2-Methoxyestradiol mediates apoptosis through caspase-dependent and independent mechanisms in ovarian cancer cells but not in normal counterparts

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Abstract

Objective The estrogen metabolite 2-methoxyestradiol has shown antitumorigenic action in some epithelial tumors. In the present work we investigate its effects in ovarian cancer used alone or in combination with other apoptotic-inducing reagents such as tumor necrosis factor-related apoptosis-inducing ligand. Methods To assess the effect of 2-methoxyestradiol, dose response and time courses in ovarian cancer and normal cells were conducted. Apoptosis was confirmed through DNA laddering, by flow cytometry, and Western blotting of proteins involved in the apoptotic cascade. Results 2-Methoxyestradiol induced apoptosis in ovarian cancer cells but not in normal counterparts. 2-Methoxyestradiol activates both the intrinsic and extrinsic apoptotic pathways. 2-Methoxyestradiol–mediated apoptosis involves reactive oxygen species generation and caspase-dependent and caspase-independent mechanisms. We also demonstrate that 2-methoxyestradiol selectively induces an additive/synergistic apoptotic response in ovarian cancer cells when used in combination with tumor necrosis factor-related apoptosis-inducing ligand. Conclusions 2-Methoxyestradiol, alone or in combination with tumor necrosis factor-related apoptosis-inducing ligand, should be considered as a potential treatment for ovarian cancer.

Keywords

AIF, 2ME, TRAIL, Death receptors, Chemotherapy, Ovarian cancer.