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VIII НАЦІОНАЛЬНИЙ КОНГРЕС ПАТОФІЗІОЛОГІВ УКРАЇНИ

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Method: In rats with the kindling syndrome induced by i.p. injections of PTZ (35.0 mg/kg daily, for three weeks). tDCS was performed with the cathode on the skull surface oriented to the cerebellar cortex (300 μA, 10.0 min). Pioglitazone (100.0 mg/kg, i.p.) was administered in 60.0 min before tDCS. Fouls stimulated kindled rats were used as a control.

Results: The latent period of seizures induced by a test injection of PTZ (35.0 mg/kg) increased significantly (by 42.2% on average $P < 0.05$ vs. control) after pioglitazone administration (100.0 mg/kg, i.p.) and tDCS, Also, combined usage of tDCS and pioglitazone prevented the precipitation of generalized tonic-clonic seizure fits in 8 out of 10 rats ($P < 0.05$), reduced seizure severity by 31.3% ($P<0.05$), and shortened the duration of ictal discharges by 45.0% ($P < 0.05$).

Discussion and Conclusion: Gained data revealed that tDCS (300 mcA, 10 min) of the paleocerebellar cortex and pioglitazone (100.0 mg/kg, i.p.) delivered separately suppress kindled seizures induced with pentylenetetrazole administration. Combined usage of tDCS and pioglitazone is followed by more pronounced increase the latency of first seizures, prevent generalized seizure fits, and inhibit ictal epileptogenesis in the frontal cortex and hippocampus of kindled rats.

Key words: seizures, pentylenetetrazol (PTZ), pioglitazone

Ключові слова: судоми, пентилентетразол (PTZ), піоглітазон

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THE EFFECT OF BISPHENOL A ON THE ENDOMETRIUM

ВПЛИВ БІСФЕНОЛУ А НА ЕНДОМЕТРІЙ

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Topicality: Bisphenol A (BPA) is an organic polymer used in dental materials, plastic utensils, food containers, as well as in the production of polycarbonate plastic materials and resins covering metal cans and water pipes and in many other industries. People are exposed to BPA through the consumption of water and food stored in plastic containers. BPA is inhaled

with dust from the air or absorbed through the skin. Because BPA is a xenoestrogen in its structure, BPA may have a significant effect on the endometrium, although its effects have not been fully studied.

Aim: The aim of the study was to analyze the literature in order to reveal the mechanism of BPA's effect on the endometrium and the main effects of its action.

Results: BPA can bind to both alpha (ERα) and beta (ERβ) estrogen receptors and trigger genomic and non-genomic mechanisms under the influence of both low and high doses of BPA.

BPA can cause hypomethylation of CpG islands, which are present in the promoter of the ERβ gene in endometrial stromal cells. Changes in epigenetic modification in the promoter region of the gene can lead to long-term changes in gene expression and phenotype. In the normal endometrium, ERβ is poorly expressed in the epithelium and stromal cells. However, epigenetic modification caused by BPA leads to high expression of ERβ in both the epithelium and the stroma. Enhanced ERβ function induces an increase in IL-1β levels, enhances adhesion and proliferative activity in the endometrium.

At the same time, BPA binds to the GPER receptor and may increase the invasion of endometrial stromal cells. GPER stimulation activates several classic signaling pathways. The PI3K / mTOR pathway regulates cell growth, proliferation, differentiation, and apoptosis in response to internal and extracellular signals, including oxygen levels, inflammation, and growth factors. Thus, the effects of BPA can increase the incidence of endometriosis.

The effect of BPA is also associated with increased vascular formation and branching points, as well as increased mRNA and vascular endothelial growth factor (VEGF) production in human endometrial endothelial cells, which also express ERβ. These data suggest that BPA may alter normal vasculogenesis in the endometrium and affect its development and possibly embryo implantation. In addition, BPA has recently been shown to alter decidualization of endometrial stromal cells in vitro. BPA is able to prevent decidualization, proliferation and alter the expression of ERα genes, PGR and cell cycle.

The effect of BPA on the endometrium during the early phase of proliferation can change the time of inhibition of miR-27b and, consequently, increase the expression of its targets, VEGFB and VEGFC, prematurely leading to dysregulation of angiogenesis. Disruption of

endometrial cell division by BPA may contribute to the development of gynecological disorders, including increased angiogenesis and VEGF gene expression in conditions such as endometriosis, abnormal decidualization, or failed implantation.

If decidualization is taken into account directly, BPA may impair the ability of endometrial stromal cells to undergo this process. Thus, BPA at a dose of 1 μm destroys decidualized stromal cells, if the cells were exposed to BFA after decidualization.

BPA is able to significantly reduce the expression of CCND2 mRNA (encoding cyclin D2) in endometrial cells, and this molecular event coincides with a decrease in proliferation. Because the Cyclin D2 / CDK complex is required to enter the S-phase of the cell cycle, without sufficient Cyclin D2, the cell will enter a state of rest without proliferating. For decidualization proliferation of stromal cells is necessary. Thus, it is possible that the lack of proliferation observed in endometrial cells exposed to BPA, reduces the potential for decidualization.

In addition, it was confirmed that BPA is able to alter estrogen synthesis and inhibit the expression of estrogen-1 receptor (ESR1) in endometrial stromal fibroblast cells. Dysregulation of ESR1 and prostaglandin receptor (PGR), as observed in BPA-treated endometrial cells, provides a potential explanation for the ineffectiveness of decidualization. In addition, the transmission of estrogen and progesterone signals is important for successful implantation in the endometrium, and if the receptors of decidual cells change during exposure to BPA, the blastocyst will be in a non-viable environment.

Conclusions:

1. The effects of BPA on the endometrium can disrupt the process of decidualization of the endometrium and can potentially lead to failed implantation and fertility problems in women.

2. Exposure to BPA can increase the risk of endometriosis.

3. Activation of proliferation in endometrial cells and the production of vascular endothelial growth factor (VEGF) in human endothelial endothelial cells may contribute to pathological changes in endometrial vasculogenesis.

Key words: Bisphenol A, endometrium.

Ключові слова: Бісфенол А, ендометрій