hour after splenocyte injection, FDG was mainly detected in the heart and lungs. It was then further distributed to other organs, and from the second hour, the highest tracer concentration was located in the abdomen. Liver FDG uptake was similar between syngeneic, allogeneic, and sensitized allogeneic groups at 4 and 7 days after islet transplantation.

Discussion. No islet rejection was detected by ^{18}F-FDG-leukocyte imaging. The amount of transplanted tissue was only few millilitres and the additional related inflammation in case of rejection is small and difficult to detect. The liver showed a relatively high spontaneous tracer uptake; the related background prevented detection of a potential increase in tracer uptake in cases of islet rejection.

ALTHOUGH islet graft positron emission tomography-imaging (PET) is an option to improve posttransplant monitoring, current positron-emitting tracers are poorly specific, have short half-lives, and are not stable enough in pancreatic islets to allow long-term follow-up.[1] Only short-term assessment has been achieved so far.[2] The aim of the present study was to assess the applicability of 2-[^{18}F] fluoro-2deoxy-D-glucose (FDG)-labeled leukocyte imaging to detect rejection after islet transplantation.

MATERIALS AND METHODS

Male Lewis and Sprague-Dawley rats (Janvier, Le Genest, France), weighing 380 to 500 g, were used according to protocols approved by the institutional animal care and use committee. Transplantation was performed by injecting 2000 islet-equivalents (IEQ) into the portal vein through a 22-G catheter (Optiva 2, Johnson and Johnson, Spreitenbach, Switzerland). Recipient rats were Sprague-Dawleys, and donors were either Sprague-Dawley in the syngeneic model or Lewis rats in the allogeneic group.

Splenocytes were isolated from naïve or sensitized Sprague-Dawley rats. After harvesting, the spleen was chopped. Splenocytes were purified in a density gradient (histopaque-1077; Sigma, Busch, Switzerland). In sensitized animals, splenocytes were isolated 12 days after intraportal transplantation of 2000 Lewis IEQ.

Clinical-grade FDG was produced by a cyclone 18/9 cyclotron (IBA, Belgium). Splenocytes were labeled with FDG in 250-μL glucose-free DMEM for 1 hour. After incubation, splenocyte radioactivity was measured with an ISOMED 2000 ionization chamber (Nuklear Medizintechnik, Dresden, Germany).

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Infusion of 10^8-labeled splenocytes was performed at 4 or 7 days after islet transplantation via a 22-G central venous catheter (Optiva 2; Johnson and Johnson, Spreitenbach, Switzerland). This time point was selected because in a preliminary experiment rat islet recipients were hyperglycemic at 1 week after allogeneic transplantation.

PET scanning was performed on a whole-body 3D only ECAT ART tomograph (CTI/Siemens, Knoxville, Tenn), as previously described.[2] Imaging started 5 minutes after infusion of splenocytes and was performed hourly for 4 hours. For each studied organ, regions of interest were drawn on transaxial slices, and total radioactivity calculated and corrected for radioactive decay considering the time of injection. Finally, the specific organ uptake was calculated by computing the ratio between the injected radioactivity and specific organ radioactivity.

RESULTS

Similar numbers of splenocytes were isolated in each group: 267 ± 46, 297 ± 64, and 392 ± 291 × 10^6 cells from Sprague-Dawley, Lewis, and sensitized Sprague-Dawley rats. In vitro uptake of FDG was also similar for naïve and sensitized splenocytes (1 ± 0.6 and 2.2 ± 0.81 MBq). One hour after injection, FDG was mainly detected in the heart and lungs. From the second hour, the highest tracer concentration was located in the abdomen. Similar distributions were observed in the three groups at 4 or 7 days after transplantation. Liver FDG uptake was similar between the syngeneic, allogeneic and sensitized allogeneic groups, 4 and 7 days after islet transplantation (Fig 1). Similar results were obtained when comparing the ratios of activity between the liver and the spleen.

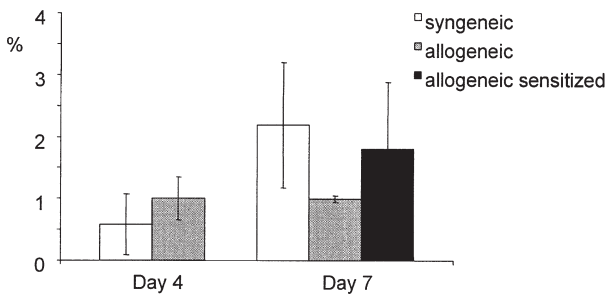

Fig 1. Liver radioactivity, 2 hours after injection of naïve or sensitized FDG-labeled splenocytes, 4 and 7 days after syngeneic or allogeneic rat islet transplantation.

DISCUSSION

FDG-labeled splenocyte imaging is feasible, as demonstrated by previous studies.[3] This technology has only been used to assess strong inflammation so far, like liver ischemia after occlusion of the hepatic artery.[3] In our study however, it failed to demonstrate islet rejection. Several attempts to monitor rejection, using scintigraphy with labeled monocytes or platelets have been performed in solid organ transplantation. Most studies demonstrated some increase of uptake, related to rejection.[4,5] In cases of islet transplantation, the amount of transplanted tissue is only a few millilitres and the related inflammation is small and difficult to detect. Moreover, the liver shows a relatively high uptake, already at 4 days after syngeneic transplantation. This finding was attributed to the spontaneous uptake of the liver or to some nonspecific posttransplant inflammation. As a consequence, the related background was much higher than the potential increase of uptake that one could detect in the case of islet rejection. The present technology appears not sensitive enough to allow detection of an islet graft rejection.

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