Prevalence of hyperuricemia and gout in post transplant renal recipients

Thesis

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بسم الله الرحمن الرحيم

" وعلمك ما لم تكن تعلم وكان فضل الله عليك عظيما "

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Mahmoud Temraz

Abstract

Background : Hypeuricemia is a common problem among renal transplant recipients, and may adversely affect graft survival. Its prevalence is clearly attributable to cyclosporine (CsA) use, although individual patients may have other risk factors as well. Hyperuricemia may add on to several other factors in contributing to progressive deterioration of graft function and ultimately graft loss.

Patients and methods : A cohort study was performed on 60 post-transplant renal recipients in the transplantation outpatient clinic , Kasr Al Aini Hospital. This study aimed to assess the prevalence of hyperuricemia and gout in renal transplant patients and to correlate between hyperuricemia and patient variables such as cyclosporine level, dyslipidemia, diabetes mellutes and renal impairment. 60 patients were analyzed including 40 (66.6%) males and 20 (33.3%) females with mean age of 32±12 years. We measure serum uric acid levels in each routine visit approximately every six months for two years in the transplantation outpatient clinic. Also we Measure cyclosporine level, blood sugar, lipid profile and kidney functions (urea, creatinine). We also record the general characteristics of the patients, history of gout and diabetes, underlying renal disorders, donor type, diuretic prescription, type of immunosuppressive regimen and urate lowering therapy. The patients were divided into two groups : *group (A)* : patients on cyclosporine, steroid & azathioprine. *group (B)* : patients on cyclosporine, steroid & MMF (cellcept).

Results : We found that mean uric acid level in all patients in the 1st year post-transplant is 6.2±1.7, while the mean uric acid level in the 2nd year post-transplant is 7±1.8 with percentage of change of 12% in uric acid level during the two years.

There is a statistically significant difference between the 1st and 2nd year post-transplant with increase uric acid level from the 1st to the 2nd year.

We found that patients with hyperuricemia represent 65% of the studied cases. Also we found that there was a significant positive correlation between mean uric acid post transplant versus cyclosporine, cholesterol and creatinine. on the other hand there was no significant correlation versus other variables such as age, sex and donor type.

Conclusion : We concluded that there is a significant increase in the prevalence of hyperuricemia in post-transplant renal recipients.

Key words : Hyperuricemia, Renal transplantation, Cyclosporine.

List of abbreviations

AHS : Allopurinol hypersestivity syndrome.
ALL : Acute lymphoplastic leukaemia.
AMP : Adenosine monophosphate.
ARF : Acute renal failure.
AT1 : Angiotensin type 1.
AZA : Azathioprine.
AII : Angiotensin II.
CAN : Chronic allograft nehropathy.
CIN : Contrast induced nephropathy.
CKD : Chronic kidney disease.
COX-2 : Cyclo-oxygenase enzyme.
Crcl : Creatinine clearance.
CRF : Chronic renal failure.
CRP : C- reactive protein.
CsA : Cyclosporine.
CVD : Cardiovascular disease.
EDTA : Ethylenediamine-tetraacetic acid.
eGFR : estimated glomerular filteration rate.
GFR : Glomerular filteration rate.
GMP : Guanosine Monophosphate.
G-6-PD : Glucose-6-phosphate dehydrogenase.
GHPRT: Hypothanxine-guanine phosphoribosyl transferase.
HD : Haemodialysis.
HU : Hyperuricemia.
IMP : Inosine Monophosphate.
MCP-1 : Monocyte chemotactant patient-1.
MMF : Mycophenolate mofetil.
NO : Nitric oxide.
NSAIDs : Non steroidal anti –inflammatory drugs.
PRPP : Phosphoribosyl pyrophosohate.
RBF : Renal blood flow.
RTRs : Renal transplant recipients.
TLS : Tumor lysis syndrome.
TNF : Tumor necrosis factor.
UA : Uric acid.

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Introduction & Aim of the Thesis

Introduction

Despite the association of gout with renal disease, controversy exists as to whether uric acid has an etiologic role. First, it has been difficult to ascribe the generalized renal injury in gout to the deposition of urate crystals, for they are often only focally present. Second, many patients with gout have hypertension or are elderly, and the renal lesions might simply reflect hypertensive or aging-associated renal damage. Third, results of the studies are mixed as to whether lowering uric acid will slow renal progression in patients with gout. The inability to resolve this issue has emphasized the need for additional studies.

Hyperuricemia is a common feature of renal disease of all etiologies; as GFR falls the serum uric acid increases due to reduced renal excretion. The hyperuricemia in renal failure patients is generally mild, due to a compensatory increase in fractional excretion, reduced production, and increased excretion of uric acid via nonrenal (gastrointestinal) routes ***(Kang et al., 2002)***.

In many situations, ARF is associated with a rise in serum uric acid as a result of both increased generation and decreased excretion. Although it is widely recognized that markedly elevated levels of uric acid can cause ARF via supersaturation within the tubules with crystallization and intrarenal obstruction (acute urate nephropathy), the possibility that uric acid may

affect renal outcomes at concentrations that do not lead to tubular obstruction have not been considered.

Most nephrologists will ignore uric acid values if they are <10mg/dl. However, even milder elevations of uric acid have been found to predict ARF in some patients (i.e. patients who receive cisplatin) ***(Ejaz et al., 2007)***.

Hyperuricemia is a common complication in post-transplant renal recipients, and frequently is associated with chronic cyclosporine immunosuppressive therapy. Studies of renal transplant recipients (RTRs) have shown rates of asymptomatic HU ranging 50-80 % with cyclosporine (CsA) and 11-25 % with azathioprine (AZA) therapy with the prevalence of gout with use of these agents ranging 4-28% and 0-8%, respectively. Gout is the most common inflammatory arthritis seen in transplant recipients, can result in loss of productivity and diminished quality of life. Furthermore, the interactions between immunosuppressive drugs, gout medications and organ dysfunction pose a therapeutic challenge ***(Stamp et al., 2006).***

Risk factors for hyperuricemia include decreased glomerular filtration rate (GFR), diuretic use, and preexistent history of hyperuricemia. The influence of hyperuricemia in patient and graft survival is unclear because uric acid is not usually considered a common risk factor for cardiovascular disease that affects graft and patient survival. However, there

have been small studies that have suggested that control of uric acid levels contributes to recovery of renal function (in heart and liver transplant recipients) and in an improvement in GFR in renal transplant recipients. Despite controversies in the need for hyperuricemia treatment in transplant patients, strategies to decrease uric acid levels includes a decrease or avoidance of cyclosporine treatment, adequacy of antihypertension treatment, avoidance of diuretics, nutritional management, and use of uric acid–decreasing agents (***Mazzal M, 2005***).