Chronic exposure to sodium arsenite alters the expression of renin–angiotensin system, apoptosis and oxidative stress markers in Wistar rat

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The renin–angiotensin system (RAS) of the kidney is responsible for renal regulation and homeostasis, and patients with chronic kidney disease frequently receive RAS blockades. The purpose of this study was to determine the connection between the stimulation of arsenic in rats and changes in transcription levels of RAS hormones, biochemical parameters and antioxidant enzymes. Twenty-five Wistar rats were divided into five groups (control, low, middle, high dose and high dose + α-tocopherol groups) and given oral doses of 8.2, 12.3 and 16.4 mg/kg sodium arsenite ($NaAsO_2$) and 50 mg/kg α-tocopherol for two months. RT-PCR analysis in nephrocytes revealed that mRNA expression of p53, p21, p27, caspases (3, 7 and 9), ACE, AGT, AT1R, CYP1A1 and Bax was found to be upregulated by ~1.9, ~1.6, ~1.5, ~2.3, ~3.3, ~3, ~2, ~1.9, ~2.4, ~1.7 and ~3.3-fold, whereas that of cyclin A, cyclin B1, cyclin E1, CDK 1, CDK 2, Bcl-2, CAT, SOD, GPx, GR and GST was downregulated consistently in renal tissues of arsenic-exposed groups by ~0.6, ~0.5, ~0.4, ~0.5, ~0.6, ~0.5, ~0.6, ~0.4, ~0.6, ~0.5 and ~0.6-fold respectively. The activities of alkaline phosphatase, acid phosphatase and antioxidant enzymes were significantly reduced by 63%, 71%, 40%, 37% and 44% respectively, upon treatment with $NaAsO_2$. Through this study, we can gain knowledge about the potential function of RAS enzymes and antioxidant enzymes against the detrimental effects of arsenic-induced oxidative stress due to altered transcription levels of RAS enzymes in Wistar rats.

Arsenic is the most potent inhibitor of cell-cycle progression (arrest in G0/G1 phase), resulting in increased expression of p27 (a particular inhibitor of S-phase entry), decreased expression of cyclin E1, and cyclin-dependent kinases[4]. Sodium arsenite ($NaAsO_2$) exposure causes cytotoxicity and cell death, as it inhibits the expression of the eIF4E and cyclin D1 genes in different human cell lines[5]. In the kidney of rats, arsenic-induced nephrotoxicity causes epithelial cell necrosis and oxidative stress[6]. According to reports, tubular cell apoptosis (caspase-3-mediated) in the renal tissue of rats is caused by arsenic[7].

Renin–angiotensin system (RAS) is a type of renal hormone system that controls systemic vascular resistance, electrolyte balance and blood pressure in the kidney[8]. Hyperactivation of RAS causes the activation of pro-inflammatory factors and an increase in oxidative stress, which can result in hypertension, damage to the renal glomeruli and sclerosis[9]. Moreover, it has been suggested that RAS genes may act as significant risk factors for diabetic nephropathy[10]. Although previous studies have demonstrated the importance of renal damage caused by arsenic, it is still unknown if gene susceptibility influences arsenic-related chronic kidney disease (CKD). Therefore, in this study we examined the impact of arsenic on the synergistic effects of genes in order to ascertain their combined effects on cell cycle, apoptotic and antioxidant enzyme markers, as well as on RAS enzymes (ACE, AGT and