[P-24]

INORGANIC ARSENIC INCREASES VASOCONSTRICTION THROUGH CALCIUM-SENSITIZATION IN VASCULAR SMOOTH MUSCLES

Moo-Yeol Lee[1], Young-Ho Lee[2], Seung-Min Chung[1], Ok-Nam Bae[1] and Jin-Ho Chung[1]

[1]College of Pharmacy, Seoul National University, Seoul 151-742, Korea
[2]College of Medicine, Yonsei University, Seoul, 120-752, Korea

Chronic exposure of arsenic is well known to be the cause of cardiovascular disease such as hypertension. In order to investigate the effect of arsenic on blood vessels, we examined whether arsenic affected agonist-induced contraction of aortic rings in isolated organ bath system. Treatment with arsenite increased vasoconstriction induced by phenylephrine or serotonin in a concentration-dependent manner. Similar effects were also shown in the aortic rings without endothelium, suggesting that vascular smooth muscle played a key role in enhanced vasoconstriction induced by arsenite. Arsenite is the most potent form among arsenic species tested. These alterations were well correlated with myosin light chain (MLC) phosphorylation induced by arsenite in smooth muscles. Direct calcium measurement using fura-2 dye in aortic rings revealed that arsenite enhanced contraction by high K+ without further increase in intracellular calcium levels. Calcium-sensitization of contractile machinery, therefore, may contribute to the enhanced vasoconstriction by arsenite. Consistent with these in vitro results, intravenous administration of 1.0 mg/kg arsenite augmented blood pressure increase induced by phenylephrine in conscious rats. These results suggest that arsenite increases agonist-induced vasoconstriction mediated by MLC phosphorylation and calcium-sensitization in smooth muscles was one of the key mechanisms for the arsenite-induced hypercontraction in blood vessels.

Keyword : Arsenic, Arsenite, Blood Vessels, Contraction, Calcium-sensitization