



The effect of Trimetazidine on Contrast-Induced Acute Kidney Injury (CI-AKI) in chronic kidney disease (CKD) Patients

Contrast-Induced acute kidney injury (CI-AKI), is a sudden decline of renal function following contrast media injection, which defined as an increase of serum creatinine (SCr) > 0.5 mg/dl or 25% increase of SCr from baseline in 48-72 hours after exposure to contrast media.¹ CI-AKI considered the third most common causes of hospital-acquired AKI.² CI-AKI is associated with increased morbidity, mortality, cost and decreased quality of life.³ Recently urine Neutrophil Gelatinase-associated Lipocalin (uNGAL) has been introduced as a novel marker for early detection of AKI,⁴ since it excreted in urine and highly accumulated in kidney cortical tubules, blood and urine in case of nephrotoxicity and ischemic damage.⁵ Trimetazidine (TMZ) (an anti-oxidant agent) has beneficial effect in ischemia reperfusion at the cellular and mitochondrial level with a strong antioxidant effects.^{6,7} Numerous trials have been conducted to evaluate different pharmacological agents for prevention of CI-AKI, but most of them were unable to determine any benefit in decreasing CI-AKI incidence rate.⁸

A recent single blinded, randomized, controlled trial was published in May 2019, which was carried out in Firoozgar hospital from March 2016 to September 2017, aimed to evaluate the effects of periprocedural administration of TMZ on the incidence of CI-AKI in CKD patients based on changes of uNGAL level, by recruiting CKD patients who were candidates for coronary angiography with estimated Glomerular Filtration Rate (eGFR) 30-60 ml/min, and ejection fraction (EF) more than 45% with no urgent for angiography. A total of 100 patients who agreed to participate in the study and were meeting the inclusion criteria were included in the study. The patients were divided into two groups randomly either to the intervention or control group. Furthermore, there is no significant difference in demographic characteristics and risk factors including age, gender, eGFR, contrast dose, EF, DM, and HTN ($P > .05$). TMZ was applied to the first group (Intervention group) (n=50) and the second group was assigned as the control group (n=50), both group received parenteral hydration as isotonic saline in a rate of 1ml/Kg/hr, and Visipaque (non-ionic contrast media) 320mg I/mL. Prior to coronary angiography, serum creatinine and urea concentrations were measured and repeated 24h, and 48h after the procedure, urine samples also were gathered before and 12h after angiography. The laboratory results and patient's data was collected from the patient's chart. A total of 100 patients formed the sample of the study. The patients in the intervention group were given TMZ 35 mg twice daily orally starting 48h before the procedure up to 24h after the procedure.



The results show that CI-AKI occurred in 4 patients (8%) in the intervention group compared to 10 patients (20%) in the control group, which indicate a significant rise in SCr before and after the procedure in the control group ($P < .05$). However, there was no significant change in serum creatinine in the intervention group ($P > .05$). Although, there was no significant change in serum creatinine between the two group based on SCr ($P > .05$). Furthermore, uNGAL is inversely correlated with eGFR and its increment level among intervention and control groups were (16.04 ± 48.55 vs. 87.77 ± 188.30 ng/mL), respectively, Regarding the uNGAL cutoff point of 1.7 times, the overall incidence of CI-AKI was 16%. the incidence of CI-AKI based on uNGAL level was 4 patients (8%) in the intervention group and 12 patients (24%) in the control group ($P < .05$), which confirmed the protective effect of TMZ in the intervention group.⁹

In conclusion, the incidence of CI-AKI was significantly lower in the group treated with TMZ compared to the control group based on uNGAL level, which suggested that TMZ administration had a protective effect on prevention of CI-AKI. These results should be reevaluated in a larger study with different doses of TMZ.

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