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Menopause, cognition, hot flashes and COVID-19: is estrogen a fundamental piece in the puzzle?

In December 2019, Wuhan (China) reported the first case of a severe acute respiratory syndrome caused by the coronavirus SARS-COV-2. On March 11, 2020, the WHO declared COVID-19 a global pandemic. Feelings of insecurity in all aspects of life, from the collective to the individual perspective, from the daily functioning of the society to changes in interpersonal relationships, social isolation, and lockdown that have been implemented since then have adverse effects on our mental health.

In our daily clinical practice, we observe that the pandemic exacerbates typical symptoms of the menopausal transition and postmenopausal period, therefore we must consider the management of the countless complaints these women have during such difficult times. They certainly deserve to be heard and taken care of. Providing adequate medical care while maintaining social distancing is a challenge but we cannot leave these women at home having to deal with their complaints and their symptoms without appropriate medical care wondering whether it is safe to use menopause hormonal therapy (MHT) .

Furthermore, women suffering with the uncomfortable symptoms of perimenopause such as vasomotor symptoms (VMS) may have difficulty in finding a doctor who will prescribe MHT to alleviate their symptoms. Many of these women will hear from their doctor that the symptoms of perimenopause are transient, and hormones should not be used due to numerous contraindications and risk of cancer, especially breast cancer. What should we do to improve this scenario? What I have witnessed as well as other doctors around the world is that the interest of gynecologists and primary care doctors are not keen on providing adequate individualized care to women during the menopausal transition.

On one side, published studies and reports on COVI-19 indicate that men develop more significant symptoms and have increased mortality rates when compared to women. On the other side, clinical observations have shown that women are the most vulnerable to the adverse effects of the imposed restrictions. The first relevant question regarding vulnerability to the disease itself is why women would be less susceptible than men and, if so, whether and how estrogen and progesterone are involved. Considering that the menopausal transition is characterized by estrogen fluctuations or hypoestrogenism, leading to uncomfortable symptoms like hot flashes, recent memory loss, forgetfulness, loss of concentration, and sleep disturbances, understanding the role of estrogen in adverse circumstances as the pandemic should be considered.

Memory problems occur mainly during the menopausal transition. In postmenopause, this decreased cognitive performance appears normal (Maki 2015). Nevertheless, under high levels of stress and depression, the cognitive decline/cognitive impairment may persist into post-menopause (Maki et al. 2021). The pandemic has increased the burden women have to face as they had to adapt to working from home, manage and provide support to their families while doing most of the housework. In such a stressful setting, one cannot blame the menopausal transition as the only culprit for increasing complaints of memory loss, low concentration, or forgetfulness.

In addition to the established effectiveness of MHT in relieving VMS and probable performance in cognitive disorders, hormonal therapy's effective potential is suggested to modulate the immune response to increase resilience to adverse COVID-19 outcomes as higher levels of estrogen and progesterone may help switch a more robust immune response. In the meantime, we are awaiting the results of two clinical studies designed to investigate the effectiveness of estrogen and progesterone therapy to decrease the severity of COVID-19 (Okpechi et al. 2021).

So, is estrogen a fundamental piece in the puzzle? Health care providers and physicians must intensify their efforts by encouraging women who are taking MHT not to interrupt therapy, support

those who have not yet started and suffer from exacerbation of their symptoms during this terrible pandemic time, as perhaps the studies that are underway may conclude that estrogens are an alternative therapy to mitigate the impacts of COVID-19 on these women.

Thus, under stressful conditions as the current COVID-19 pandemic, MHT for eligible symptomatic women can have additional benefits for mood, cognition, and quality of life. Future studies will answer whether estrogens and progestogens have any role in modulating the immune response and potential effectiveness in alleviating the severe symptoms of COVID-19. Healthcare providers, physicians and researchers have a considerable challenge to seek new therapies capable of reducing the severity of symptoms and the devastating impact that we have experienced in this unique period of human history and perhaps estrogen may be the answer.

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