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Invited Editorial

Starting and stopping menopausal hormone therapy and antidepressants for hot flushes: A case-based approach

Menopausal hot flushes are common, can be very annoying and may go on for years, but their underlying pathophysiology is rather poorly understood. Menopausal vasomotor symptoms (VMS) can last for more than 7 years for more than 50% of women and persist for 4.5 years after the final menstrual period (FMP) [1]. Longer duration of VMS has been associated with factors such as lower levels of education, younger age, greater perceived stress and symptom sensitivity, as well as higher depressive symptoms and anxiety at first VMS report.

Although anxiety can be a risk factor for VMS [2], it is not clear whether it is a precursor or a consequence of the symptoms and whether it has an impact on the individual perception of hot flushes and their intensity. In a 14-year follow-up study [2], there was a strong predictive association of somatic (but not affective) anxiety with the risk of menopause-related hot flushes. Several treatments targeting somatic anxiety are under investigation.

Hormonal, non-hormonal and non-pharmaceutical (e.g. cognitive behavioural therapy - CBT) treatments have been used for menopause-related VMS [3]. Menopausal hormone therapy (MHT) may improve low mood and CBT may improve low mood and decrease menopause-related anxiety.

Menopausal hormone therapy has been widely used to treat hot flushes and other menopause-related symptoms (vaginal dryness, vaginal atrophy, sexual dysfunction). Several health-related issues should be considered before treatment initiation, however.

Although MHT can be effective, the symptoms may reappear following discontinuation. It appears that a gradual MHT discontinuation may limit the recurrence of symptoms in the short term, but not in the long term. This remains a controversial issue. In one study, conjugated equine estrogens (CEE) improved vaginal dryness and VMS in women with baseline symptoms [4], although they increased breast tenderness. There was a likelihood of experiencing symptoms following the discontinuation of CEE, even after long-term treatment. A similar study in women under 60 years of age also found that symptoms may reappear during the first post-treatment year; however, they usually subsided or disappeared within three years [5]. Discontinuation of estrogen plus progestogen therapy (EPT) for hot flushes, regardless of an abrupt or taper-down method, can cause recurrence of VMS and a deterioration in health-related quality of life (HRQoL) [6]. It has been reported that there may also be an increased cardiovascular mortality risk in the first year after the discontinuation of MHT [7,8].

According to the North American Menopause Society (NAMS), continuing systemic MHT after the age of 65 years should be a matter of clinical choice made on an individual basis after discussing the treatment plan with the woman [9].

Non-hormonal treatments for menopause-related VMS include antidepressants. Patient-specific treatment with selective serotonin reuptake inhibitors (SSRIs), especially paroxetine, citalopram and escitalopram, and serotonin and norepinephrine reuptake inhibitors (SNRIs), especially venlafaxine and desvenlafaxine, may be effective in reducing menopause-related hot flushes [10].

Nausea, constipation and other adverse effects usually subside early in treatment. SNRIs should be used with caution in women with hypertension. SSRIs may interfere with tamoxifen metabolism and should be avoided by women with breast cancer who take this medication [10].

Several other antidepressants are being studied for the treatment of menopause-related symptoms. Fluoxetine and sertraline are considered second-line treatment options. Concomitant depressive and anxiety symptoms are expected to subside with the use of antidepressants.

Discontinuation of antidepressant treatment may trigger a relapse of VMS [11]. Potential drug interactions, specific concerns (e.g. the issue of increased risk of suicidality with paroxetine, usually reported in young individuals) and potential adverse effects should be taken into account before prescribing. Sexual adverse effects may occur. Drug-related adverse effects are expected to subside or cease altogether following discontinuation of treatment.

Antidepressant discontinuation syndrome, following an abrupt stoppage of the medication, may occur within a few days. The symptoms are usually mild and include flu-like symptoms, nausea, insomnia, sensory disturbances, imbalance and hyper-arousal. Tapering is generally recommended, although there may be a few exceptions (e.g. with fluoxetine) [12]. Possibly titrating up and tapering down the antidepressant may improve tolerability. The length of treatment which is required has not been established.

It appears that SSRIs and SNRIs should not be the first-line treatment for VMS alone (i.e. without the presence of depression). Clinicians are advised to discuss the treatment options with the woman and to explain the risks and benefits.

In conclusion, menopause-related hot flushes may be distressing and may considerably impair the woman's HRQoL. MHT and antidepressants have been used for menopause-related VMS, often with good results. However, there are risks and benefits that have

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to be assessed by the clinician and discussed with the woman on an individual basis. Several issues, such as the tapering of the dose and the length of treatment, remain unclear. Further research is expected to provide data that could be used in planning an effective therapeutic approach.

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References

[1] N.E. Avis, S.L. Crawford, G. Greendale, J.T. Bromberger, S.A. Everson-Rose, E.B. Gold, R. Hess, H. Joffe, H.M. Kravitz, P.G. Tepper, R.C. Thurston, Study of Women's Health Across the Nation, Duration of menopausal vasomotor symptoms over the menopause transition, JAMA Intern. Med. 175 (2015) 531–539.
[2] E.W. Freeman, M.D. Sammel, R.J. Sanders, Risk of long-term hot flashes after natural menopause: evidence from the Penn ovarian aging study cohort, Menopause 21 (2014) 924–932.
[3] NICE guidelines [NG23]. Menopause: diagnosis and management. November 2015 https://www.nice.org.uk/guidance/ng23/resources/menopause-diagnosis-and-management-1837330217413. (Accessed 02 October 2019).
[4] R.L. Brunner, A. Aragaki, V. Barnabei, B.B. Cochrane, M. Gass, S. Hendrix, D. Lane, J. Ockene, N.F. Woods, S. Yasmeen, M. Stefanick, Menopausal symptom experience before and after stopping estrogen therapy in the women's health initiative randomized, placebo-controlled trial, Menopause 17 (2010) 946–954.
[5] G. Perrone, O. Capri, P. Galoppi, F.R. Patacchioli, E. Bevilacqua, M.G. de Stefano, R. Brunelli, Menopausal symptoms after the discontinuation of long-term hormone replacement therapy in women under 60: a 3-year follow-up, Gynecol. Obstet. Invest. 76 (2013) 38–43.
[6] L. Lindh-Astrand, M. Bixo, A.L. Hirschberg, I. Sundström-Poromaa, M. Hammar, A randomized controlled study of taper-down or abrupt discontinuation of hormone therapy in women treated for vasomotor symptoms, Menopause 17 (2010) 72–79.
[7] T.S. Mikkola, P. Tuomikoski, H. Lyytinen, P. Korhonen, F. Hoti, P. Vattulainen, M. Gissler, O. Ylikorkala, Increased cardiovascular mortality risk in women discontinuing postmenopausal hormone therapy, J. Clin. Endocrinol. Metab. 100 (2015) 4588–4594.
[8] M. Venetkoski, H. Savolainen-Peltonen, P. Rahkola-Soisalo, F. Hoti, P. Vattulainen, M. Gissler, O. Ylikorkala, T.S. Mikkola, Increased cardiac and stroke death risk in the first year after discontinuation of postmenopausal hormone therapy, Menopause 25 (2018) 375–379.
[9] The North American Menopause Society statement on continuing use of systemic hormone therapy after age 65, Menopause 22 (2015) 693.
[10] C. Stubbs, L. Mattingly, S.A. Crawford, E.A. Wickersham, J.L. Brockhaus, L.H. McCarthy, Do SSRIs and SNRIs reduce the frequency and/or severity of hot flashes in menopausal women, J. Okla. State Med. Assoc. 110 (2017) 272–274.
[11] H. Joffe, K.A. Guthrie, J. Larson, L.S. Cohen, J.S. Carpenter, A.Z. Lacroix, E.W. Freeman, Relapse of vasomotor symptoms after discontinuation of the selective serotonin reuptake inhibitor escitalopram: results from the menopause strategies: finding lasting answers for symptoms and health research network, Menopause 20 (2013) 261–268.
[12] M. Gabriel, V. Sharma, Antidepressant discontinuation syndrome, CMAJ 189 (2017) E747.

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