**Role of neuropeptides in Patients with Endometriosis: A Literature Review**

*Hamidreza Mosleh \*1, Sedighe Hosseini 2, Nazanin Hajizadeh 2, Leila Majdi 2, Marziyeh Ajdary3,* *Zahra Shams Mofarahe 1*

1. Department of Biology and Anatomical Sciences, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. Preventative Gynecology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3. Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran

\*Corresponding author

Email: mosleh.hamidreza@sbmu.ac.ir

**Abstract**

While the exact pathogenesis of endometriosis is not fully understood, researchers have explored endocrine, paracrine, and immunological influences to better understand the disease. Neuropeptides, which play a significant role in regulating communication among endometrial cells, have been extensively studied and found to have effects on neurons and other somatic cells. The interplay between neuropeptides, pain, and the immune response suggests that neuropeptides may play a significant role in the development and progression of endometriosis. We investigate the role of nerve fibers and neuropeptides, Estrogen and Estrogen receptors, and new biomarkers in promoting inflammation and pain in endometriosis. Here are some results:

1. Decreased *PNX-14* levels are associated with increased LH/FSH ratio and elevated 17b-estradiol levels in endometriosis with ovarian localization.

2. Lower expression of *Kisspeptin* and its receptor may contribute to the invasiveness of endometriosis.

*3. Galectin-3*, which is overexpressed in eutopic endometrial stromal cells of patients with endometriosis, plays a role in supporting the survival and engraftment of endometrial cells in the peritoneal cavity. It enhances the adhesion and migration of endometrial stromal cells and reduces natural killer cell cytotoxicity.

4. *Urocortin* (*UCN*): It is suggested that *UCN* and *CRH* might play immunoregulatory roles in endometriotic sites, influencing reproductive functions.

5. Sensory nerve-derived neuropeptides (such as *SP* and *CGRP*) and sympathetic nerve-derived neurotransmitters (such as noradrenaline) may promote the development of adenomyosis through their respective receptors on adenomyotic lesions.

6. Inhibition of *NPSR1* gene expression reduces inflammatory cytokines and monocytes in endometriosis, suggesting *NPSR1* as a therapeutic target for reducing chronic inflammation and pain in endometriosis patients.

In conclusion, the data presented in this article highlight the significant involvement of the nervous system, neuropeptides, and estrogen in the pathogenesis of endometriosis. Understanding these molecular mechanisms can aid in the development of targeted therapies for managing inflammation, pain, and disease progression in endometriosis patients.

**Key words:** Neuropeptides, Endometriosis, Pain, Inflammation.