Capsaicin and Related Sensory Receptors in Menopausal Hot Flashes, Postpartum Shivering, and Vulvodynia: A Sensory Receptor Target Group that Requires Further Investigation in Women’s Health

Menopausal hot flashes, postpartum shivering, and vulvodynia represent three different clinical complaints that women’s health clinicians may observe on a regular basis. Their causes are still unknown, and their treatments are primarily directed at the patient’s symptoms.

The 2021 Nobel Prize in medicine or physiology was awarded to David Julius and Ardem Patapoutian who discovered the molecular receptors for temperature sensation and mechanical force sensation, respectively [1-4]. Dr. Julius investigated the molecular basis of the burning sensation associated with capsaicin, which is the ingredient in chili peppers that cause the sensory taste in the hot peppers. Dr. Julius and his research group isolated an ion channel known as TRPV1 (transient receptor potential cation channel subfamily V member 1), which was found to be the unique single receptor activated by capsaicin in chili peppers and also by temperatures that humans perceive as burning hot. Their findings explain the sensory events that a person feels when chili peppers are eaten, with an initial burning sensation and then followed by the subsequent physiologic response in the body, which is accompanied by intense sweating [1-4]. Additional studies by the Julius research group identified transient receptor potential (TRP) channels that serve as the molecular receptors that detect low temperatures [4].

The identification of the TRPV1 and associated group of sensory receptors allows investigators to focus on their possible roles in common issues regarding women’s health, menopausal hot flashes, postpartum shivering, and vulvodynia.

GAPS THAT NEED TO BE ADDRESSED

The gaps in the understanding of the TRPV1 class of sensory receptors regarding women’s health include the following: how do steroid and peptide hormones control their expression, what are the differences in the expression of the receptors in different individuals, what disease states cause a disruption of the receptor actions, and are there blockers of the actions of the receptors?

Menopausal hot flashes represent one important area for additional studies of these sensory receptors [5, 6]. Menopausal hot flashes occur in up to 80 percent of perimenopausal and menopausal women. They significantly impact the quality of life, as they are associated with sleep disturbance and other issues related to vasomotor symptoms. Hence, first, studies need to address and focus on the following questions: What is the relationship between steroid and peptide hormone levels and the expression of the receptors? What are the relative roles of estrogens and progestins in the regulation of the receptors? What is the role of blood flow in relation to the activation of the receptors? Is there an individual or ethnic difference in the expression of the receptors? Are there individual responses to menopausal hot flashes? Can different agents allow the alleviation of the symptoms by the sensory receptors? Hot flashes attenuate and disappear over time; therefore, how do the capsaicin receptors affect the spontaneous attenuation and disappearance of the symptoms? Could changes in the regulation of the receptors accelerate the process, which leads to a decrease in hot flashes?

A second common condition that can be investigated in the context of the sensory TRP cool receptors is postpartum shivering [7, 8]. A number of postpartum women have a shiver response. Most commonly, this occurs immediately postpartum. However, the shivering response could be found after the delivery process. Therefore, studies need to be conducted to examine the following: Could the shiver response be due to the cold sensing receptors that belong to the same class as the capsaicin receptors? Could the rapid decline in the serum steroid or peptide hormones with delivery activate the receptors so that the women respond to the hormonal changes by shivering? Are there blockers to this reaction to make the new mother more comfortable? Are there conditions in which there is an abnormal shiver response by the cool sensing receptors in postpartum women?

Vulvodynia represents another important condition regarding Women’s Health in which investigating the capsaicin receptors would be beneficial. The patients with vulvodynia have a burning pain sensation in the vulva [9-10]. Vulvodynia is diagnosed when the patient has symptoms for 3 months or more, and there are no abnormal physical findings. Currently, there is no known etiology for the chronic and potentially debilitating discomfort. These women with vulvodynia may have other associated conditions, such as fibromyalgia, irritable bowel syndrome, or painful bladder syndrome. Sometimes, women have associated risk factors, such as anxiety, depression, or post-traumatic stress disorder. The diagnosis is made when other causes of vulvar pain, such as infections, have been ruled out. Questions that need to be considered while treating patients with vulvodynia include whether there is abnormal activation of the capsaicin receptors? Is there an association between hormone levels and the expression of the receptors? Could blockers of the capsaicin receptors block the burning sensations experienced by these patients? Is there a simple and non-invasive way to diagnose TRPV1 receptor abnormalities in these women?

CONCLUSION

The discovery of the TRPV1 receptor for capsaicin and its surprising identification as the identical receptor both for the chili pepper sensation and the human sensory response receptor for burning hot sensation has paved the way for future advan-
This ion channel is required for the detection of capsaicin and burning hot sensation, with subsequent physiologic changes when activated, including intense sweating. This group of hot and cool receptors may impact the three common conditions regarding women’s health, such as menopausal hot flashes, postpartum shivers, and vulvodynia. Additional translational medicine studies that address the effects of steroid and peptide hormones on the expression of these receptors, the differential expression of the receptors in different women, the post-receptor effectors of these receptors, and the blockage of the receptor actions may lead to advances in reducing the discomfort in women suffering from menopausal hot flashes, postpartum shivers, and vulvodynia.

REFERENCES


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