中文題目: 尿毒素對於急性腎損傷動物模式腎素-血管擴張素系統的影響

英文題目: Uremic toxins influence renin-angiotensin system in animal model with acute kidney injury

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BACKGROUND

Renal ischemia/reperfusion (I/R) rapidly elevates the protein-bound uremic toxin, indoxyl sulfate, and promotes the activation of the renin-angiotensin system (RAS). In this study, we examined the protective effects of RAS blockers by attenuating the loss of angiotensin-converting enzyme 2 (ACE2) and its product, angiotensin 1–7 (Ang 1-7), in experimental model of acute kidney injury and indoxyl sulfate.

METHODS

The animal protocols and procedures were handled in accordance with the guidelines of the National Taiwan University College of Medicine and College of Public Health for the care and use of laboratory animals (NIH publication No. 86-23, revised 1985) with institutional Animal Care and Use Committee (IACUC) approval.

RESULTS

When human proximal tubular epithelial cell lines (HK-2) underwent the management of indoxyl sulfate in the association with hypoxia, the RAS components including angiotensinogen and ACE were up-regulated other than the ACE2. The imbalance of cellular ACE/ACE2 ratio induced reactive oxygen species (ROS), activated Erk, and inhibited AMPK, but these events were reversed by aliskiren and losartan. In IS-treated AKI mice, the inflammation, fibrosis, epithelial mesenchymal transition, dedifferentiation and ROS were alleviated in RAS blockers by reestablishment of the expression of ACE2. Moreover, both of them could improve the level of Ang1-7 and reduce the level of 8-Hydroxy-2'-deoxyguanosine in patients with hyperreninemic hypertension.

CONCLUSION

These findings suggested that RAS blockers possessed anti-oxidative activity to ameliorate the IS-induced renal damage, which may be partly attributed to modulation of ROS/ERK and ROS/AMPK pathways as well as downstream ACE2/Ang1-7 axis.