Estetrol: a new natural estrogen providing a safe therapeutic window for the treatment of menopause

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Introduction

Estetrol (E4) is a natural estrogen exclusively produced by the human fetal liver during pregnancy. E4 has recently been characterized as the first natural SERM. It exhibits estrogen-like effects on the brain, bone, uterus, ovulation and atheroma prevention. E4 also presents anti-estrogenic properties in vascular and central nervous systems since it prevents estradiol (E2) actions on endothelial NO synthase activation, acceleration of endothelial healing and on allopregnanolone synthesis. Additionally, several evidences highlight that E4 is a promising compound for menopausal hormone therapy. The aim of this study is to define the impact of E4 on mammary gland and breast cancer.

Results

ERα is the predominant receptor mediating E4 effects on breast and breast cancer

E4 antagonizes E2-induced breast and breast cancer growth

E4 does not antagonize E2-dependent ERα nuclear activity, but inhibits ERα extranuclear effects

Conclusions

While estrogen receptor alpha (ERα) is the predominant receptor mediating its effects, the dual weak-estrogenic/anti-estrogenic feature of E4 results from differential signaling pathways activation. Altogether, our results highlight that E4 has a low or very limited impact on breast and breast cancer growth and offers a safe therapeutic window for menopausal symptom treatment.

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