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Mechanism of Piperacillin/Tazobactam nephrotoxicity

Jihyun Yang, Ki Joon Lim, Jun Yong Lee, Se Won Oh, Myung-gyu Kim, Sang-Kyung Jo, Won-Yong Cho
Department of Internal Medicine-Nephrology, Korea University Anam Hospital, Korea, Republic of

Objectives: Piperacillin/tazobactam (pipe/tazo) is one of the most commonly used antibiotics in critically ill patients. Several epidemiologic studies revealed that the pipe/tazo has nephrotoxicity and it could lead worse outcome, but the underlying mechanism of nephrotoxicity of this antibiotics is not well studied. In this study, we investigated the effect of pipe/tazo on renal aspect.

Methods:

We injected pipe/tazo intraveously to 6-7 week old C57L/B6. Tabaxin 4.5g (piperacillin 4.0g + Tazobactam 0.5g) was dissolved in destilled water to achieve 5.625mg/ml/mouse. We injected 0.9% normal saline in the sham group. We measured serum blood urea nitrogen (BUN), serum creatinine and renal pathology 24hr after IV pipe/tazo administration.

Results: Serum creatinine and BUN was increased in pipe/tazo group (normal vehicle vs pipe/tazo, 0.19±0.02 vs 0.31±0.05, p=<0.01, n=3-5/group) (18.75±0.02 vs 26.5±1.71, p=0.043, n=3-5/group). This renal injury was accompanied with tubular cell apoptosis which is accessed by TUNEL positive cell in the kidney. Also, we could observe increased IGFBP7 expression in the proximal tubules. There was minimal tubulitis, only few inflammation cell infiltration in pipe/tazo group. Transmission electron microscopy (TEM) revealed there was also glomerular damage with foot process effacement, mitochondrial damage in a glomerular interstitial cell were observed in pipe/tazo group.

Conclusions: These results provide that pipe/tazo has direct nephrotoxicity, which could be associated with mitochondrial damage and tubule apoptosis. Therefore, we should provide individualized care in patients who are at high risk of AKI, or may have impaired renal function so we could prevent progressive renal function detorioration.