THE IMPACTS OF INDOXYL SULFATE-INDUCED OXIDATIVE STRESS ON RENAL CELL DEATH

Su Hyun Kim, Jung-ho Shin, Dae-Hwan Oh, Ki Hyun Park, Jin Ho Hwang,
Department of Internal Medicine, Chung-Ang University College of Medicine

Background

- Indoxyl sulfate (IS) is one of major protein-bound uremic toxins and is markedly increased in chronic kidney disease (CKD) patients.
- Besides IS as a marker of renal dysfunction, it has a substantial role in the progression of CKD.
- To address IS-induced renal progression, production of reactive oxygen species (ROS) has been explained as a major mediator.
- This study investigated the ROS production and signal pathways which were induced by exposure to IS.

Methods

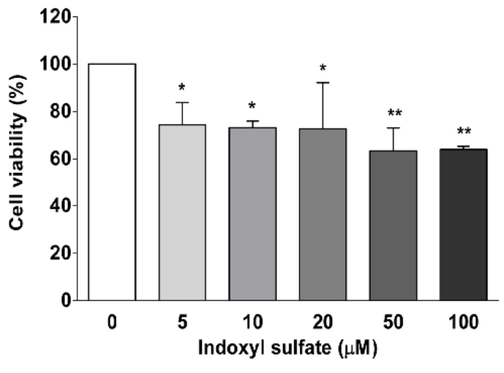
Cell culture
- Human proximal tubular cells (HK-2 cells) were cultured.

Treatment
- Cells were treated with a serial concentration of IS.
- Cells were treated with medication, including catalase, irbesartan and probenecid, in addition to IS of 100 μM.

Cell viability, ROS production and protein expression were evaluated.

Results

Cell viability according to exposure to IS

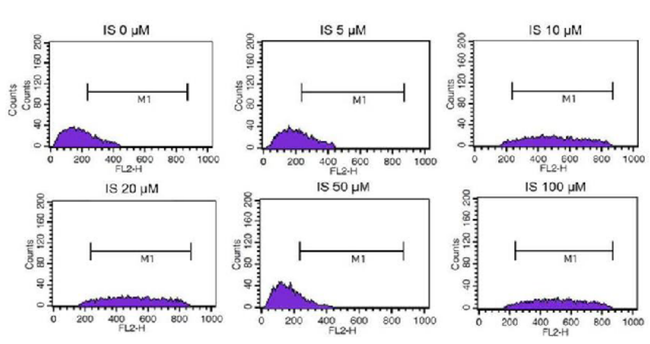


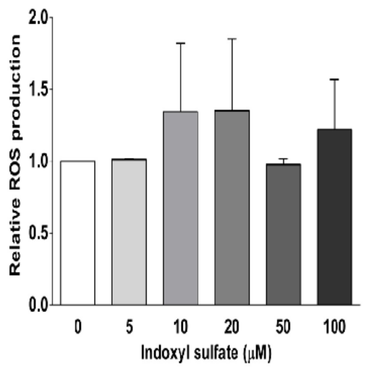
*P<0.05; **P<0.01

- Cell viability was assessed using MTT assay. As shown, IS had a dose-dependent cytotoxicity in HK-2 cells (P=0.001).
- Compared to IS of 0 μM, exposure to IS of 5, 10, 20, 50 and 100 μM resulted in decreases of cell viability by 25.7%, 26.9%, 27.3%, 36.6% and 36.1%, respectively.

ROS production after exposure to IS

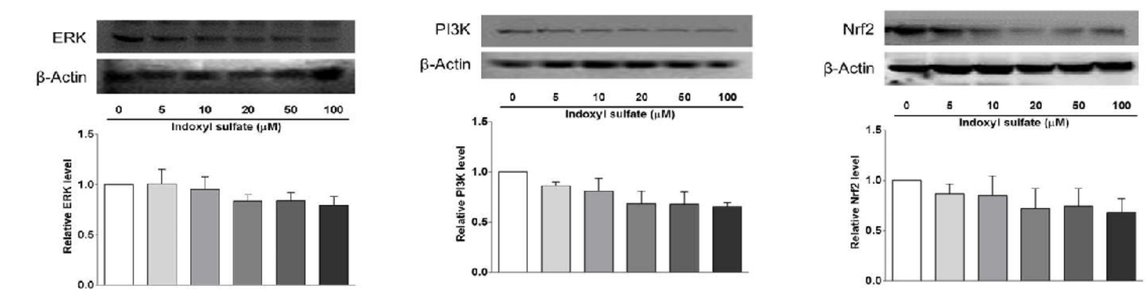
- Exposure to IS of 10, 20 and 100 μM increased ROS production by 34.4%, 35.2% and 37.3% (NS)





Protein expression in IS-induced cell injury

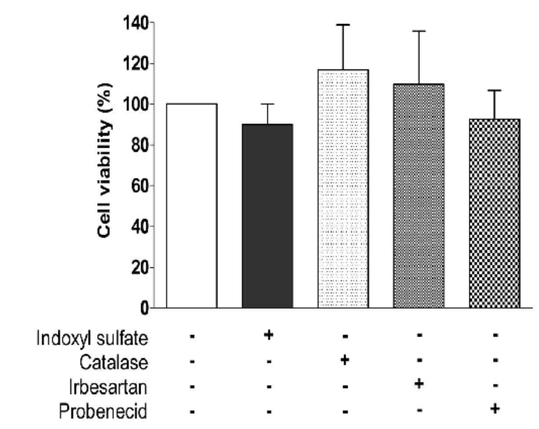
- ERK, PI3K, Nrf2, HO-1, JNK and NOS3 expression were quantified.



*P<0.05; **P<0.01

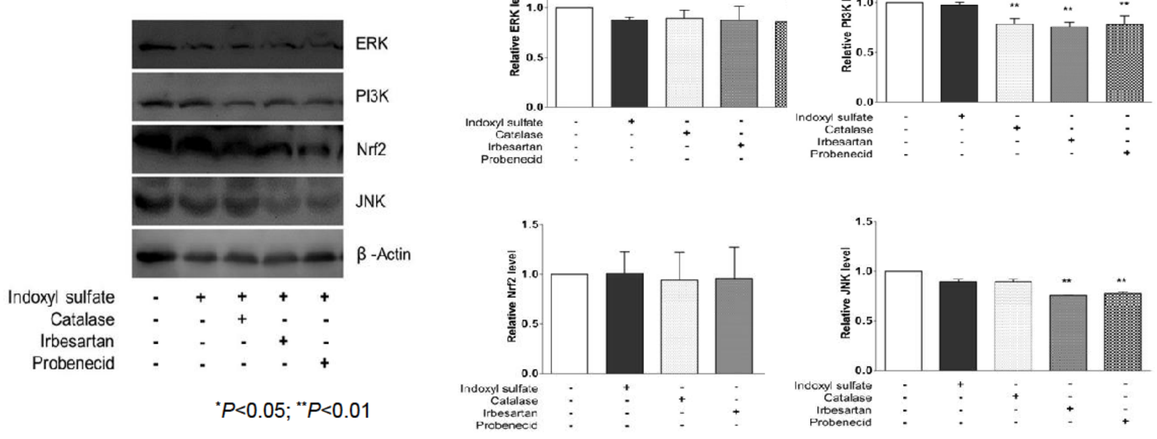
- Expression of ERK, PI3K, Nrf2 and JNK decreased, while expression of HO-1 and NOS3 increased in a dose-dependent manner.

Cell viability after medication in HK-2 cells exposed to IS



- Cell viability increased by treatment with catalase and irbesartan, compared to cells exposed by IS only (NS).

Effects of medication on IS-induced protein expression



*P<0.05; **P<0.01

- Unfortunately, we could not find the changes of protein expression according to the medication in HK-2 cells exposed by IS.

Conclusion

- IS had a dose-dependent cytotoxicity in HK-2 cells and that might be related with increased ROS production. This mechanism might include the ERK, PI3K-AKT, Nrf2-keap1 and JNK pathway.
- Despite negative results regarding effects of antioxidants and angiotensin receptor blockers on protein expression, they might have potentials to improve cell viability exposed to IS.

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