2-hydroxyoestradiol and 2-methoxyoestradiol, two endogenous oestradiol metabolites, induce DNA fragmentation in Sertoli cells

Valencia, C., Molina, C., Florez, M., Buñay, J., Moreno, R. D., Orihuela, P. A., ... & Parada■Bustamante, A. (2016). 2■hydroxyoestradiol and 2■methoxyoestradiol, two endogenous oestradiol metabolites, induce DNA fragmentation in Sertoli cells. Andrologia, 48(10), 1294-1306. <10.1111/and.12576> Accessed 18 Dec 2020.

Abstract

Elevated intratesticular levels of hydroxyoestradiols and methoxyoestradiols, two classes of endogenous oestradiol metabolites, have been associated with male infertility. The aim of this study was to explore the effects of 2■hydroxyoestradiol (2OHE2), 4■hydroxyoestradiol (4OHE2), 2-methoxyoestradiol (2ME2) and 4■methoxyoestradiol (4ME2) on Sertoli cell viability. For this, TM4 cells were incubated with different concentrations of these metabolites for 24 h to then evaluate the viability and DNA integrity by MTS and TUNEL assay respectively. The participation of classical oestrogen receptors and the involvement of oxidative stress and apoptotic mechanisms were also evaluated co■incubating TM4 cells with these estradiol metabolites and with the drugs ICI182780, N■acetylcysteine and Z■VAD■FMK respectively. Only high concentrations of 2OHE2 and 2ME2 decreased cell viability inducing DNA fragmentation. In addition, ICI182780 did not block the effect of 2OHE2 and 2ME2, while N■Acetylcysteine and Z■VAD■FMK only blocked the effect of 2OHE2. Moreover, 2OHE2 but not 2ME2induced PARP and caspase■3 cleavage. Finally, lower 2OHE2 and 2ME2 concentrations (0.01–0.1–1.0 μmol l–1) decreased Sertoli cell viability 48 h post■treatment. Our results support the hypothesis that elevated intratesticular 2OHE2 or 2ME2 concentrations could be related to male infertility since 2OHE2 by apoptosis and 2ME2 by undetermined mechanisms induce DNA fragmentation in Sertoli cells..