Assessment of Nonimmunologic Factors in Kidney Transplant Recipients According to Kidney Disease Improving Global Outcomes


ABSTRACT

Introduction. Cardiovascular disease is the primary cause of death among kidney transplant recipients (KTRs), whereas chronic allograft nephropathy (CAN) is the main reason leading to end-stage chronic kidney disease. The etiologies of both entities include immunologic and nonimmunologic factors. The management of modifiable nonimmunologic parameters has recently been identified by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. The aim of our study was to assess the implementation of these guidelines in the outpatient kidney transplantation clinic of our hospital.

Patient and Methods. We retrospectively monitored the records of 48 transplanted KTRs including 32 males of overall mean age 45.1 ± 10.7 years regarding control of anemia, dyslipidemia, mineral bone disorder (MBD), and blood pressure (BP) levels. Data were recorded every 6 months for 2 years, starting 1 year after renal transplantation.

Results. The estimated glomerular filtration rate of patients at baseline was 60.3 ± 18.8 mL/min/1.73 m² with no significant change during 2 years of follow-up. The control of anemia was satisfactory in 42 patients (88%) with hemoglobin values ≥ 11 g/dL during the follow-up. Regarding dyslipidemia management, the aggregate of patients showed fasting triglycerides ≤ 500 mg/dL in all measurements. The percentage of KTRs with LDL ≤ 100 mg/dL tended to improve from baseline versus the end of the study period (20.8% vs 41.7%). Serum calcium was satisfactorily controlled in 77% of patients, serum phosphorus in all patients, whereas parathyroid hormone (PTH) was abnormal in 60% of KTRs with chronic kidney disease stages 3–5. Finally, the BP goal of < 130/80 mm Hg was achieved in approximately half of the patients.

Conclusion. Control of nonimmunologic factors was satisfactory in terms of renal anemia and MBD, whereas dyslipidemia and BP levels were inadequately controlled. There is a clear need for better integration into clinical practice of KDIGO guidelines with regard to modifiable nonimmunologic factors.

The last decade has witnessed improved survival of kidney transplant recipients (KTRs) and better graft survival rates. However, KTRs continue to show an increased risk of premature cardiovascular (CV) mortality. Moreover, long-term allograft survival is restricted by chronic allograft nephropathy (CAN), which is the main cause leading to end-stage chronic kidney disease (CKD). The etiology of the increased CV burden and of CAN includes mutual nonimmunologic risk factors such as traditional CV risk factors, previous chronic renal failure with dialysis therapy, and transplantation itself.

Evidence-based medicine is a clinical discipline that has emerged in the 1990s. It formalized long-practiced principles of basing clinical practice on scientific evidence. Clinical practice guidelines have emerged as useful tools for experienced doctors to improve outcomes. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines have recently been identified by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. The aim of our study was to assess the implementation of these guidelines in the outpatient kidney transplantation clinic of our hospital.

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Disease Improving Global Outcomes (KDIGO; 2009) establishes clinical practice guidelines to monitor, manage and treat KTRs. These guidelines make recommendations for immunosuppression, graft monitoring, as well as prevention and treatment of CV disease, infection, malignancy, and other complications that are common among KTRs, including hematologic and bone disorders.

However, the implementation of these guidelines is difficult despite the efforts of healthcare providers. The aim of our study was to assess the implementation and achievement of these guidelines with regard to modifiable immunologic parameters in the outpatient kidney transplantation clinic of our hospital.

PATIENTS AND METHODS

We retrospectively reviewed data on KTRs from the outpatient clinic in our recently established transplantation center. We considered eligible patients to have received a kidney graft at least a year before the analysis assessing hematologic and biochemical screening at 4 biannual visits starting 2 years after the publication of KDIGO. The cases eligible for analysis included 48 transplant recipients with 32 males showing an overall mean age of 45.1 ± 10.7 years. Renal replacement therapy was hemodialysis (66.7%) or peritoneal dialysis (33.3%) with a mean period of 36.6 ± 37.6 months before transplantation.

We assessed the implementation of clinical practice guidelines for anemia, dyslipidemia, mineral and bone disorders (MBD), and hypertension. The evaluated parameters were as follows: estimated glomerular filtration rate (eGFR), Cockcroft-Gault formula; hemoglobin (Hb), total cholesterol (TChol), low-density lipoprotein (LDL), triglycerides (TRG), serum calcium (Ca) and phosphorus (P), and parathyroid hormone (PTH). Arterial blood pressure as well as systolic and diastolic values (SBP and DBP) were measured in the sitting position after 15 minutes of rest and we evaluated mean values of 2 measurements (5 minutes apart from each other) Moreover, we recorded antihypertensive medications.

According to KDIGO clinical practice guidelines, the recommended target for Hb is ≥11 g/dL and ≤13 g/dL when the patient is receiving erythropoietic-stimulating agent (ESA) therapy. The targets for lipid control are TRG <500 mg/dL and LDL <100 mg/dL. As concerns MBD, for KTRs with CKD of stages 3–5, the serum levels of Ca, P, and PTH should be within normal ranges. The target for control of hypertension is <130/80 mm Hg. The study was approved by our Local Ethics Committee.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (Version 16.0; SPSS Inc., Chicago, Ill, United States). Variables are presented as percentages and mean values ± standard deviations (SD). Descriptive statistics were used to summarize the demographic characteristics of the patients. For comparison of the variables we applied students t test. P < .05 was considered significant.

RESULTS

Mean ± SD of eGFR of KTRs at baseline was 60.3 ± 18.8 mL/min/1.73 m² with no significant change during the period of monitoring. Baseline and final biochemical parameters of patients are shown in Table 1. The control of anemia was considered satisfactory in 42 patients (88%) among whom the target value of Hb was ≥11 g/dL. The other subjects had a mean Hb level of 10.8 ± 1.25 g/dL. Four patients who were receiving ESA therapy had Hb levels <13 g/dL. Patient lipid profiles improved as the levels of LDL were significantly reduced from 153.8 ± 61.1 mg/dL to 124.8 ± 47.5 mg/dL (P = .031), TChol from 223.7 ± 63 mg/dL to 191.1 ± 38.9 mg/dL (P = .015), and TRG from 151.2 ± 59.1 mg/dL to 123.1 ± 66.8 mg/dL (P = .038). In parallel, the number of KTRs achieving LDL targets increased from 20.8% at baseline to 42% at the end of study, whereas the number of KTRs receiving statins remained the same (n = 12; 25%). For KTRs with CKD stages 3–5 (n = 26), parameters of MBD did not change significantly during study. Particularly, serum Ca was within normal range in 77% (n = 20) and serum P in all patients. Values of PTH between 12 and 72 pg/mL were found in 62% (n = 16).

A history of arterial hypertension was present among 46% of patients, whereas 8 KTRs (17%) developed post-transplantation arterial hypertension. Systolic BP was <130 mm Hg in 26 patients (54%) at baseline and in 22 patients (46%) at the end of the study. Diastolic BP was <80 mm Hg in 20 patients (42%) at baseline and in 28 patients (58%) at the end of the study. The mean number of antihypertensive agents per patient was 1.6 ± 0.8 at baseline and 1.7 ± 1.1 at the end of monitoring. One of 2 KTRs was prescribed a calcium channel blocker (50%), whereas 30% (16) used a renin-angiotensin system blocker and 8% used diuretics. Beta-blockers were used in 22 patients (45.8%) at the beginning and in 26 patients (54.2%) at the end of the follow-up period. Two patients (4.2%) were diabetic before transplantation, whereas 10 patients (20.8%) developed post-transplantation diabetes mellitus displaying a mean serum fasting glucose level of 146 ± 42 mg/dL on treatment.

DISCUSSION

Our study confirmed the difficulty of implementing and achieving that targets among KTRs. According to our

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Note: Data shown as mean ± SD. Abbreviations: BMI, body mass index; CG, Cockcroft-Gault formula; NS, not statistically significant.
results the control of anemia was satisfactory. The proportion of our patients with Hb >11 g/dL was higher compared with other reports, since their reported prevalence ranged from 20%–40% depending on the time of evaluation after transplantation. A recent publication by Jones et al reported that the prevalence of anemia decreases from 189% at the time of transplantation to 44% at 2 years thereafter. Moreover, only 4 of our patients (8%) received ESA, whereas published data have shown a percentage to be 20%.

Control of dyslipidemia in our study was rather poor. We managed to double the proportion of patients who met the criteria for successful dyslipidemia treatment by lifestyle modifications mainly; nevertheless, the percentage remained rather low. Dyslipidemias are frequent in renal transplant recipients, occurring among approximately 60% of them within the first year posttransplantation. It has been suggested that this factor may relate to the development of CAN. Moreover, a large, randomized, multicenter trial showed that management of dyslipidemia with fluvastatin produced safe, effective reduction in LDL-cholesterol associated with a reduced risk of major CV events. Our result supports the difficulty of managing dyslipidemia in KTRs due to the multifactorial etiology.

Biochemical abnormalities of MBD which are common among KTRs, fluctuate dramatically depending on the time after kidney transplantation. Unfortunately, there is a paucity of data describing the risk relationship of these abnormalities to mortality among KTRs. Two investigative groups have observed a relationship between serum Ca, P disturbances, and an increased risk of kidney allograft loss. Our results to meet MBD targets were satisfactory, although there are no large databases including routinely collected data for systematic evaluation. Therefore, the predictive value of statutory treatment criteria remains obscure.

Finally, although BP control was poor, namely half of our patients achieved the suggested target range, it was an expected finding because this goal is difficult to reach among KTRs. Hypertension affects approximately 80% of KTRs presented a calcineurin inhibitor. Data from the Collaborative Transplant Study clearly showed that poor hypertensive control with a SBP >130 mm Hg was deleterious to graft function in the long term. Our result was consistent with the findings of Hillebrand et al.

According to our knowledge there is no report that evaluates KDIGO guidelines with regard to nonimmunologic parameters among KTRs. We hypothesized that these guidelines have set high standards for the management of modifiable nonimmunologic factors that predict both CVD and CAN in KTRs. Theere goals are difficult to achieve. Moreover, it seems that healthcare providers involved in the treatment of KTRs might, justifiably, mainly focus on the management of immunologic factors affecting patient and graft survivals. The results of our small study support the clear need for better implementation of KDIGO guidelines into clinical practice with regard to modifiable nonimmunologic parameters.

REFERENCES

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5. KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients: Am J Transplant 9(suppl 3):S1, 2009