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Renal function in patients on long-term home parenteral nutrition and in intestinal transplant recipients

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ABSTRACT

Objective: A decrease of renal function was described in patients on long-term home parenteral nutrition (HPN) for benign intestinal failure. The risk for chronic renal failure (CRF) due to frequent episodes of dehydration despite optimal HPN, is an indication for intestinal transplantation (ITx). ITx is the solid organ transplant at highest risk for developing CRF. The aim of this study was to compare the prevalence and the probability of CRF occurring in adults on HPN and after ITx.
Methods: A cross-sectional and retrospective follow-up study was carried out in 2011. Renal function was evaluated at cross-sectional and at time of starting HPN or ITx, by serum creatinine concentration (mg/dL) and estimated glomerular filtration rate (eGFR), according to the Modification of Diet in Renal Disease equation (mL·min·1.73 m^2). CRF was defined as eGFR <60. Duration of follow up was from time of starting treatment to time of cross-sectional.
Results: We enrolled 33 patients on HPN and 22 who had undergone ITx. The frequency of CRF was 6% in the HPN group and 9% in the ITx group ($P = 0.67$) at start of treatment, and 21% and 54%, respectively ($P = 0.01$) at the time of the cross-sectional evaluation. During the follow-up, the annual decline of eGFR was 2.8% and 14.5%, respectively ($P = 0.02$). The 5-y probability of maintaining an eGFR ≥60 was 84% in the HPN group and 44% in the ITx group ($P < 0.001$).
Conclusions: The decrease of renal function and the risk for developing CRF are greater after ITx than during HPN. The risk for CRF on HPN, as a criterion for ITx, should be revised.

Introduction

Intestinal failure (IF) results from a reduction in the functioning gut mass characterized by the inability to maintain protein–energy, fluid, electrolyte, and/or micronutrient balance [1]. Patients with irreversible IF are destined to be dependent on lifelong home parenteral nutrition (HPN) or to undergo intestinal transplantation (ITx). HPN is currently the primary therapy and patients are usually listed for ITx when a life-threatening condition occurs due to complications of HPN or because of the underlying disease [2].

A few studies have investigated the renal function in adults on HPN for chronic benign IF [3–5]. One retrospective follow-up showed a progressive decline of glomerular filtration rate (GFR) [3], and two cross-sectional studies reported a decreased renal function in about 50% of patients on HPN [4,5]. The occurrence of frequent and severe episodes of dehydration, potentially causing chronic renal failure (CRF), was included among the Medicare indication criteria for ITx [2,6]. However, several studies on adult and pediatric ITx recipients have showed that ITx is the solid organ transplant at highest risk for patients to develop CRF, with a 21% incidence at 5 y post-ITx and an associated increased risk for death [7–12].

In order to further investigate the outcome of the renal function of patients on HPN and of ITx recipients, we carried out a comparative study to analyze the prevalence and probability of

LP conceived and designed the study, analyzed the data, and drafted the manuscript. AL and CZ generated and collected the data on the intestinal transplantation recipients. VS, FA, MG, and CP generated, collected, and assembled the data on the patients receiving home parenteral nutrition. ADP revised the manuscript and all authors approved its final version.

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developing CRF in two adult patient cohorts who were cared for at the same hospital.

Materials and methods

This was a cross-sectional and retrospective follow-up study, based on data prospectively recorded during the patients' scheduled clinical monitoring. For the purpose of the study, baseline was the time of starting HPN or of ITx, cross-sectional was the time of inclusion and of data collection, and the duration of the follow-up was the time from baseline to cross-sectional study.

In 2011, all the patients followed at the Center for Chronic Intestinal Failure [13] and at the Transplantation Unit [14] of the S. Orsola-Malpighi University Hospital of Bologna, Italy, who were on HPN for benign IF or who had undergone ITx were included in the study, if all the following criteria were present: age 18 to 60 y, duration of treatment >6 mo, stable at home.

Age, sex, body mass index (BMI, kg/m^2), primary disease, and cause of IF were recorded for all patients. The characteristics of the HPN program and the number of episodes of central venous catheter (CVC)–related sepsis were collected for those on HPN. Type of ITx, the induction of immunosuppressive therapy, the number of acute cellular rejection (ACR) episodes, and the duration of HPN before ITx were analyzed for ITx recipients.

Renal function was assessed using serum creatinine concentration (sCr, mg/dL) to calculate the estimated glomerular filtration rate (eGFR) according to the Modification of Diet in Renal Disease Study equation (mL·min·1.73 m^2 body surface) [15]. Renal function was classified as normal when eGFR was ≥90 mL·min·1.73 m^2. Decreased renal function was classified as mild when eGFR was 89 to 60 mL·min·1.73 m^2, moderate when eGFR was 59 to 30 mL·min·1.73 m^2, and severe when eGFR was <30 mL·min·1.73 m^2. A permanent reduction in eGFR to <60 mL·min·1.73 m^2 was defined as CRF [15].

Serum creatinine at cross-sectional study, was analyzed by Jaffe's assay on fully automated and run on Modular E 170 analyzer (Roche Diagnostic International Ltd, Rotkreuz, Switzerland S.P.A.). Normal value is ≤1.2 mg/dL.

The history of the patients with normal renal function at baseline and an eGFR <60 mL·min·1.73 m^2 at cross-sectional, was reviewed to identify the time when permanent CFR occurred.

The study was carried out according to the institutional review board and ethical committee approval was given for studies based on the retrospective analysis of data collected during the routine clinical practice (no. 1248/2007).

Statistical analysis

Variables are reported as mean ± SD, median, and percentages. Differences between means were analyzed by the Student's *t* test and those between median by the Mann-Whitney *U* test. Differences between frequencies were analyzed by the χ^2 test. Spearman Rank Correlation was used to evaluate the association between the variables. The probability of developing CRF was calculated using the Kaplan-Meier method, including those patients who had eGFR >60 mL·min·1.73 m^2 at baseline. The end point was the time from baseline to the time of occurrence of CRF or to the end of the follow-up. Group comparison was made with the log-rank test. *P*-values < 0.05 were considered significant. The Statgraphics® Centurion XV statistical package 2008 (StatPoint, Inc, Warrenton, VA, USA) was used for the analyses.

Results

Fifty-five patients were included in the study. Of the participants, 33 were on long-term HPN and 22 were ITx recipients. The characteristics at baseline of the two patient cohorts are shown in Table 1. The groups significantly differed for the percentage of female patients (higher in the ITx group), age (younger in the ITx group), BMI (lower in the HPN group), and primary disease (presence of Crohn's disease in the HPN group). The type of ITx was isolated small bowel in 19 recipients, multivisceral with liver in 2, and modified multivisceral (no liver) in 1. The induction immunosuppressive therapy was alemtuzumab in 16 patients, daclizumab in 5, and thymoglobulin in 1. The duration of HPN before ITx was 32 ± 78 mo. Before starting treatments, renal function was normal in most of the patients and did not differ between the groups. In the four patients who had CRF, sCr was increased in three (range: 1.4–1.9 mg/dL) and normal in one (1.1 mg/dL).

The duration of the follow-up and the outcome of the renal function are reported in Table 2. At the end of the follow-up, BMI did not differ between the groups, eGRF was significantly lower and frequency as well as degree of CRF were higher in the ITx group. One ITx recipient was on hemodialysis. In the 21 patients who had CRF, sCr was increased in 14 (range: 1.3–10 mg/dL) and normal in 6 (0.8–1.2 mg/dL). During the follow-up,

Table 1
Characteristics of the patient cohorts at baseline: time of starting HPN or of ITx

	HPN (n = 33)	ITx (n = 22)	*P*-value
Males/females	13/20	15/7	0.036
Age (y)			
Mean ± SD	43.8 ± 10.8	32.6 ± 9.2	0.000
Median	43.8	32.1	0.000
BMI (kg/m^2)			
Mean ± SD	19.4 ± 5.1	21.5 ± 3.6	0.095
Median	18.3	21.6	0.027
Cause of intestinal failure, n (%)			0.500
Short bowel syndrome	21 (63.6)	15 (68.2)	
Motility disorder	11 (33.3)	6 (27.3)	
Others	1 (3.1)	1 (4.5)	
Primary disease, n (%)			0.020
Mesenteric ischemia	6 (18.2)	9 (40.9)	
CIPO	10 (30.3)	6 (27.3)	
Crohn's disease	11 (33.3)	0	
Desmoids in FAP	3 (9.1)	2 (9.1)	
Others	3 (9.1)	5 (22.7)	
Baseline renal function			
sCr (mg/dL)			
Mean ± SD	0.82 ± 0.28	0.83 ± 0.25	0.884
Median	0.78	0.80	0.629
eGFR (mL·min·1.73 m^2)			
Mean ± SD	101.6 ± 36.3	117.3 ± 53.4	0.198
Median	94.0	107.0	0.191
Renal function degree, n (%)			
eGFR ≥ 90 (mL·min·1.73 m^2)	19 (57.6)	16 (72.7)	0.342
eGFR 89–60 (mL·min·1.73 m^2)	12 (36.4)	4 (18.2)	
eGFR 59–30 (mL·min·1.73 m^2)*	2 (6.0)	2 (9.1)	

BMI, body mass index; CIPO, chronic intestinal pseudo-obstruction; eGFR, estimated glomerular filtration rate; FAP, familial adenomatous polyposis; HPN, home parenteral nutrition; ITx, intestinal transplantation; sCR, serum creatinine
* eGFR < 60 mL·min·1.73 m^2 indicates the presence of chronic renal failure.

Table 2
Outcome of the renal function during HPN or after ITx

	HPN (n = 33)	ITx (n = 22)	*P*-value
Duration of follow-up (y)			
Mean ± SD	8.4 ± 6.6	6.2 ± 3.1	0.152
Median	7.2	6.7	0.434
BMI (kg/m^2)			
Mean ± SD	20.3 ± 4.1	21.9 ± 4.4	0.162
Median	20.2	22.32	0.183
Cross-sectional*			
sCr (mg/dL)			
Mean ± SD	0.93 ± 0.29	2.10 ± 2.18	0.003
Median	0.93	1.40	0.000
eGFR (mL·min·1.73 m^2)			
Mean ± SD	84 ± 34	62 ± 41	0.031
Median	74.0	55.5	0.011
Renal function degree, n (%)			
eGFR ≥ 90 (mL·min·1.73 m^2)	13 (39.4)	2 (9.1)	0.013
eGFR 89–60 (mL·min·1.73 m^2)	13 (39.4)	8 (36.4)	
eGFR 59–30 (mL·min·1.73 m^2)†	7 (21.2)	9 (40.9)	
eGFR <30 (mL·min·1.73 m^2)†,‡		3 (13.6)†	
Annual decline of eGFR (% of baseline value)			
Mean ± SD	−2.8 ± 8.3	−14.5 ± 28.4	0.029
Median	−1.5	−7.4	0.007

BMI, body mass index; eGFR, estimated glomerular filtration rate; HPN, home parenteral nutrition; ITx, intestinal transplantation; sCr, serum creatinine
* Cross-sectional data collected at end of follow-up.
† eGFR <60 mL·min·1.73 m^2 indicates the presence of chronic renal failure.
‡ One ITx recipient was on hemodialisis.