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NON-HORMONAL ALTERNATIVES FOR TREATMENT OF PERIMENOPAUSAL VASOMOTOR SYMPTOMS

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Vasomotor symptoms, more commonly known as “hot flashes”, are sudden, abrupt alterations in temperature regulation caused by decreased levels of estrogen during physiological and pathological menopause, which is explained by disrupted thermoregulation in hypothalamus. These episodes of thermal dysregulation generally present themselves as sweating, with skin reddening most often on the face, neck and chest; the episodes vary in frequency and severity, in most severe cases having a considerable negative impact on a woman’s quality of life, especially social and professional performance.

Even though the most sought out treatment is hormonal therapy (HRT; estrogen and progesterone replacement), for some patients other alternatives must be regarded due to serious health concerns, such as medical history of an estrogen-sensitive cancer (including breast cancer), coronary heart disease, myocardial infarction, stroke, venous thromboembolism, or a genetically high risk of thromboembolic disease that prevents them from using HRT including patients that refuse the hormonal therapy without underlying medical contraindications.

The options available in non-HRT include the following: as first line treatment – antidepressants (SSRIs), followed by gabapentin and pregabalin (anticonvulsant drugs), oxybutynin (anticholinergic agent), clonidine (alpha-2 adrenergic agonist). These medications are included in most up-to-date guidelines and have proven efficacy, therefore being evidence-based. However, psychotropic medications, such as antidepressants and anticonvulsants still remain a source of stigma among women, which inhibits their use.

Alternative medicine offers other options, such as purified pollen extract (supplement sourced from pure pollen extract), black cohosh, soy derivatives and others. However, it should be noted that none of these methods are evidence-based, and their sporadic efficacy is mostly explained by placebo-effect. Some of the non-pharmacological approaches are weight loss, yoga and exercise, cognitive behavioral therapy, relaxation therapy, acupuncture, cooling strategies, and stellate ganglion block (vertebral cervical block by local anaesthetic injection).

Some of the newly emerging therapies should be mentioned, such as neurokinin B antagonist – fezolinetant undere the brand name “Veozah”, – is the first one to receive approval from the FDA, while dual neurokinin 1 and 3 antagonist are also mentioned as potentially effective. Uncertainties remain regarding the pathophysiology of VMS. It involves, however, kisspeptin-neurodiverdial (KNDy) neurons, which innervate the hypothalamic thermoregulatory centre and respond to estradiol negative feedback. Hot flashes are caused by an increase in neurokinin B signalling at the KNDy neurons in the thermoregulatory zone, which is a consequence of the decline in estrogen during menopause, though the precise mechanism is still unknown. Fezolinetant dampens neuronal signalling and reduces hot flashes by blocking neurokinin B binding on the hypothalamic KNDy neurons.

As mentioned before, vasomotor symptoms can have a detrimental impact on a woman's overall quality of life and are still widely underdiagnosed and undertreated, therefore, novel therapeutic approaches should be profoundly studied and implemented in practical healthcare.

While there are many options available, clinicians should ultimately individualize therapy based on the patient’s needs and goals while mitigating bothersome side effects.