POSTERS

CELLULAR AND MOLECULAR MECHANISMS OF GADOLINIUM TOXICITY IN SERTOLI CELLS

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The increasing environmental release of gadolinium (Gd), due to both industrial and clinical applications, has raised concerns about human health. Following ingestion/absorption, Gd exerts toxic effects across various tissues, but its consequences for male reproductive health are still poorly understood. Our previous studies demonstrated that oral Gd administration to adult rats adversely affects steroidogenesis and spermatogenesis, with direct effects on Leydig and germ cells. However, the impact of Gd on Sertoli cells, which provide vital support and energy (e.g., lactate) to germ cells, remains unreported. Therefore, in the present study we exposed mouse Sertoli (TM4) cells to increasing concentrations (5-1000 µM) of GdCl3 or Gd2O3 for 24h. Our results showed a dose-dependent decrease in TM4 cell viability and proliferation. Gd cytotoxic effects reflect a significant impairment of Sertoli cell functions. Specifically, Gd inhibited both the expression of the AR protein and the activity of LDH, as such as Blood-Testis Barrier integrity was also compromised. Gd induced oxidative stress and activated autophagic and apoptotic processes, mediated by the inhibition of the Akt pathway. Finally, we documented mitochondrial dysfunction and alteration in Mitochondrial-Associated Endoplasmic Reticulum Membranes (MAM) integrity. In conclusion, our findings highlight novel cellular and molecular mechanisms underlying Gd-induced testicular damage, specifically implicating that Gd-induced impairment to spermatogenesis may also result from compromised Sertoli cell function.

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