POSTERS

OBESITY-INDUCED TESTICULAR DYSFUNCTION: PROTECTIVE ROLES OF THYROID HORMONES IN HIGH-FAT DIET-FED RATS

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Obesity, through chronic lipotoxicity and oxidative stress, adversely affects multiple aspects of testicular function and represents a significant risk factor for male infertility. 3,5-diiodo-L-thyronine (T2), an endogenous thyroid hormone metabolite with recognized metabolic and mitochondrial regulatory effects, has emerged as a potential modulator of oxidative stress–related damage. This study evaluated the effects of a high-fat diet (HFD) on male reproductive physiology in adult Wistar rats and investigated the potential protective role of T2. HFD induced a marked reduction in serum testosterone levels (~87%), associated with impaired steroidogenesis, as evidenced by decreased 3β-hydroxysteroid dehydrogenase (3β-HSD) expression in Leydig cells. This was accompanied by enhanced apoptosis, as shown by increased active caspase-3, an elevated BAX/BCL2 ratio, and a higher number of TUNEL-positive cells. In parallel, spermatogenesis was significantly compromised, as indicated by reduced expression of proliferating cell nuclear antigen (PCNA) and synaptonemal complex protein 3 (SYCP3), reflecting impaired germ cell proliferation and meiotic progression. HFD markedly increased oxidative stress markers (TBARS and 4-HNE), and altered antioxidant defenses (SOD, CAT enzymatic activities) alongside impaired NRF2 signaling, characterized by its reduced nuclear translocation. Moreover, mitochondrial homeostasis was disrupted, as evidenced by altered PINK1/PARKIN signaling, reduced PGC-1α expression, and dysregulation of mitochondrial dynamics (DRP1, OPA1). Importantly, T2 treatment partially restored steroidogenesis, reduced apoptosis, improved spermatogenic markers, enhanced NRF2 nuclear translocation, and ameliorated mitochondrial dysfunction. Overall, these findings confirmed that obesity impairs male reproductive function through oxidative stress, defective antioxidant response, apoptosis, and mitochondrial dysfunction, while T2 exert protective effects, supporting its potential as a therapeutic strategy to preserve fertility in metabolic disorders.