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Correction of Serum Leptin after Successful Kidney Transplantation

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Authors' contributions

This work was carried out in collaboration between all authors. Authors PKK and MD designed the study and principal investigators. Author RMP wrote the protocol. Authors STR performed the statistical analysis and author KR performed biochemical analysis. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Introduction: Serum leptin levels are increased in chronic kidney disease (CKD) patients primarily due to decreased clearance by kidneys. As leptin is a 16 Kda protein, it is also not cleared even by dialysis using conventional dialyzers or by continuous ambulatory peritoneal dialysis (CAPD). Studies have shown that elevated leptin levels are corrected after successful renal transplantation. With this intention, we determined if restoration of renal function with kidney transplantation can reduce serum leptin concentration in CKD patients.
Materials and Methods: A total of 21 Patients undergoing living donor kidney transplantation were studied. There were 13 men and 8 women, from 16 to 45 years of age. All patients were receiving Hemodialysis prior to transplant. All patients received triple immunosuppressant therapy after the surgery. There were no graft rejections. Blood samples were collected under fasting conditions before and 6 days after transplantation.

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Results: The mean age of the patients was 28.38±9.38 years. Pre transplantation leptin concentration was 9.96 + 3.48 ng/ml and this decreased to 4.07±1.7 ng/ml within six days of transplantation ($p<0.0001$). However there was no concomitant change in Body Mass Index (BMI) as the follow-up was too short. Plasma Creatinine level declined from 7.5±1.6 mg/dl to 1.1±0.7 mg/dl within six days after transplantation.
Conclusion: Successful renal transplantation immediately reduces serum leptin levels along with serum creatinine. The reduction in serum leptin levels after renal transplantation is likely due to reversal of renal function. Neither pre nor post transplant plasma Leptin levels correlated significantly with BMI in our study.

Keywords: Serum leptin; chronic kidney disease; kidney transplantation.

1. INTRODUCTION

Protein-energy malnutrition is a common problem in patients with End stage kidney disease which contributes significantly to the increased morbidity and mortality. In uremic patients poor intake and increased catabolism could be responsible for malnutrition. Leptin is a large molecular protein mainly produced by adipocytes, which signals the brain and regulate food intake [1]. In uremia, increased serum leptin levels may contribute to anorexia and malnutrition [2]. Serum Leptin levels are increased in chronic kidney disease as it is not cleared by dialysis using conventional dialyzers or by CAPD [3]. Elevated leptin levels are corrected after successful renal transplantation [4]. Hence we studied serum leptin concentration in CKD patients on Hemodialysis for more than three months and determined if restoration of renal function with successful kidney transplantation can reduce serum leptin concentration in these patients

2. MATERIALS AND METHODS

A total of 21 Patients undergoing living donor kidney transplant were studied. The Institutional ethics committee approved the study protocol (IRB approval number is NIEC 312/2012) and informed consent was obtained from all study participants. All patients were receiving hemodialysis prior to transplant. All patients received triple immunosuppressant therapy post operatively consisting of Tacrolimus, mycophenolate mofetil and Gluco-corticoids. Patients on dialysis for less than 3 months, patients not regular for dialysis, those suffering with intercurrent illness, patients undergoing preemptive transplant and patients with acute rejection were excluded from study. Blood specimen were collected under fasting conditions between 8-10am from antecubital vein under aseptic conditions before the start of hemodialysis session within 1 week before transplant and 6 days after transplant. Samples for leptin levels were not analyzed if they had graft rejections as serum leptin levels are elevated in graft dysfunction. The BMI was calculated from weight in kilograms divided by the square of the height in meters. The samples were centrifuged and serum separated. Serum samples were stored at -80°C and analyzed within 6 months. Samples were thawed only once. Hemolysed and lipemic samples were discarded. Serum leptin was estimated by using Elisa method. Leptin assay was carried out on BIO-RAD CODA, fully automated ELISA system, using commercial kit obtained from BIOSOURCE. The leptin assay had a good inter and intra assay precision. This assay detects only free leptin levels. The minimum detection limit was 0.1ng/ml. The reference interval according to the manufacturer for lean men and lean women were 2.4±1.1ng/ml and 6.6±3.0ng/ml respectively.

2.1 Statistical Analysis

The data was entered in Microsoft excel spread sheet 2007 and normally distributed data was expressed as mean±SD. Statistical analysis was performed by using SPSS-11.5. Paired Student's' test was used to study serum leptin levels before and after kidney transplantation. Pearson correlation analysis was performed between serum leptin and BMI, serum creatinine. P<0.05 was accepted as statistically significant.

3. RESULTS

The cohort contained 13 men and 8 women age ranging from 16 to 45 years. The mean age of the patients was 28.38±9.38 years. The body mass index of the cohort was 22.09±2.48 Kg/m2. The average duration of dialysis was 14.9±4.9 months. The most assumed cause of native kidney disease was chronic glomerular nephritis, however one patient had chronic interstitial nephritis and another had Autosomal dominant polycystic kidney disease. The mean pre transplantation leptin concentration was 9.96±3.48 ng/ml and this decreased to 4.07±1.7 ng/ml (P<0.0001) within six days of transplantation. Plasma Creatinine level declined dramatically from 7.5±1.6 mg/dl to 1.1±0.7 mg/dl (P<0.0001) within one week Fig. 1. There was no graft rejection in any of these patients. In our study, there was no concomitant change in BMI (P>0.05). Neither pre (r=0.03, p>0.05) nor post transplant (r= -0.01, p>0.05) plasma Leptin levels correlated significantly with BMI.

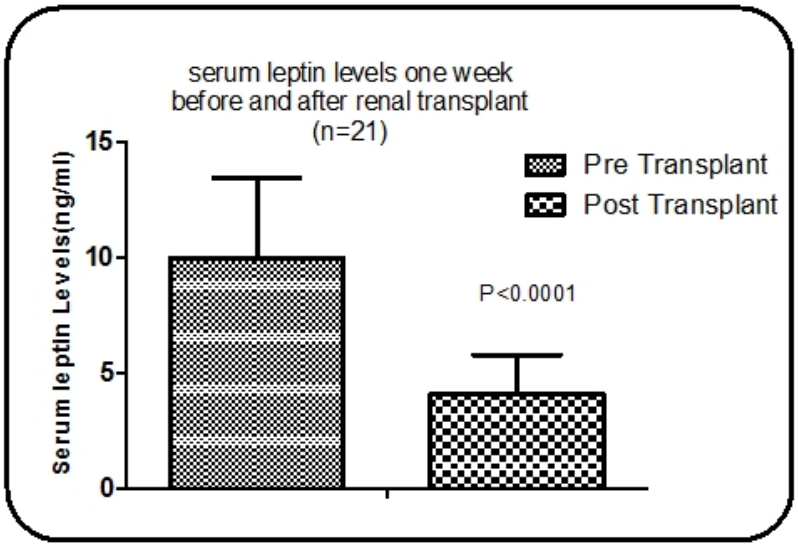

Fig. 1. Showing serum leptin levels one week before and after renal transplant

4. DISCUSSION

Serum leptin levels are increased in CKD patients due to lack of elimination by kidneys and increased production [3,5]. The underlying mechanism of increased leptin concentration remains unknown, but a recent study found a correlation of plasma insulin and leptin levels independent of adiposity in kidney disease, suggesting a link between leptin and insulin

homeostasis [6,7]. In our study, the serum leptin level was decreased by approximately 50% within one week of transplantation. Similar observation was noticed by Michael Landt et al. and such a reduction persisted up to 60 days post transplant [8]. The decline in plasma leptin concentration observed in these patients cannot be ascribed to the effect of steroids used as post transplantation immunosuppressant, though some effect of steroid administration cannot be ruled out. In a study, methyl predinisolone given at a rate of 0.6mg/kg/day to human volunteers had no effect on plasma leptin concentration [9]. However, in obese humans, administration of steroids increased plasma leptin concentration [10,11]. It is also important to consider other factors such as diurnal variation, fasting or over feeding, and heterogeneity among patients in plasma could influence the result of the study. Samples for serum leptin are preferably collected during day time as leptin levels are relatively steady [12]. To avoid the influence of diurnal patterns in leptin level, we measured leptin levels during day time after 10 hours of fasting. Studies have shown that fasting more than 12hrs decreased [13-14] and over feeding for 10 hours increased [15] day time plasma leptin concentration. In our study, diet was not controlled and there was no evidence that the subjects were over eating, since average BMI values were nearly identical pre and 6 days post-transplant. It could be due to short follow-up to detect a significant change in BMI. Neither pre nor post transplant plasma Leptin levels correlated significantly with BMI in our study which was in contrast to Michael Landt et al; observation. Caution has to be executed in understanding our study results, since fewer subjects has participated in our study and an attempt of long term follow-up was not made due to technical reasons.

5. CONCLUSION

Successful renal transplantation immediately reduces serum leptin levels along with serum creatinine. The reduction in serum leptin levels after renal transplantation is likely due to reversal of renal function. Neither pre nor post transplant plasma Leptin levels correlated significantly with BMI in our study.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee(IRB approval number - NIEC 312/2012) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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