



## THE ADVANTAGES OF TRANSDERMAL ESTROGENS

Piette P (BE) [1]

Hormone Therapy (HT) remains the most effective treatment for vasomotor symptoms including sleep disturbances and the genitourinary syndrome of menopause. This was confirmed in the very recent updated Position Statement of the North American Menopause Society (2017) and in most of international guidelines. It is definitely safe in more healthy subjects when initiated within 10 years from menopause for at least 5 to 10 years, provided it had been initiated before the age of 60 years. Standard or even lower daily doses of oral HT, contrary to transdermal route of estradiol administration (by gel or patch ie) are mainly associated with an increased risk of venous thromboembolism (VTE), gallbladder disease and stroke. In a double-blind randomized active-controlled, multicenter, 12-week phase 3 study, a transdermal estradiol gel at several concentrations and the transdermal patch used in the KEEPS trial were evaluated on long-term clinical effectiveness and safety, on serum concentration-effect relationship and withdrawal effects. In the safety study, estradiol median serum concentrations (and estradiol/estrone ratio) suggest estradiol gel for 1.25 g (32,0 pg/mL) and 2.5 g (60,0 pg/mL) daily doses should be therapeutically effective, and comparable from the patients receiving the patch. The change from baseline in the frequency of moderate-to-severe hot flushes was not affected by the serum estradiol concentration but non-responders rate was suggested to increase by decreasing the daily dose. Transdermal 17 $\beta$ -estradiol therapy in recently postmenopausal women was associated with a reduced amyloid- $\beta$  deposition in KEEPS trial.

In conclusion, nonoral routes of administration may offer potential advantages because nonoral routes bypass the first-pass hepatic effect. Risk of gallstones, cholecystitis, and cholecystectomy is increased with oral estrogen-alone and combination HT. The use of transdermal as compared with oral HT may be considered less likely to produce thrombotic risk and perhaps the risk of stroke and coronary artery disease (AACE 2017); women with advancing age will also beneficiate from this safe route of administration. Transdermal estradiol in a gel or in a patch will allow us to treat safely symptomatic women in the early menopause for as long as required with a regular evaluation of the benefit/risk ratio for the patient as confirmed recently in the KEEPS trial and several meta-analysis.

[1] Besins Healthcare