Medium-dose estrogen ameliorates experimental autoimmune encephalomyelitis in ovariectomized mice.

Haghmorad D\textsuperscript{1}, Salehipour Z\textsuperscript{2}, Nosratabadi R\textsuperscript{3}, Rastin M\textsuperscript{2}, Kokhai P\textsuperscript{1}, Mahmoudi MB\textsuperscript{4}, Amini AA\textsuperscript{5}, Mahmoudi M\textsuperscript{2}.

Author information

Abstract

Estrogen is a neuro-protective hormone in various central nervous system (CNS) disorders. The present study evaluated the role of estrogen during experimental autoimmune encephalomyelitis (EAE) at doses selected to mimic any suppressive potential from the hormone during pregnancy. Here, mice were ovariectomized and then 2 weeks later treated with MOG antigen to induce EAE. Concurrently, mice then received (subcutaneously) an implanted pellet to deliver varying estrogen amounts over a 21-day period. Clinical scores and other parameters were monitored daily for the 21 days. At the end of the period, brain/spinal cord histology was performed to measure lymphocyte infiltration; T-cell profiles were determined through ELISA, flow cytometry, and real-time PCR. Transcription factor expression levels in the CNS were assessed using real-time PCR; T-cell differentiation was evaluated via flow cytometry. The results demonstrated that estrogen inhibited development of EAE. Histological studies revealed limited leukocyte infiltration into the CNS. High and medium dose of estrogen increased $T_{H2}$ and $T_{reg}$ cell production of interleukin (IL)-4, IL-10, and transforming growth factor (TGF)-$\beta$, but concurrently resulted in a significant reduction in production of interferon (IFN)-$\gamma$, IL-17, and IL-6. Flow cytometry revealed there were also significant decreases in the percentages of $T_{H1}$ and $T_{H17}$ cells, as well as significant increase in percentages of $T_{reg}$ and $T_{H2}$ cells in the spleen and lymph nodes. Real-time PCR results indicated that high- and medium-dose estrogen treatments reduced T-bet and ROR-$\gamma$t factor expression, but enhanced Foxp3 and GATA3 expression. Collectively, these results demonstrated that a medium dose of estrogen - similar to a pregnancy level of estrogen - could potentially reduce the incidence and severity of autoimmune EAE and possibly other autoimmune pathologies.

KEYWORDS:

EAE; Estrogen; central nervous system; multiple sclerosis; transcription factor