

Characteristics of metformin induced acute kidney injury with or without lactic acidosis

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Background: Metformin is a common medication used for the treatment of type 2 diabetes. Metformin associated lactic acidosis (MALA) is the most serious potential adverse effect of metformin with high mortality rate. Moreover metformin can induce infrequently acute kidney injury (AKI) without LA, but little clinical data exist about this topic. We investigated the clinical characteristic differences between metformin-associated AKI with or without LA. **Methods:** We retrospectively reviewed all patients who were diagnosed with metformin associated AKI at Konyang University hospital between 2012 and 2017. The KDIGO criteria were applied to all patients to diagnose AKI. We divided them into groups (AKI with MALA vs AKI without MALA). **Results:** Nine patients were identified as having metformin associated AKI. One was excluded because the level of lactic acid was not measured. Six patients showed AKI with MALA (>3 mmol/L). AKI without MALA were two. Median duration of diabetes were 10 years (4 - 14 yrs). Predisposing factors of metformin associated AKI were hypertension (9), congestive heart failure (CHF) (5), chronic kidney disease (CKD) (4), concomitant consumption of nonsteroidal anti-inflammatory drugs (NSAIDs) (5), malignancy (2), cerebrovascular accident (CVA) (1) and radioccontrast media exposure for coronary angiography (1). Among these predisposing factors, CHF and CKD were risk factors of AKI without MALA group ($p=0.03$). Mean daily dose of metformin was significantly higher in AKI with MALA group (24.9 ± 10.7 mg/kg/day vs 8.4 ± 1.6 mg/kg/day, $p=0.007$). pH was lower in AKI with MALA group but p -value was not significant (7.14 ± 0.18 vs 7.43 ± 0.03 , $p=0.073$). Six patients (67%) received renal replacement therapy as treatment for AKI. Among them, two patients received a continuous renal replacement therapy (CRRT) and four patients received intermittent hemodialysis (HD). Three patients (33%) were treated with bicarbonate and fluid resuscitation. The two patients in AKI without MALA group treated with intermittent HD. One patient died despite renal replacement therapy in AKI with MALA group. **Conclusions:** In patients with metformin associated AKI, LA was associated with higher metformin dose.

EFFECT OF OMEGA-3 FATTY ACID AND MENAQUINONE-7 ON AORTIC CALCIFICATION IN ADENINE INDUCED RAT MODEL

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Introduction & Aims: Vascular calcification is common and progressing in CKD and dialysis patients. Diet with high-dose menaquinone-7 (MK-7) inhibited the development of cardiovascular calcification in 5/6 nephrectomy rat combined with high phosphate diet. Eicosapentaenoic acid, one of omega-3 fatty acid (FA), attenuates arterial calcification induced by warfarin. We evaluated whether the effect of omega-3 FA and MK-7 on aortic calcification in adenine and low protein diet induced vascular calcification rat model. **Methods:** Male Sprague Dawley rats were fed the diets containing 0.75% adenine and 2.5% protein for 3 weeks. After 3 weeks, 4 rats were sacrificed. Thirty two rats were randomly divided into four groups, which were treated and fed the diets containing 2.5% protein for 4 weeks: adenine control (0.9% saline), adenine control treated with omega-3 FA (300mg/kg/day), adenine control treated with MK-7 (50ug/kg/day), adenine control treated with omega-3 FA and MK-7. Serum creatinine, BUN, calcium and phosphate were measured. Normal control was fed the diets containing 2.5% protein for 7 weeks. For quantitative assessment of aortic calcification, von Kossa stain of aorta was done and calcium contents were measured. **Results:** Serum creatinine of adenine control group treated with omega-3 FA and MK-7 was lower than adenine control group without treatment. Serum calcium and BUN were not significantly different between adenine control group with treatment and without treatment. All treated groups and group without treatment were exposed to higher serum phosphate level without difference. Two rats among 4 rats showed aortic calcification at 3 weeks. After 4 weeks, aortic calcification was progressed in adenine control group without treatment on von Kossa stain and calcium contents analysis of aorta. Aortic calcification on von Kossa stain and calcium contents was the least progressed in adenine control group treated with combination of omega-3 FA and MK-7 compared to omega-3 FA or MK-7 single therapy. **Conclusions:** Combined treatment with omega-3 FA and MK-7 definitely prevents progression of aortic calcification compared to rat without treatment in adenine and low protein diet induced vascular calcification rat model.