GESTACIONAL CO-EXPOSURE TO PHTHALATES AND NANOPLASTICS IMPAIRS TESTICULAR REDOX HOMEOSTASIS ACROSS GENERATION

Mirella Franco Moreira[1]; Vanessa Aguiar Rocha[1]; Natália Magosso[1]; Patrick Vieira de Souza[1]; Débora Hipólito Quadreli[2]; Matheus Naia Fioretto[1]; Isabela Silva Ferreira[1]; Victória Cristina Pinha[1]; Glaura Scantamburlo Alves Fernandes[2]; Wellerson Rodrigo Scarano[1]

[1]Universidade Estadual Paulista (UNESP) - Botucatu - São Paulo
[2]Universidade Estadual de Londrina (UEL) - Londrina - Paraná

INTRODUCTION: The widespread use of plastics has resulted in the continuous release of nanoplastics (NPs) and plasticizers such as phthalates into the environment. Since phthalates are not chemically bound to the plastic matrix, they are easily released and absorbed by the body, where they can act as endocrine disruptors. When in mixtures or combined with NPs, their toxic effects become even more concerning, particularly due to the limited understanding of their interactions within the human body. The testis is especially vulnerable during critical developmental windows, and exposure during this period may impair male reproductive function and lead to multigenerational consequences, highlighting the importance of studying these compounds in co-exposure scenarios. **OBJECTIVE:** To investigate the multigenerational effects of gestational exposure to a phthalate mixture (PM), alone or in combination with NPs, on oxidative stress markers in the testes of male offspring (F1) during pubertal and adult stages. **MATERIALS AND METHODS:** Pregnant Sprague Dawley rats (n=6–8) were divided into six groups: CTRL: control; LPM: 20 µg/kg/day PM; HPM: 200 mg/kg/day PM; NP: 1 mg/kg/day polystyrene NPs (100 nm); LPM+NP: 20 µg/kg/day PM + 1 mg/kg/day NPs; HPM+NP: 200 mg/kg/day PM + 1 mg/kg/day NPs. Exposure occurred via gavage from gestational day 10 to postnatal day (PND) 21 (CEUA: 1174020523). On PND22 and PND120, one male per litter was euthanized for oxidative stress analysis (n=5-8). **RESULTS AND CONCLUSION:** At puberty (PND 22), early oxidative stress was observed, with increased TBARS in NP, decreased GSH in LPM+NP, and reduced GGT and GSSG in HMP+NP, indicating antioxidant depletion and redox imbalance. The rise in SOD in LPM+NP and HMP+NP suggests a compensatory response, while the decrease CAT in NP may contribute to hydrogen peroxide accumulation. In adulthood (PND 120), effects were more pronounced in co-exposed groups: TBARS increased in HPM; GSH, GGT, and GSSG increased in LPM and NP, but decreased in LPM+NP and HPM+NP, which also showed reduced SOD and CAT levels. These findings suggest progressive antioxidant system exhaustion and possible mitochondrial dysfunction, impairing energy metabolism essential for testicular function.

Keywords: Nanoplastics; Oxidative stress; Phthalates; Testicle.

Financing: FAPESP 2024/03207-0