Elucidating Novel Mechanisms: Berberine Mitigates Cisplatin-Induced Hepatorenal Mitochondrial Dysfunction Through Preservation of Electron Transport Chain Integrity

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A high incidence of hepatorenal impairment in cancer patients treated with cisplatin has been reported. Berberine, a plant alkaloid possesses wide range of medicinal properties. Mitochondrial accumulation of cisplatin and subsequent damage to electron transport chain (ETC) plays a key role in the cisplatin-induced cell death. This study was aimed to elucidate the mitigative role of berberine against cisplatin-induced hepatorenal injury with an in depth focus on mitochondrial functions. Clone 9 and Human renal mesangial cells were treated with 10 μM berberine for 24 h followed by 20 μM cisplatin. Cell morphology and intracellular ROS generation (DCFDA), mitochondrial ROS and antioxidant status (RTPCR and Western Blotting), mitochondrial membrane pore transition (Swelling assay), apoptosis (Incucyte), membrane potential (TMRM uptake), respiration and oxygen consumption rate (Seahorse Pro analyzer), protein expression and activities of complexes II, III and IV, and ATP content were measured. Berberine pretreatment significantly reduced intracellular ROS levels and prevented cisplatin-induced cell death. An increase in mitochondrial oxidative stress and reduced antioxidant enzymes by cisplatin subsequently increased mitochondrial swelling and mPTP opening, apoptosis, membrane depolarization, and inhibition of electron chain complexes . Berberine effectively mitigated these deleterious effects, ameliorated mitochondrial functions and prevented cell death. In conclusion, this study has provided significant evidences that berberine preserved the integrity of ETC and mitigated cisplatin-induced hepatic and renal mitochondrial dysfunction Hence, berberine may be considered as a potential adjuvant drug during and after chemotherapy with cisplatin.

Awards Won:
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