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CORRELATION BETWEEN PROGRAF AND CYCLOSPORINE LEVEL AND LIPID PROFILE IN SUDANESE POST-RENAL TRANSPLANT PATIENTS

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ABSTRACT

Background: Hyperlipidemia is an important metabolic disorder that is common among renal transplant recipients. The objective of this study is to correlate between tacrolimus (prograf) and cyclosporine level and lipid profile in Sudanese post-renal transplant patients. **Methodology**: This is a case-control study. Clinical and biochemical data (lipid profile, cyclosporine and prograf levels) of 50 Kidney transplant recipients, referred to Sudanese Kidney Transplantation society and 50 apparently healthy control persons matched for age and sex. **Results:** mean of serum level total cholesterol(TC),Triglycerides(TG),Low density lipoprotein (LDL) were significantly increased in post-renal transplant patient compare to healthy individuals (Cholesterol P=0 .000),(Triglycerides P=0 .000),(LDL P-value= 0.000), but HDL is insignificant increased (HDL P-value= 0.071). There was no difference between patient receiving prograf and cyclosporine on lipid profile (TC p=0.292, TG p=0.875, LDL p =0.959, HDL p=0.723). There was weak correlation between lipid profile and duration of transplantation, and lipid profile level with drugs (Prograf, Cyclosporine) (TC P- value = 0.292, r= -0.152), (TG P-value= 0.875, r= -0.023), (LDL P-value=0.959, r= 0.007), (HDL P-value= 0 .723, r=-.051). **Conclusion**: Lipid profile level is high in post renal transplant patient receiving Prograf and Cyclosporine.

KEYWORDS: Post-renal Transplantation; Hyperlipidemia; Tacrolimus (prograf); Cyclosporine.

INTRODUCTION

Renal transplantation is an established method of renal replacement therapy in patients with end stage renal failure.[1] Despite the improvement, after transplantation, in the overall survival of patients and renal grafts, cardiovascular diseases still the prime cause of death accounting for almost 50% of mortality in this population.[2,3]

Several metabolic disturbances that may contribute to long-term morbidity and mortality occur with increased frequency after renal transplantation. The cause of these disorders is multifactorial, resulting from an interaction of inherent genetic susceptibility effects of immunosuppressant and antihypertensive drugs and weight gain as well as other factors.[4]

Dyslipidemia has been identified as a major risk factor for cardiovascular diseases in the general population and particularly among renal transplant recipients.[5] In addition to the significant risk factor of advanced age and male gender in the general population ,transplant patients frequently display disorders that produce or exacerbate hyperlipidemia.[6] In addition, drug therapy with cyclosporine[7] and steroids[8] may produce hyperlipidemic effects.[6]

Tacrolimus (prograf), a calcineurin inhibitor, remains the centerpiece of the maintenance treatment scheme in renal transplant recipients. Both its narrow therapeutic index and its highly pharmacokinetic variance may lead to over treatment and toxicity or insufficient treatment and transplant rejection, conditions that are usually seen in clinical practice. Thus, it is obvious that the optimal tacrolimus dose has to be achieved soon after transplantation and must be preserved thereafter.[9]

The relative role of steroids and tacrolimus in the development of hyperlipidemia after renal transplantation has not yet been clearly established.[9]

Tacrolimus is chemically known as a macrolide. In T-cells, activation of the T-cell receptor normally increases intracellular calcium, which acts via calmodulin to activate calcineurin.[10]

Tacrolimus reduces peptidyle-prolyl isomerase activity by binding to the immunophilin FKBP (FK506 binding protein) creating a new complex. This FkBP12-FK506 complex interacts with and inhibits calcineurin thus inhibiting both T-lymphocyte signal transduction and IL-2 transcription.[11]

Cyclosporine is an immunosuppressant drug widely used in organ transplant recipients and people with autoimmune disorders. long term treatment with cyclosporine is associated with many side effects including hyperlipidemia and increased risk of atherosclerosis. While its immunosuppressive effects are closely linked to its effects on T-cell activation via the inhibition of the nuclear factor of activated Tcells pathway. These include inhibition of calcineurin activity and intracellular cyclophilin peptidylprolyl isomerase and chaperone activities.[12]

Although short-term immunosuppression concerning patient and graft survival is found to be similar between the two drugs, tacrolimus results in a more favorable lipid profile and this may have important long-term implications given the prognostic influence of rejection on graft survival.[13]

MATERIALS AND METHODS

Case-control study conducted at Sudanese Kidney Transplantation society. The study was carried out in the period of (2016 to 2017). A number of 50 kidney-transplant adult recipients and 50 apparently healthy individual matched for age and sex as control. Patients who diagnosed with diabetes mellitus, hypertension, liver disease and autoimmune diseases before renal transplantation, were excluded. Data were collected from the patient by the information was filled into pre – designed questionnaire, which included personal data, after reception of ethical approval from Ministry of Health and a permission was taken from the Sudanese Kidney Transplantation society Administration, under aseptic precautions 3ml of venous blood on lithuimheparin container was collected both from patients and controls, 3ml of whole blood on EDTA container was collected from patients.

Lipid profile was determined by Cobas C311, full automation. Prograf and Cyclosporine levels were determined using Cobas e411, full automation. The laboratory tests were all performed using control sera.

The sample size was calculated and the data were analyzed by computer using SPSS.

RESULTS

The mean of serum level total cholesterol(TC),Triglycerides(TG) and Low density lipoprotein (LDL) were significantly increased in post-renal transplant patient compare to healthy individuals (TC P=0 .000,TG P=0 .000, LDL P-value= 0.000), but HDL was insignificant increased (HDL P-value= 0.071). There was no difference between patient receiving prograf or cyclosporine on lipid profile (TC p=0.292,TG p=0.875, LDL p =0.959,HDL p=0.723). There was weak correlation between TC, TG, LDL and HDL and duration of transplantation [(p= 0.577, r= 0.081), (P=0.892, r= -0.20) (p=0.494, r= -0.099) (p=0.396, r= -0.123)] respectively. Also there was weak correlation between TC, TG, LDL and HDL and drugs (Prograf, Cyclosporine) (P =0 .292 ,r= -0.152),(P =0.875, r=-0.023),(P=0.959, r=0.007),(P = 0.723,r= -0.051) respectively.

Table 1: shows mean Lipid Profile level between control and patient:

MG/DL	CONTROL (n=50)	Patient (n=50)	P. Value
TC	135 ± 24	218 ±38	.000
T.G	100 ±32	176 ±89	.000
LDL	89 ±24	1.56±47	.000
HDL	55 ±16	63 ±26	.071

TC= Total cholesterol, TG= Triglycerides, LDL= Low density lipoprotein, HDL= High density lipoprotein

Table 2: shows the Comparison between Patients received Prograf and Cyclosporine drugs:

MG/DL	Prograph (n=31)	Cyclosporine (n=19)	P. Value
TC	223 ± 42	211 ±30	.292
T.G	178 ±97	174 ±78	.875
LDL	1.56 ±50	1.1.57 ±41	.959
HDL	64 ±27	61 ±25	.723

TC= Total cholesterol, TG= Triglycerides, LDL= Low density lipoprotein, HDL= High density lipoprotein.

DISCUSSION

This study focused on the occurrence of the lipid abnormalities in post renal transplantation and the pattern of hyperlipidemia was also defined. Results of the study showed high level lipid profile in post renal transplant patients. These results are confirmed with previous studies.[14, 15, 16] and contradicted with another studies.[16, 17] In this study there were high levels of TC, TG (90%, 52%) respectively. HDL was insignificant increased. Increased in HDL is beneficial for renal transplant patients, because it's protective against coronary heart disease.[14] In agreement with Gunjotikar et al.[18] LDL reported negative correlation with duration of transplantation. In this study there was weak correlation with cyclosporine and lipid profile in agreement with other studies.[19,20] Hypertension is an important factor causing renal dysfunction and also can be caused by renal dysfunction.[21,22] Other factors can produce hyperlipidemic effect such as advanced age, male gender and use of steroids.

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CONCLUSION

The study found that Lipid profile level is high in post renal transplant patients receiving Prograf and Cyclosporine.

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