Menopause Live prepared for Dr Alberto Calderon Zuniga

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Menopause Live Case Series

MHT and Systemic Lupus Erythematosus

Mrs. X is 50 years old and recently postmenopausal, having had her last menstrual period a year ago. She laments climacteric symptoms and asks about the risks and benefits of menopausal hormone therapy (MHT). During the consultation, she refers that she has been affected by Systemic Lupus Erythematosus (SLE) since the age of 38 years. She has no other health problem. Mrs. X experienced a miscarriage at the age of 24 years and then had a live birth at the age of 25. The pregnancy was uneventful. In her family, there is no history of breast or ovarian cancer; her father has had type 2 diabetes since the age of 6O, with some vascular complications, and her mother suffers from hypertension and hypercholesterolemia. Her first SLE flare occurred at the age of 37 years and presented with fatigue, joint pains, hair loss and skin lesions especially on the face and the upper thorax. She first consulted her general practitioner who prescribed some tests and suspected SLE. She was sent to a specialist who confirmed the diagnosis based on clinical and biological criteria; arthritis, skin lesions, alopecia, fatigue and an increase in c-reactive protein, discrete leukopenia, a decrease in total complement levels and positive anti-DNA and anti-smooth muscle antibodies. She underwent a series of tests that excluded kidney, brain, heart or lung involvement and antiphospholipid antibodies. It was concluded therefore that Mrs. X had cutaneous articular SLE. She took hydroxychloroquine for 10 years but had to stop it. She has had several flares over the years with increasing involvement of joints but of no other sites. She has taken corticosteroids 3 times for short periods. She is currently without treatment and her last flare occurred more than 5 years ago.

How will we answer her question on the benefits and risks of MHT? [for details see reference 1]

SLE is an autoimmune disease that can be worsened by estrogens. Before puberty and after menopause, the female: male ratio is about 2-3:1, whereas, during childbearing age, this ratio reaches 10-13:1. Genetic factors linked to chromosome X are also associated with the prevalence in women. In 30% of the cases, SLE antiphospholipid antibodies or lupus anticoagulant (APL) may be present. SLE is associated with an increase in cardiovascular disease and osteoporosis at a young age. The frequency of cardiovascular events is proportional to the duration of SLE and associated with renal involvement.

Can we thus prescribe a combined MHT?

There are two rather reassuring randomized trials published in women with SLE using conjugated estrogens and medroxyprogesterone acetate versus placebo. The first study [2] included quiescent or low active SLE without APL. A significant number of patients dropped out. There was no difference after one year of treatment in severe flares, 13 of the 174 patients (7.5%) in the active group and 8 of the 177 (4.5%) in the placebo group, but a significant difference in mild-moderate flares, 1.14 flares/person-year for MHT and 0.86 flare/person-year for placebo, RR= 1.34 (1.07-1.66). Women with stable-active lupus had a higher risk of severe flares, RR = 2.87 (1.19 – 6.92), especially if renal involvement was present. Two venous thromboses, one stroke and one thrombosis in an arteriovenous graft occurred in the treated group versus one venous

thrombosis in the placebo group. In the second study, (3), the presence of an APL was not a contraindication. There was no difference after one year in the index of SLE activity, the SLEDAI, or the number of flares RR=0.96 (0.70–1.32). Three patients in the active group developed a thrombosis (1 venous and 2 arterial) versus 1 arterial thrombosis in the placebo group in a patient with an APL. The number of drop-outs, however, precludes any firm conclusions on the safety of MHT. Several retrospective studies have reported no increase in the risk of flares but some bias of selection of the patients can be suspected. In practice, APLs may be considered a contraindication because of the risk of autoimmunity exacerbation by estrogens and the high risk of thrombosis. Active SLE also contraindicates the treatment. In our patient, Mrs. Martin, MHT may be considered under careful clinical and biological follow-up. In this case, transdermal estradiol and micronized progesterone or dydrogesterone should be preferred and prescribed at the lowest dose of estradiol necessary to alleviate symptoms. Transdermal estradiol is associated with a lower incidence of thrombosis and stroke in patients without SLE (no study in this specific group). Micronized progesterone is also known to help alleviate vasomotor symptoms and sleep disorders. This systemic MHT can be easily combined with vaginal estrogens. In case of a history of severe SLE, which is associated with an increased risk of cardiovascular events and accrual damage, we suggest using non-hormonal treatment such as SSRI or SNRI as first-line treatment.

Further reading: Review published in IMS Official Journal Climacteris *by Anne Gompel "Systemic lupus erythematosus and menopause."* https://www.tandfonline.com/doi/full/10.1080/13697137.2019.1679113

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