

Comparison of the possible side effects of cyclosporine and tacrolimus on renal function in kidney transplant patients

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Abstract

Background: Cyclosporine and Tacrolimus are two main immunosuppressants of kidney transplant patients and are commonly used in hospitals with renal transplantation.

Aim of the study: The goal of this study is to demonstrate potential harmful effects, not only from kidney failure as a disease, but also the use of immunosuppressants before and after renal transplants.

Materials and Methods: An analysis of tacrolimus or cyclosporine immunosuppressive regimes has been conducted in Baghdad hospital using data from patients with kidney transplants. The study excluded patients who received other types of immune suppressant drugs, and those who switched from cyclosporine to tacrolimus.

Conclusion: Effectiveness and side effects should be tested in kidney transplantation patients with cyclosporin and tacrolimus and other immunosuppressive medications, tacrolimus treated patient has shown an increase in glucose level and decrease in WBC , hemoglobin and calcium level in comparing to cyclosporine treated group.

This finding may allow scientists and physicians to make a better choice between immunosuppressive drug s according to the patient's medical condition.

Keywords: Cyclosporine, Tacrolimus, renal failure, renal transplant.

Introduction

Chronic kidney disease [CKD] is a major threat to public health with a rapid rise in its global prevalence and occurrence, particularly in the developing countries, resulting in end-stage renal disease [ESRD], premature mortality, poor quality of life and large health systems burden. There are currently clear guidelines and an internationally agreed system for CKD staging that facilitates diagnosis and management of the CKD amongst the nations and populations involved in the studies [1, 2].

In most instances, a prolonged path of gradual renal function loss is followed by end stage renal disease. The population with earlier stages of CKD is an ideal target for interventions to slow progression to ESRD and for optimizing management of co-morbid conditions, e.g. cardiovascular disease, anemia, etc., in order to improve long-term outcomes [3].

As an end result of the rise in non-communicable diseases, the number of patients with end stage kidney disease [ESKD] is growing worldwide. ESKD is a medical condition for a lifetime which has a significant impact on clinicians, communities and the health sector. Over 2 million people worldwide have been estimated to need life support therapy for ESKD. In reality the number might be 10 folds higher than the estimated figures as the access to renal replacement therapy [RRT] is restricted or not available in over 112 countries and before accessing diagnostic and therapeutic health services, many patients die [4].

The diagnosis of renal failure in addition to physical exams and complete medical history may include: blood and urine analysis, ultrasound and kidney biopsy [5].

End stage renal failure has a number of different causes. Chronic renal disease risk factors include growing of age, type II diabetes mellitus and hypertension. In contrast to glomerulonephritis, polycystic kidney, atherosclerosis and obstructive uropathy, untreated hypertension is the most common cause [6].

Renal transplantation is a preferred cure for a minority of patients with ESRD. Improved early graft survival and long term graft function have increased the cost-effectiveness of kidney transplantation as an alternative to dialysis [7].

The defense against harmful foreign molecules is the importance of the immune system. However, this protection may in some cases lead to a serious problem. For example, the introduction of an allograft can bring out a damaging immune response, causing rejection of the transplanted tissue [8].

Two of a major immunosuppressant drugs that is used for kidney transplant patient is Cyclosporine and Tacrolimus. Cyclosporin consisted of eleven amino acids it's a lipophilic cyclic polypeptide used to prevent rejection of the kidney, liver and heart transplant allogeneic. By combination with corticoids and anti-metabolite drugs, cyclosporine is most effective in preventing the acute rejection of transplanted organs. Cyclosporine appears to inhibit immune cell induced responses, whereas humeral immunity is much less impaired. Treatment may be linked to several potentially serious side effects: enlarged gum, seizures, peptic ulcers, fever, vomiting, high blood pressure nephrotoxicity, hypercholesterolemia and hepatotoxicity [9].

Tacrolimus, On the other hand, is approved for rejection protection for liver and kidney transplant and is administered with a corticosteroid or anti-metabolites. This medicine was found to be beneficial in compare to cyclosporine because of its potential and decreases in rejection and also because less corticosteroid doses are used with it. , thus decreasing the likelihood of steroid-associated side effects. Tacrolimus performs like cyclosporin in its immunosuppression reaction, except that it bind to a different immunophilin .and also a wide numbers of side effects are recognized vary between nephrotoxicity and anaphylactic reactions [10]. The purpose of the study is to highlight the potential serious effect not only from renal failure but also from the use of immunosuppressive drugs after renal transplantation, and the safety differences between these drugs.

Materials and methods

A study of tacrolimus or cyclosporine immunosuppressive regimens in the Baghdad clinics has been performed using evidence from patients undergoing kidney transplantation.

Also the study included only incident patients who underwent transplantation in 2015 and were followed-up for at least 3 months.

2 Patient was from both gender and age from (40 -65) included in this study Patients who received more types of immune suppressant drugs than that we include in this study was excluded and those who switched from cyclosporine to tacrolimus-based regimens.

SPSS22 analytical method used to estimate the p value. A significance level of 5% was considered.

Group design

Renal transplant Patients was divided into 2 main groups:

Group (1): 11 patient received cyclosporine as there immunosuppressant drug in addition to corticosteroid.

Group (2): 11 patient received Tacrolimus as there immunosuppressant drug in addition to corticosteroid.

Laboratory analysis

All patients had been examined after the kidney transplantation for kidney function tests, glucose level and electrolyte concentration as follows:

- 1- Creatinine serum concentration.
- 2- Urea blood concentration.
- 3- Glucose blood concentration.
- 4- Sodium serum concentration.
- 5- Potassium serum concentration.
- 6- Calcium serum concentration.
- 7- WBC count.
- 8- Platelet count.
- 9- Hemoglobin level.

Results

A. Biochemical results

Table (1): the means of biochemical parameters levels in group (1 , 2) in patient after kidney transplant

	Normal values	Group 1	Group 2
Glucose levels mg/dl	70-100	137.88±21.54	147.66±24.5*
UREA levels mg/dL	8-21	79.1±19.9	85.6±34.0
Creatinine levels mg/dL	0.8-1.3	2.7±0.95	2.5±1.2
WBC levels/μL	4000-10,000	12388.8±4168.16	7066.66±2003.33*
Platelet levels/μL	150,000-350,000	234000±85287.74	156000±121622.36 *
Hemoglobin levels g/dL	14-17	8.2556±2.4	6.9333±1.5

Group (1): cyclosporine treated group, Group (2): Tacrolimus treated group * represent a significant deference between group (1) and group (2) [p<0.05] SPSS22 analytical method used to estimate the p value.

B. Electrolyte results

Table (2): the means of electrolyte levels in group (1 , 2) and (3) in patient after kidney transplant

	Normal Ca level mg/dL	Ca1 Group 1	Ca2 Group 2	Norml K level meq/L	K1 Group 1	K2 Group 2	Normal sodium level meq/L	Na1 Group 1	Na2 Group 2
Mean Electrolyte	9-10.5	8.6±0.28	7.7±0.01*	3.5-5.0	4.17±1.1	3.8±0.55	136-145	139.2±4.34	134±0.001

Group (1): cyclosporine treated group, Group (2): Tacrolimus treated group * represent a significant deference between group (1) and group (2) [p<0.05] SPSS22 analytical method used to estimate the p value.

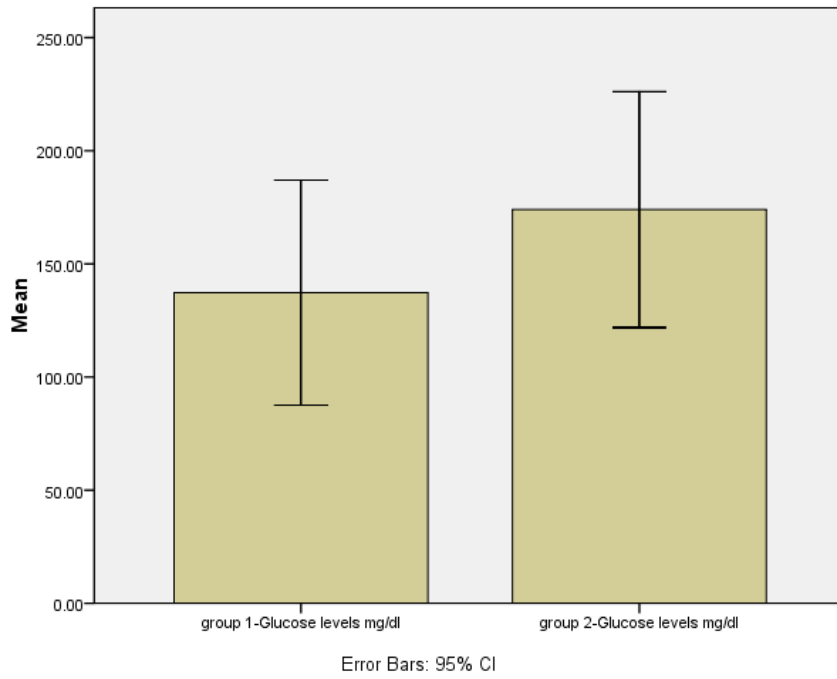


Figure (1): represent the differences between group (1) and (2) in glucose level after 3 months of kidney transplant surgery

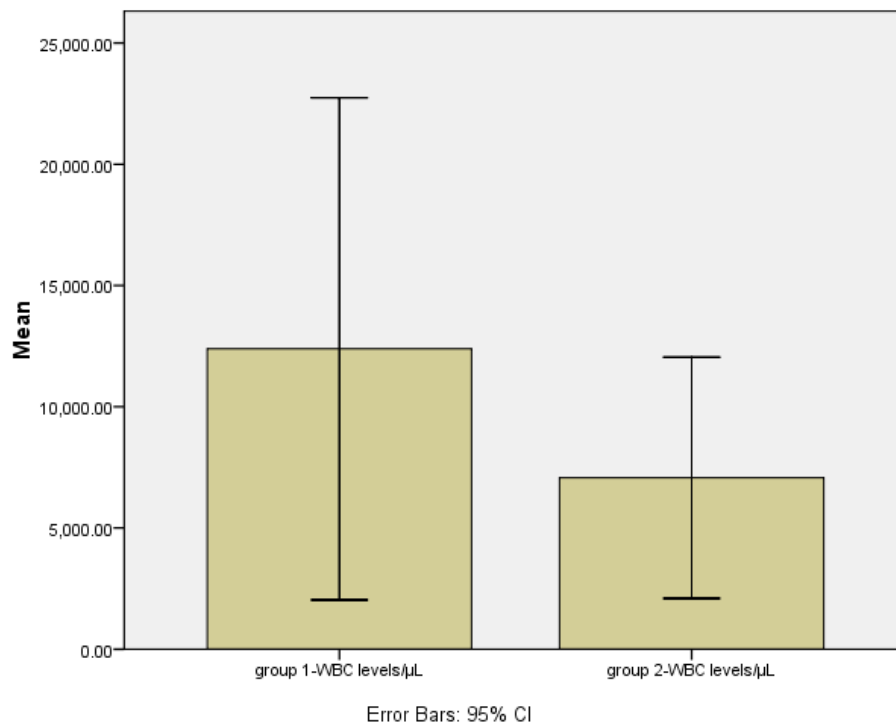


Figure (2): represent the differences between group (1) and (2) in WBC count after 3 months of kidney transplant surgery

Discussion

Tacrolimus and cyclosporine are thought to contribute to Hyperglycemia through a variety of mechanisms, including the inducement of insulin resistance coupled with direct beta cell effects. The differential impact of individual immunosuppressive agents on incidence of PTDM [post-transplant diabetes mellitus] and glycemic control has been examined. Bouchta *et al.* studied patients who developed PTDM following renal transplantation and were converted from tacrolimus to cyclosporine, he found that Tacrolimus conversion to cyclosporin for PTDM is associated with a significant improvement in glucose metabolism and frequent reversal of diabetes [11].

In our study it was found that patients who were treated with Tacrolimus showed a significant increase in glucose level in compare to cyclosporine treated group. Figure (1), Table (1).

Regarding to the renal function tests elevations in serum creatinine and blood urea are common during cyclosporine therapy and do not necessarily indicate allograft rejection. A case of hemolytic uremic syndrome [HUS] associated with cyclosporine therapy has been reported. Another fatal case of acute tubular necrosis has been also reported. In addition, cyclosporine-induced hyperuricemia may predispose the patient to renal calculi [12].

In rare cases, long-term cyclosporine use has induced chronic kidney toxicity. Causing high blood urea or creatinine [13].

Serum creatinine and blood urea levels in cyclosporine treatment are not unusual to increase. These increases do not necessarily indicate rejection in renal transplants and before starting dosage adjustments, each patient should be fully evaluated [14].

In the study it was found that urea and creatinine concentration in both cyclosporine and tacrolimus treated group show un-significant differences in comparing to each other. Table (1)

Looking for the hematological changes that could be associated with renal transplant patient it was found that the incidence of leucopenia and neutropenia in kidney transplant recipients ranges from 10% to 55.5% and from 4.9% to 37.5%, respectively [15].

The first year following transplant occurrence of neutropenia was 28 percent, and was significantly associated with tacrolimus combination therapy, according to a new retrospective study of kidney receivers. These results have been lined with this study in which WBC concentration in cyclosporin treated group found to be $12388.8 \pm 4168.16/\mu\text{L}$ while tacrolimus treated group shows a significant decrease to $7066.66 \pm 2003.33/\mu\text{L}$. Figure (2)

Peter *et al* noted that initial reports had shown that tacrolimus (TC) therapy might have severe anemia. The degree of anemia under TC treatment in comparison to cyclosporine A (CsA) treatment after renal transplantation has been investigated. There is a correlation between Hb and creatinine clearance among children with functioning renal graft. There was no significant difference in the degree of anemia between children treated with TC- and CsA [16].

These results found to be compatible with our results that shown HB concentration for both cyclosporine and tacrolimus are lower than the normal range 8.2556 ± 2.4 g/dL and 6.9333 ± 1.5 g/dL, respectively.

In conjunction with previous works, hyperuricaemia is more popular with treatment with cyclosporin, These findings consist of qualitative differences in cyclosporine and tacrolimus nephrotoxicity [17].

In isolated incidents, shortly after the medication was introduced in clinical usage, a salt loss nephropathy linked to Tacrolimus has been identified. Hyponatraemia has been reported in patient of combined pancreas with kidney transplants disease, and also was correlated to sodium losses in exocrine secretions because the pancreatic duct will drain into the bladder. A clinical study of kidney transplant recipients found that Tacrolimus was less associated with distal renal tubular acidosis than with Cyclosporin [18].

In our study it was found that calcium level was significantly lower than normal level with un-significant differences in potassium and sodium concentrations. Table (2)

Conclusion

Cyclosporine and tacrolimus and other immunosuppressant drugs which are used in kidney transplant patient can be selected depending on their efficiency and side effects associated with their use, tacrolimus treated patient has shown an increase in glucose level and decrease in WBC, hemoglobin and calcium level in comparing to cyclosporine treated group these result could help researcher and physician for better choice between immunosuppressant drugs depending on patient medical condition.

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