Methylmercury-induced mouse sertoli cells apoptosis via regulation of mitochondrial-dependent pathway.

Abstract

The most toxic form of mercury, methylmercury (MeHg), is an organic form of mercury, existing as a toxic environmental pollutant which usually poisons people and wildlife during ingest fishes, or wildlife that are at the top of aquatic foodchains from polluted areas. And due to its bioaccumulative property, MeHg could be ingested more quickly and excreted more slowly in the body compared with other forms of mercury, damages to immune system, genetic and central nervous systems were widely studied before, but the part of MeHg-induced reproductive toxicity and associated molecular mechanisms were limited, furthermore, on the strength of MeHg existing both in nature and as contaminants, exposed to such an environment containing MeHg might be unconsciously. For these reasons, we used TM4 cell line to proceed this study for further investigation of possible mechanisms involving in MeHg-induced reproductive toxicity. Initially, we determined cell viability after MeHg treatment for 24h in a dose-dependent manner with range from 0.25 to 10 μM. Expressions of endoplasmic reticulum (ER)-stress regulated apoptotic cell death proteins (including: glucose-regulated protein (GRP)78, GRP94, and CHOP), caspase 12 and calpain activation. were detected by western blot analysis and Q-PCR. Whether MeHg would cause mitochondrial dysfunction, we detected mitochondrial membrane potential (MMP) via fluorescence, and used western blot analysis to measure the release of apoptosis-inducing factor (AIF) from mitochondrial to cytoplasm, poly(ADP-ribose) polymerase(PARP) cleavage, and activation of caspase cascades. All of above could be reversed by antioxidant N-acetylcysteine (NAC) pretreatment. In sum, these results indicate that MeHg may be capable of inducing TM4 cells apoptosis and functional damage, revealing MeHg may be a latent risk factor in causing reproductive toxicity.

Keyword: Methylmercury (MeHg); reproductive toxicity ; apoptosis ; mitochondria dysfunction; endoplasmic reticulum-stress (ER-stress).