Sleep Disturbances and Quality of Life in Patients After Living Donor Liver Transplantation

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ABSTRACT

Background. Following improvements in patient and graft survival after liver transplantation (LT), the recipients' quality of life has become an important focus of patient care. Sleep is closely related to physical and mental health; however, sleep disturbances in LT patients have not yet been evaluated.

Methods. We assessed 59 LT patients (aged ≥18 years) between September 2011 and September 2012. The patients completed the restless legs syndrome (RLS), 36-item short-form health survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS) questionnaires. In addition, laboratory data were obtained and neuropsychological tests (NPT) were performed during study entry.

Results. Thirty-eight patients (64%) were included in the poor sleep group (PSQI ≥6 or ESS ≥10). The SF-36 scores were lower in the poor sleep group than in the good sleep group. Eleven patients (18%) had RLS. An NPT score ≥3 indicated minimal hepatic encephalopathy (MHE3). The MHE3 group consisted of 22 patients (43%). The time after LT was shorter; serum albumin, branched chain amino acid/tyrosine molar ratio (BTR), and role limitations due to poor physical health were lower; and serum ammonia levels were higher in the MHE3 group than in the MHE0-2 group. When the poor sleep group was divided into subgroups (control, MHE, RLS, and unknown), MHE patients had high model for end-stage liver disease scores, high ammonia levels, and low BTR, whereas RLS patients showed a short time after LT.

Conclusion. Sixty-four percent of recipients were classified as poor sleepers. SF-36 scores were lower for poor sleepers than good sleepers. RLS and MHE are major diseases that cause sleep disturbances in patients after LT.

RECENTLY, it has been reported that the general quality of life (QOL) of patients improves after liver transplantation (LT) when compared with that of healthy controls. However, liver transplant recipients have significant deficits in QOL. Consequently, the previously reported QOL benefits after LT may have been overstated [1]. Following improvements in patient and graft survival after LT, the QOL of recipients has become an important focus of patient care and clinical outcomes research. Although QOL improves within 1 year after LT, not all patients achieve or sustain the same level of QOL for 12 years [2]. Efforts should be made to improve QOL and function during the initial recovery period in liver transplant recipients [2]. However, the factors that influence the QOL of liver transplant recipients have not been fully analyzed. Additionally, the lack of a gold-standard QOL instrument for liver transplant recipients is problematic [3].

Patients with liver cirrhosis (LC) experience a wide range of symptoms. Some cirrhotic patients are affected by

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sleep disturbances [4]. In recent years, it has been reported that sleep disturbances in cirrhotic patients is closely related to survival [5] and mental health [6,7]. Córdoba et al reported that sleep disturbances were observed in 47.7% of cirrhotic patients [4]. Sleep disturbances are a major complication in chronic liver disease (CLD) patients. The relationship between sleep disturbances and various cirrhotic symptoms remains unclear. Recently, we determined the prevalence of restless legs syndrome (RLS) in Japanese CLD patients and reported that the prevalence of RLS was 16.8% [8]. In addition, we clarified that RLS worsens the quality of sleep and life in CLD patients. In this report, we found that many cirrhotic patients (40%) without RLS suffered from poor sleep. In another report [9], we showed that branched chain amino acids (BCAAs) are useful for cirrhotic patients who do not have any overt encephalopathy but suffer from sleep disturbances. Barbara et al reported that somnolence in cirrhotic patients is related to minimal hepatic encephalopathy (MHE) [10]. However, the frequency and type of sleep disturbance after LT has not been evaluated.

Rodrigue et al stated that sleep disturbances are common before and after kidney transplantation [11]. They reported that kidney transplant recipients with severe fatigue and poor sleep quality had significantly lower QOL scores than those with low fatigue levels. In their study, the origins of the sleep disturbances were unclear. They suggested that kidney transplantation programs should develop a collaborative relationship with a sleep health center to assist in the clinical evaluation and management of sleep-related problems [11]. Living-donor LT is associated with a lower incidence of neurological complications than cadaveric LT [12], although neurological complications are more common in LTs than in other solid organ transplants (eg, kidney transplantations) [13]. These differences were attributed to the complexity of the surgical procedure, unfavorable clinical conditions of the patients awaiting transplantation (malnutrition, coagulopathy, and low platelet count), and hepatic encephalopathy before LT [14,15]. Sleep disturbances are likely one of the worst problems facing liver transplant recipients.

In this study, we evaluated the QOL of recipients after LT, compared QOL after LT with sleep disturbances, and explored the origins of these sleep disturbances.

PATIENTS AND METHODS

Patients

Our research team included a sleep specialty clinician. The study participants were recruited from among LT patients who were admitted for liver biopsy at Nagasaki University Hospital in Nagasaki, Japan, between September 2011 and September 2012. The eligibility criteria included that patients were ≥18 years of age and on the LT waitlist or a liver transplant recipient. All questionnaires were completed in writing by the patients at entry (Table 1). In addition, laboratory data were obtained at study entry (Table 1). Medical data at the time of LT were extracted from the patients' medical records (Table 2).

Table 1. Clinical Characteristics at Entry

Characteristics	N = 59
Age (mean ± SD)	58.4 ± 11.7
Postoperative weeks to entry	187.3 ± 137.5
BMI (kg/m^2: mean ± SD)	24.2 ± 3.7
Recurrent hepatitis	24
ALT (IU/L: mean ± SD)	33.5 ± 25
Total bilirubin (mg/dL: mean ± SD)	1.1 ± 0.6
Prothrombin time (%: mean ± SD)	82.8 ± 23.8
Branched chain amino acid/tyrosine molar ratio (mean ± SD)	6.87 ± 2.08
Albumin (mg/dL: mean ± SD)	4.0 ± 0.5
Hemoglobin (g/dL: mean ± SD)	12.3 ± 2.4
Ferritin (ng/mL: mean ± SD)	115 ± 136
NEFA (μEq/L: mean ± SD)	0.60 ± 0.26
Creatine (mg/dL: mean ± SD)	0.954 ± 0.264
Ammonia (μg/dL: mean ± SD)	35.3 ± 24.7
Immunosuppressant (PSL/Tac/CyA)	5/33/18
Diabetes	15
Hypertension	25
Thyroid disease (hyper/hypo)	1/3
Cirrhosis-related symptoms score (CSS)	7.1 ± 4.9
Pittsburgh Sleep Quality Index (PSQI)	7.0 ± 3.8
Poor sleeper (PSQI)	34
Epworth Sleepiness Score (ESS)	5.3 ± 3.8
Poor sleeper (ESS)	12
Restless legs syndrome (RLS)	11
Neuropsychological test (NPT)	2.01 ± 1.61
Physical functioning (PF)	76 ± 22
Role limitations due to poor physical health (RP)	70 ± 26
Bodily pain (BP)	71.8 ± 24.5
General health perception (GH)	51 ± 19
Vitality (VT)	59 ± 21
Social functioning (SF)	80 ± 22
Role limitations due to poor emotional health (RE)	74 ± 21.2
Mental health (MH)	67.2 ± 21.2
Respiration quotient (RQ)	0.88 ± 0.19
Resting energy expenditure (REE)	1203 ± 190
% REE	114 ± 190

Normal values in laboratory tests: ALT (IU/L), 5–40; AST (IU/L), 10–40; γ-GTP (IU/L), <70 in men, <30 in women; TP (g/dL), 6.7–8.3; ALB (g/dL), 4.0–5.0; WBC (cells/μL), 3500–9000; RBC (×10^4/μL), 450–580 in men, 380–480 in women; Plt (×10^4/μL), 14–33; PT (%), 70–130; BUN (mg/dL), 8.0–22.0; Cr (mg/dL), 0.61–1.04 in men, 0.47–0.79 in women; ALP (IU/L), 115–359; LDH (IU/L), 119–229; TB (mg/dL), 0.3–1.5; BTR, 5–9.5; NH_3 (μg/dL), <75; ChE (IU/L), 214–466; TC (mg/dL), 128–220; TG (mg/dL), 38–150 (mg/dL), 70–110; BMI, body weight (kg)/height (m^2).

Abbreviations: BMI, body mass index; ALT, alanine aminotransferase; PSL, prednisolone; Tac, tacrolimus; CyA, cyclosporine A; NEFA, non-esterified fatty acid.

Laboratory Measurements

Laboratory data, anthropometric measurements, and questionnaire results were obtained on the day of entry. Body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m^2). Laboratory measurements included white blood cell (WBC) counts, red blood cell (RBC) counts, platelet (Plt) counts, prothrombin time (PT), blood urea nitrogen (BUN), creatinine (Cr), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyltranspeptidase (γ-GTP), alkaline phosphatase (ALP), total bilirubin (TB), total protein (TP), albumin (Alb), total cholesterol (TC), cholinesterase (ChE), triglyceride (TG), fasting blood glucose (FBG), ammonia (NH_3), and BCAA/tyrosine ratio (BTR).