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Letter to the editor

Two-hit theory by estrogen in burning mouth syndrome

KEYWORDS

Burning mouth syndrome;
Estrogen;
TRPV1

Burning mouth syndrome (BMS) is characterized by chronic burning pain in a normal-appearing oral mucosa. An important implication regarding the mechanism of pathogenesis is that the disease generally develops in post-menopausal women. I read with great interest the paper by Seol et al. on the regulation of transient receptor potential vanilloid 1 (TRPV1) as an estrogen-dependent nociceptor in BMS patients.¹ They argued that estrogen has both pronociceptive and anti-nociceptive effects via modulation of nociceptors. Estrogen upregulates TRPV1 through classical genomic and non-classical pathways, resulting in pronociceptive effect. On the other hand, estrogen alleviates pain by downregulating nerve growth factor (NGF), which can translocate TRPV1 to the cell surface membrane.

How do the opposing effects of estrogen on pain perception affect the development of BMS? As a first hit by estrogen, increased estrogen during puberty increases TRPV1 expression, making at-risk individuals more sensitive to pain and more pain induced by dental treatment. In fact, BMS patients may have migraine headaches related to TRPV1 and neuroinflammation prior to the onset of BMS.² As a second hit by estrogen, when estrogen decreases during menopause, NGF increases, TRPV1 increases at the cell surface, pain sensitivity increases, neuroinflammation also occurs, and BMS develops in at-risk individuals. In fact, TRPV1 expression is increased in the oral mucosa of BMS patients.³ Two-hit by estrogen may explain gender

differences in BMS patients. However, future studies on changes in estrogen and TRPV1 expression and rigorous investigation of pre-existing painful conditions in BMS patients are needed to validate this.

Declaration of competing interest

The author has no conflicts of interest relevant to this article.

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Abbreviations: BMS, burning mouth syndrome; NGF, nerve growth factor; TRPV1, transient receptor potential vanilloid 1.

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