## Headache Medicine



# The pathophysiology of the development of migraine from estrogen in women of childbearing age: review

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#### Introduction

Changes in estrogen levels can trigger headaches, including estrogen-associated migraine. These changes can occur naturally (e.g., menstruation, pregnancy, menopause) or can be induced (e.g., hormonal contraceptives, hormone replacement therapy, anti-estrogen agents). **Objective** 

The aim of this review is to investigate the pathophysiology of the development of migraine from estrogen in women of childbearing age. **Method** 

This Integrative Literature Review was developed based on the steps described by Marcela Tavares de Souza, Michelly Dias da Silva and Rachel de Carvalho (Albert Einstein Israelita Hospital), in the article: "Integrative review: what is it? How to do it?". To assess and analyze literature data we searched for the following terms: (Estrogen ) AND ("Migraine Disorders") AND (Physiopathology) (MESH or text words) in PubMed and Medline (acess through the Biblioteca Virtual em Saúde), and yielded 19 relevant studies. We included original articles and reviews, in full, which respond to the objective of the study and which are in Portuguese or in English. We excluded research that did not reach the objective, articles that did not cover the theme or animal or in vitro testing.

### Results

The studies consistently reveal a significant association between abrupt estrogen "withdrawal" during the late luteal phase and the pathophysiology of menstrual migraine. The drop in estrogen levels may have a pro-nociceptive effect as its main route, facilitating cortical responses to painful stimuli, through its association with ERK, modulation of the trigeminovascular system and the serotonergic, opioid, noradrenergic, glutamatergic and GABAergic neurotransmitter systems. Studies also indicate that the increase in prostaglandin levels and the vasodilatory effect mediated by estrogen withdrawal are important factors in the pathophysiology of migraine. Other studies suggest an association between mineral homeostasis and oxidative stress with the incidence of headaches mediated by female sex hormones. One study suggested that high plasma concentrations of estrogen appear to be associated with migraine attacks with aura. The action of progesterone still has ambiguous results.

#### Conclusion

The action of estrogen on the pathophysiology of migration occurs through many distinct pathways. Understanding these means is necessary to develop efficient treatments that increase patients' quality of life.

