Therefore, the use of MMF during SRNS should be taken into account. However, randomized controlled studies with larger representative samples are needed to reach significant conclusions.

CONFLICT OF INTEREST

None declared.

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How Neutrophil Gelatinase-associated Lipocalin Can Be Presented in Plasma and Urine

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Neutrophil gelatinase-associated lipocalin (NGAL) is a small 25-kD protein massively released from renal tubular cells after various injuring stimuli is emerging as a promising new

biomarker for the early identification of acute kidney injury (AKI).[1] Although NGAL is widely used for early AKI detection, patients with chronic kidney disease (CKD) with higher baseline NGAL showed a considerably increased risk of worsening residual kidney function within 1 year compared with those with lower baseline NGAL values.[2] This correlation between NGAL and CKD progressions interested the investigators to searching for novel predictors of severity and progression of CKD.

In the current issue of the *Iranian Journal of Kidney Diseases*, Youssef and El-Shal[3] have reported a study to determine the correlation between the level of urinary NGAL and progression of kidney injury in children who have focal segmental glomerulosclerosis (FSGS). They found a significant negative relationship between urinary NGAL and creatinine clearance in FSGS patients both in activity and after 1 year. They cite Mori and Nakao[4] who proposed a hypothesis ("forest fire") about the correlation between NGAL and glomerular filtration rate, suggesting that increment NGAL in CKD is not just the passive consequence of kidney function impairment, but it is the consequence of a sustained production by "inflamed" but vital tubular cells, whereas increase in serum creatinine and glomerular function rate reduction are only due to loss of functional cells or nephrons. Therefore, increased NGAL in CKD is the consequence of persistent inflammation.

Several recent studies revealed a high plasma NGAL levels in CKD patients which appeared to reflect the chronic inflammatory state of these patients.[2,5] Likewise, kidney allograft dysfunction may be influenced by multiple mechanisms, including ischemia-reperfusion, inflammation, and immune processes.[6] However, this sustain inflammation process is not limited to "inflamed" and vital tubular cells rather it is a systemic phenomenon. Therefore, we need to know how NGAL can be presented in plasma and urine.

Neutrophil gelatinase-associated lipocalin is a member of the lipocalin superfamily protein, which is binding covalently to gelatinase in neutrophils and can be detected at low concentrations in normal kidneys, lungs, liver, stomach, trachea, and colon.[7-9] However, it is now well known that NGAL mRNA has been significantly expressed in other organs, especially in the liver and lungs, along with AKI, subsequently overexpressed NGAL protein releases into the plasma. In addition, NGAL is an acute-phase reactant and may be released from neutrophils, macrophages, and other immune cells into the systemic circulation. Furthermore, AKI resulted in reduced renal clearance of NGAL and plasma NGAL accumulation.[10] Then, plasma NGAL reabsorbed in the proximal tubules by endocytosis. Thus, the decreased renal clearance of NGAL with subsequent accumulation in the systemic circulation observed only when proximal renal tubular cells are injured and NGAL reabsorption is impaired or when de novo NGAL synthesis increases. In AKI, however, a rapid and massive upregulation of NGAL mRNA in the distal nephron segments, specifically in the thick ascending limb loop of Henle, and the collecting ducts is demonstrated. Therefore, a considerable portion of the urinary NGAL is resulted from synthesis and secretion of NGAL protein in the distal nephron.[7] On the other hand, urinary NGAL is mainly produced by the distal nephron after injury and is immediately secreted into the urine. In contrast, plasma NGAL is a product of multiple sources and might be a good biomarker for inflammation.[10] As a result, plasma NGAL measurements may be affected by a number of coexisting variables such as CKD, chronic hypertension, systemic infections, inflammatory conditions, anemia, hypoxia, and malignancies[7]; however, in the absence of anuria, measurement of urinary NGAL could be a more valuable predictor of AKI with less confounding variables and being more restricted to tubular damage.[10]

In the CKD population, NGAL levels correlate with the severity of kidney impairment. However, it should be considered that the increase in plasma NGAL in this condition is generally much less than those typically increase in AKI.[7] Nowadays, it is widely accepted that the rate of deterioration in kidney function is associated with the degree of renal tubulo-interstitial

impairment rather than with the severity of glomerular lesions.[11] Urine NGAL has also been shown to represent an early biomarker for the degree of chronic injury in patients with immunoglobulin A nephropathy and lupus nephritis and may be increased in urinary tract infections. However, the levels of urine NGAL in these situations are significantly blunted compared with that typically measured in AKI.[7] In CKD patients, especially in coexistence with proteinuria, urinary NGAL

expression may be resulted from inflammation and tubular damage.

CONFLICT OF INTEREST

None declared.

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Is a Lower Dose of Cyclosporine Required Among Iranian Kidney Transplant Recipients?

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Cyclosporine A is widely used as maintenance immunosuppressive regimen in solid organ transplantation and remains the base of immunosuppression therapy in most organ transplant patients.[1-3] Although, there is no consensus on the optimal dosage, the appropriate cyclosporine blood level is conventionally identified based on the therapeutic drug monitoring (TDM) of cyclosporine to reach the therapeutic level.[4-7] This is an important issue, because this approach is necessary to prevent allograft rejection and nephrotoxicity. Although cyclosporine dosage is routinely monitored by predose blood trough level (C0) or the 2-hour postdose level (C2),[3-7] there is poor correlation between clinical outcome and drug concentration assessed using this strategy.[1,5,7-9] On the other hand, cyclosporine can cause several side effects such as gingival overgrowth.[10]

Cyclosporine-induced gingival enlargement in Iranian kidney transplant patients seems to be prevalent; Ghafari and coworkers reported a frequency of 35% among Iranian kidney transplant recipients receiving cyclosporine.[11] Therefore, modification of the individual doses of cyclosporine by monitoring of cyclosporine blood level is crucial to avoid side effects.[4] Furthermore, C2 blood level