Immunosuppressive Medication Adherence in Liver Transplant Recipients

R. Promraj[a], W. Dumronggittigule[b,*], Y. Sirivatanauksorn[b], A. Ruenrom[a], C. Tovikkai[b], S. Limsrichamrern[b], P. Kositamongkol[b], P. Mahawithitwong[b], and S. Asavakarn[b]

[a]Ambulatory Care Unit, Pharmacy Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [b]Hepatopancreatobiliary and Transplant Surgery Unit, Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

ABSTRACT

Background. Immunosuppressive medication is one of the pivotal factors in the outcome of liver transplant patients. Nonadherence to immunosuppressive therapy is a common problem after transplantation and affects graft and patient survival. This study aimed to assess immunosuppressive medication adherence in liver transplant recipients.

Methods. Liver transplant recipients who underwent the Siriraj-Support Medication Adherence in Organ Transplantation (S-SMAOT) program were included in this cross-sectional study. Immunosuppressive medication adherence was assessed with the use of the Immunosuppressive Therapy Adherence Scale (ITAS, which is scored from 0 to 12; very poor to excellence adherence). The correlations between ITAS scores and the clinical profiles of the patients, duration after transplantation, and transplant educational scores post-test were also analyzed.

Results. From October 2012 to September 2014, a total of 50 liver transplant recipients (86 visits) were enrolled in this study. The ratio of male to female patients was 48:52. The proportions of patients with ITAS scores of 12, 10–11, and 0–9 were 82.6%, 16.3% and 1.2%, respectively. ITAS score was significantly correlated with the duration after transplantation ($P < .001$) and the educational scores ($P = .009$).

Conclusions. Consistent assessment of patients' immunosuppressive medication adherence is essential to avoid problems of noncompliance and to improve the outcome after liver transplantation. The S-SMAOT program was an effective approach to significantly improve the medication adherence in liver transplant recipients.

LIVER transplantation is a life-saving surgery for treating suitable patients with end-stage liver disease and hepatocellular carcinoma [1–3]. Graft survival depends on several important factors, including immunosuppressive medication adherence (compliance). Nonadherence to immunosuppressive medications after liver transplantation is not uncommon, occurring in 15%–40% of patients [4], and this problem is one of the leading causes of preventable graft loss [5,6].

The Siriraj-Support Medication Adherence in Organ Transplantation (S-SMAOT) program was developed and established at Siriraj Hospital to ensure transplant patients' immunosuppressive medication adherence. S-SMAOT includes several educational methods to emphasize the importance of immunosuppressive drugs and to teach liver transplant recipients how to use immunosuppressive drugs properly. Adherence to immunosuppressant therapy can be measured by various techniques, and there is still no criterion standard method. In the present study, the Immunosuppressive Therapy Adherence Scale (ITAS) [7] was used because it is a reliable instrument to measure recipients' adherence.

*Address correspondence to Wethit Dumronggittigule, Hepatopancreatobiliary and Transplant Surgery Unit, Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wang Lang Road, Bangkoknoi, Bangkok 10700, Thailand. E-mail: wethit.dum@mahidol.ac.th

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This study aimed to assess the effectiveness of our S-SMAOT program in improving immunosuppressive drug adherence of liver transplant recipients at Siriraj Hospital.

METHODS

A cross-sectional observational study was performed in the liver transplant patients who visited the Siriraj outpatient liver transplant clinic from October 2012 to September 2014. All patients (50 patients and 86 visits) who had received educational training under the S-SMAOT program by transplant pharmacists were enrolled in this study. This study was approved by Siriraj Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

The S-SMAOT program uses a systematic pharmaceutical educational approach to educate patients and their caregivers about immunosuppressive drugs by means of various pharmaceutical tools, such as medication flipchart, medication schedule, medication pill boxes, drug interaction card, and medical counseling by the transplant team (transplant surgeons, transplant pharmacists, transplant coordinators, and nurses). Moreover, pre- and post-counseling educational tests (Thai-language questionnaires for testing knowledge about immunosuppressive drugs) during admitting at the time of liver transplantation were evaluated to encourage adherence to immunosuppressive and other medications after liver transplantation.

All recipients received educational training under the S-SMAOT program during their admission. Immunosuppressive drug adherence was assessed in the outpatient liver transplant clinic. Patients were interviewed by transplant pharmacists according to the ITAS (Table 1).

Demographic characteristics of the patients were presented in means and standard deviations (SD) or numbers and percentages as appropriate. The correlation between ITAS scores and post-counseling educational scores was evaluated with the use of Spearman correlation test. Moreover, the correlations between ITAS scores and age groups, as well as ITAS scores and duration after liver transplantation, were evaluated. All statistical analyses were performed with the use of SPSS version 18 (SPSS, Chicago, Illinois). A P value of $<.05$ was considered to be statistically significant.

RESULTS

The mean age of the patients was 58 ± 14 years, and 52.3% were female. There were 71 patients (82.6%) having excellent (12) ITAS score. Fourteen patients (16.3%) and 1 patient (1.2%) had moderate (10–11) and poor (0–9) ITAS scores, respectively. The ITAS scores were not significantly different between male and female patients. Age groups were significantly correlated with the ITAS scores ($r = -0.280$; $P = .01$). The patients who were >60 years old had a significant proportion of poor to moderate adherence (30.4% with ITAS 0–11), whereas in patients <50 years old, there was only 1 patient (4.6%) having a moderate ITAS score and none having a poor ITAS score. Educational scores after counseling were significantly correlated with the ITAS scores ($r = 0.235$; $P = .03$). For example, almost all of the patients with high post-counseling educational scores (11 of 12 patients; 91.7%) had the excellent ITAS score, whereas only 73.3% (11 of 15 patients) of the patients with low educational scores had the excellent ITAS score (Table 2).

The most common indication for liver transplantation was hepatocellular carcinoma (26.2%), followed by hepatitis C cirrhosis (24.6%) and hepatitis B cirrhosis (22.9%). However, the ITAS scores were not significantly different among indications for liver transplantation in this study. Interestingly, durations after transplantation were significantly correlated with drug adherence ($r = -0.426$; $P < .001$). In the 1st 6 months after transplantation, the patients tended to have excellence adherence (ranging from 83.3% to 94.5%), and the adherence rate decreased after 6 months (40%–60%; Table 2).

Regarding the number of medications used, the average and SD of the number of total medications and the number of immunosuppressant were 8.6 ± 3.5 and 2.3 ± 0.6 items, respectively. The patients who administered only single immunosuppressive drug tended to have better adherence (100% having excellence adherence) than the patients who administered 2 or 3 immunosuppressive drugs (74.5%–90.6% having excellent adherence). Nevertheless, the number of immunosuppressive drugs was not significantly correlated with the ITAS scores. The number of total medications was also not correlated with the ITAS scores.

DISCUSSION

Immunosuppressive drug adherence is highly essential to maintain excellent outcomes after organ transplantation [8,9]. The incidence of nonadherence to immunosuppressants among organ transplantation varies in different countries, depending on socioeconomic, patient-related, disease-related, and environment-related factors [10–13]. This is the 1st study to evaluate immunosuppressive drug adherence after liver

Table 1. Immunosuppressive Therapy Adherence Scale (ITAS)

Question	Score			
	3: 0% (Never)	2: 1%–20%	1: 21%–50%	0: >50% (Very Frequent)
1) In the past 3 months, how often did you forget to take your immunosuppressive medication(s)?				
2) In the past 3 months, how often were you careless about taking your immunosuppressive medication(s)?				
3) In the past 3 months, how often did you stop taking your immunosuppressive medication(s) because you felt worse?				
4) In the past 3 months, how often did you miss taking your immunosuppressive medication(s) for any reason?				