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## **Chronic pelvic pain and comorbidity at menopause: what is key for the gynecologist**

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### **Background**

Chronic pelvic pain (CPP) is a challenging condition. Increasing evidence suggests that the hallmark of pain is tissue inflammation. Acute and chronic inflammation are mediated by the mastcells (MCs). They are distributed in all organs and vascularized tissue, where they work as immune sentinels. They are recruited to the sites of inflammation, where they orchestrate the inflammatory response. MCs contain different angioactive, pro-inflammatory and neurotrophic factors, packed in vesicles which differentially release their content outside the cell into the tissue, according to the type and timing of damaging factors ("agonists" of the degranulation process). The mastcell activity is modulated by sexual hormones, with estrogens having agonist and testosterone antagonist role on mastcell degranulation, at least in the fertile age. After the menopause, the hormonal modulation becomes even more complex, with tissue differentiations. The majority of gynaecologists are not familiar with MCs role in inflammation and pain.

### **Aim of the presentation**

To update the knowledge and understanding of mastcell role in chronic pelvic pain, focusing on endometriosis, vulvar vestibulitis, irritable bowel syndrome and bladder pain syndrome/interstitial cystitis, during and after the menopausal transition.

### **Method**

Review of the literature and clinical experience.

### **Results**

Increasing evidence supports the prominent role of up-regulated mastcells in the maintenance of chronic inflammation and in the shifting from nociceptive to neuropathic pain in the affected tissues, contributing to CPP. New therapeutic lines consider reduction of agonists and/or using drugs ("antagonists") that can down-regulate the release of pro-inflammatory, angiogenic and neurotrophic factors from the mastcells.

### **Conclusions**

MCs are the real conductor of the inflammatory process. In CPP, MCs are the maintaining contributors of chronic inflammation, leading to the shift between nociceptive and neuropathic pain. Gynecologists may improve CPP by understanding the pathophysiology of MCs in chronic inflammation and addressing it in a multimodal therapeutic process. Appropriate choice of Hormone Replacement Therapy may further contribute to modulate and reduce pain during and after the menopausal transition.