"Brain-Region responsiveness to DT56a (Femarelle®) Administration on Allopregnanolone and Opioid Content in Ovariectomized Rats"

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Abstract

Objective: The natural selective estrogen receptor modulator DT56a (Femarelle®), derived from soybean, has been shown to relieve menopausal vasomotor symptoms with no effect on sex steroid hormone levels or endometrial thickness. The purpose of the present study was to evaluate the neuroendocrine effect of DT56a administration through the evaluation of brain content of allopregnanolone (AP), an endogenous neurosteroid gamma-aminobutyric acid agonist with anxiolytic properties, and through the assessment of beta-endorphin (beta-END), the endogenous opioid implicated in pain mechanism, emotional state, and autonomic control.

Methods: Five groups of Wistar ovariectomized (OVX) rats received one of the following treatments: oral DT56a administration at doses of 6, 12, 60, and 120 mg kg\(^{-1}\) day\(^{-1}\) or estradiol valerate (E\(_2\)V) at a dose of 0.05 mg kg\(^{-1}\) day\(^{-1}\) for 14 days. One group of fertile and one group of OVX rats receiving placebo were used as controls. The concentration of AP was assessed in the frontal and parietal cortex, hippocampus, hypothalamus, anterior pituitary, and serum, whereas the content of beta-END was evaluated in the frontal and parietal cortex, hippocampus, hypothalamus, neurointermediate lobe, anterior pituitary, and plasma.

Results: DT56a increased AP levels in all brain areas analyzed and in serum, with a classical dose-related curve in comparison with OVX rats. In some brain areas, such as the frontal cortex, the parietal cortex, and the anterior pituitary, positive results were found even with the administration of a lower DT56a dose of 60 mg kg\(^{-1}\) day\(^{-1}\), attaining AP levels in the range of those in animals treated with E\(_2\)V. Similarly, beta-END levels were enhanced in selected brain areas such as the hippocampus, the hypothalamus, the neurointermediate lobe, and the anterior pituitary in comparison with those in OVX rats, in which the increase of the opioid was dose related and in the range of those in rats treated with E\(_2\)V.
Conclusions: This study demonstrated that DT56a positively affects brain neurosteroidogenesis and the opiate-ergic system: DT56a exerts an estrogen-like effect on selective areas related to mood, cognition, and homeostasis control, presenting a specific pattern of interaction with the brain function. These findings may, in part, explain the clinical effect of DT56a on menopausal symptoms.