Transgenerational effect of endocrine disruptors on reproductive function

Sabovic I [1], Di Nisi A [1,2], De Toni L [1], Gotti S [3], Foresta C [1], Ferlin A [1]

[1] Department of Medicine, Operative Unit of Andrology and Medicine of Human Reproduction, University of Padova, Padua, Italy; [2] Department of Psychology and Health Sciences, Pegaso Digital University, Napoli, Italy; [3] Neuroscience Institute Cavalieri Ottolenghi (NICO), Orbassano-Turin, Italy

Introduction

Endocrine Disruptors (EDs) are compounds that have the ability to affect the endocrine system by interfering with the synthesis, bioavailability, and action of hormones. Among the main EDs we can include Bisphenol A (BPA), Bisphenol S (BPS) and Perfluoroalkyl compounds (PFAS) [1-3].

Aim

In this PRIN study (Grant 20203AMKTW_002) we evaluated the possible transgenerational effects of BPA, BPS and PFOS on testicular function in male F1 mice born from mothers treated in pregnancy and during lactation with subtoxic levels within the recognized tolerability levels for these three substances: BPA (4 ug/kg b.w., N=12); BPS (4 ug/kg b.w., N=14) and PFOS (3 ug/kg b.w., N = 15).

Results

Mice were sacrificed at sexual maturity (P = 90 days), and subsequently blood was collected, testes were stocked at - 80°C, and spermatozoa were retrieved from their respective epididymis to analyze the effects of different EDs by assessment of sperm count and motility, quantification of plasma hormones by ELISA method, and analysis of protein expression by western blotting technique. Compared with the unexposed controls (49.14 ± 19.87 x106 spermatozoa), the group exposed to PFOS (12.19 ± 3.17x106 spermatozoa), or BPA (10.12 ± 4.8 x106 spermatozoa) or BPS (8.84 ± 2.0 x106 spermatozoa) showed reduced sperm concentration ($P < 0.05$). In parallel, the percentage of sperm with progressive motility dropped dramatically (-90% on average) in all three ED-exposed groups compared with the control group. Quantification of hormones in plasma showed decreased levels of testosterone and INSL3 in the three groups of exposed mice compared with controls (all $p<0.05$), while FSH and LH levels were increased in exposed mice compared with control (all $p<0.05$). Protein expression analysis in the testis showed increased FSH receptor in all three ED-exposed groups compared with the control. Finally, bioaccumulation of BPA, BPS and PFOS was evaluated by LC-MS, showing that all three EDs were concentrated at the testicular level (BPA=237.07 ± 119.02 ng/g; BPS=306.45 ± 140.09 ng/g; PFOS=60.75 ± 35.66 ng/g) compared to plasma (BPA= 216.44 ± 137.24 ng/mL; BPS=120.81 ± 62.98 ng/mL; PFOS=7.76 ± 3.78 ng/mL), all $p<0.05$
compared with control.

Conclusions

This study demonstrates for the first time a transgenerational effect of EDs at subtoxic dosages on testicular function, with direct damage on spermatogenesis and Leydig cell function, with intratesticular accumulation of these molecules

Bibliography

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