Evaluation of Pediatric Liver Transplant Recipients Using Quantitative Hepatobiliary Scintigraphy

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The first successful liver transplantation was performed in 1963. Since then, advances in surgical technique, immunosuppressive therapy, and treatment of posttransplant complications have dramatically improved the prognosis for patients who undergo this procedure. Further, refinement of preoperative nutritional management and the advent of techniques for reduced-size transplants have made liver transplantation the preferred treatment for pediatric patients with end-stage liver disease. The postoperative period is a critical and uncertain time for pediatric liver transplant recipients because of the possibility of various complications that lead to liver dysfunction. Possible complications include infection, rejection, hepatocyte damage, cholestasis, vascular occlusion, and biliary obstruction. Another important issue is that there may be no accompanying clinical signs when a graft starts to fail. Biochemical testing lacks sensitivity, especially in the early postoperative period. Biopsy is currently considered the only definitive method for identifying liver transplant problems, but this is an invasive procedure. Quantitative, noninvasive methods are needed to diagnose graft dysfunction in the early stage. Radionuclide imaging methods may meet these requirements.

The aim of this study was to assess the clinical value of serial quantitative hepatobiliary scintigraphy for monitoring graft function in pediatric liver transplant recipients.

MATERIALS AND METHODS

Patients

We studied 10 pediatric liver transplant recipients, 5 who had undergone orthotopic and 5 who had undergone heterotopic liver transplantation. Three of the patients were female, 7 were male, and the mean patient age at transplantation was 13.4 ± 1.2 years. The causes of liver failure in the group were Byler’s disease (n = 3), Wilson’s disease (n = 2), cryptogenic cirrhosis (n = 2), hepatitis B (n = 1), Budd-Chiari syndrome (n = 1), and Alagille syndrome (n = 1). Three of the grafts were from cadavers and 7 were from living-related donors. All patients received segmental liver grafts. The median follow-up period after transplantation was 4.5 years. Hepatobiliary scintigraphy was carried out at regular intervals, starting with the first week after transplantation. Graft liver biopsy was performed in all cases that showed abnormal scintigraphic parameters. Scintigraphy and biopsy results were compared.

Hepatobiliary Scintigraphy

A total of 78 hepatobiliary scans were done in the 10 patients. Each scan required an intravenous injection of 1.85 MBq/kg of Tc-99m mebrofenin (CIS Bio International, France). A large-field-of-view single-head gamma camera (Siemens, Diacam, Germany) with a low-energy all-purpose collimator was used for image acquisition. In testing parenchymal function, data were recorded every 30 seconds for 40 minutes in a 64 × 64 matrix, and the images were then evaluated quantitatively. The quantitative parameters used were hepatocyte extraction fraction (HEF), time to maximum activity (Tmax), and time to half of maximum activity (T1/2). To determine HEF, we drew similar sized regions of interest over the left ventricle of the heart and the graft liver. Time activity curves were obtained from these regions, and then HEF values were calculated by deconvolution analysis. To determine Tmax and T1/2 values, we drew a region of interest over the graft liver and drew a background region of interest below and lateral to the graft liver. Time activity curves were obtained, and we calculated the Tmax and T1/2 values from these curves.

Biopsy

All pathologic specimens were obtained by needle biopsy, and each sample was formalin-fixed and processed routinely for light microscopy. Biopsies were systematically evaluated for features of acute rejection, chronic rejection, hepatocyte damage/cholestasis, and other pathology.

Statistical Analysis

The paired-samples student t test was used for statistical analysis. P < .05 was considered to indicate statistical significance.

RESULTS

At the end of the first week, 4 patients’ grafts showed normal HEF, Tmax, and T1/2 values. In this group, the mean HEF was 95.2 ± 2.5%, the mean Tmax was 10.5 ± 1.5 minutes, and the mean T1/2 was 29.7 ± 1.8 minutes. The other 6 patients showed abnormal scintigraphic findings at this time. In this group, the mean HEF was 43.0 ± 7.1%, the mean Tmax was 28.5 ± 1.4 minutes, and the mean T1/2...
was 56.4 ± 4.3 minutes. The graft biopsies from these 6 patients revealed 1 episode of acute rejection in 1 child and hepatocyte damage/cholestasis in the other 5 cases. In 5 of the 6 patients with abnormal scintigraphy findings, the parameters normalized after the episode of acute rejection and the hepatocellular damage resolved. The remaining

Fig 1. Hepatobiliary scans in pediatric recipient at the end of the first week (A) and fourth year (B) after orthotopic liver transplantation. The scans were completely normal at both periods.
individual continued to show abnormal HEF, Tmax, and T 1/2 values.

In late follow-up period, 4 of the 9 grafts that had shown normal function previously exhibited abnormal parameters. The findings for these cases were mean HEF 44.6 ± 2.7%, mean Tmax 29.2 ± 2.5 minutes, and mean T 1/2 58.4 ± 2.8 minutes. Biopsies from these patients revealed hepatocyte damage/cholestasis. Serial follow-up scanning showed normalization of the scintigraphic parameters in 2 of the 4 cases. In the other 5 of the 9 grafts that had shown normal function, scintigraphic parameters remained normal throughout follow-up (Fig 1). In these patients, the mean HEF was 96.8 ± 2.1%, the mean Tmax was 11.5 ± 0.8 minutes, and the mean T 1/2 was 28.2 ± 2.2 minutes. The 10th patient continued to exhibit abnormal scintigraphic parameters from the early through the late phase of follow-up.

Statistical testing revealed significant differences in the HEF, Tmax, and T 1/2 values for the normal functioning and dysfunctioning grafts in early and late period after the transplantation (P < .001). We found a significant positive correlation between the biopsy and scintigraphy results (P < .001).

DISCUSSION

Liver transplantation is an accepted and successful treatment method for pediatric patients with end-stage liver disease. Monitoring of transplant liver function is important in these individuals, because graft dysfunction due to various complications may arise in the postoperative period. Hepatobiliary scintigraphy with Tc-99m iminodiacetic acid (IDA) derivatives is a useful technique for examining liver transplant recipients post-surgery. This noninvasive method permits identification of structural complications such as infarcts, abscesses, and bile leaks, as well as functional complications related to hepatic perfusion, tracer uptake, and excretion.3 Although this method has been widely used to evaluate graft liver function in adult patients,3,5–7 few studies have focused on pediatric liver transplant recipients.

Gelfand et al studied the effectiveness of Tc-99m mebrofenin scintigraphy for evaluating graft function in pediatric orthotopic liver transplant recipients.2 They performed 115 hepatobiliary scans in 30 children, showing that the method was valuable for predicting graft survival and identifying biliary complications. In addition, Roca et al came to similar conclusions in a review of the utility of hepatobiliary scintigraphy for assessing pediatric liver transplant recipients.8

In the present study, we used serial quantitative hepatobiliary scintigraphy with Tc-99m mebrofenin to assess the function of segmental liver grafts in pediatric liver transplant recipients. Unlike other investigators, in addition to assessing orthotopic liver transplant recipients this way, we also evaluated graft function in heterotopic pediatric liver transplant recipients. Graft liver biopsies were performed in all cases that showed abnormal scintigraphic parameters; biopsy and scintigraphy results were compared. We found a significant positive correlation between the biopsy and scintigraphy findings (P < .001). Overall, the study showed that quantitative hepatobiliary scintigraphy is a sensitive method for identifying liver dysfunction and establishing recovery of graft function after the complications in orthotopic and heterotopic pediatric liver transplant recipients.

We conclude that serial quantitative hepatobiliary scintigraphy is a valuable noninvasive method for monitoring graft liver function in children who have undergone liver transplantation.

REFERENCES