VPLIV NADOMEŠČANJA ESTRADIOLA NA OZNAČEVALCE VNETJA, KOAGULACIJO IN FIBRINOLIZO

THE INFLUENCE OF ESTRADIOL REPLACEMENT THERAPY IN MARKERS OF INFLAMMATION, COAGULATION AND FIBRINOLYSIS

Branka Žegura[1], Irena Keber[2], Miran Šebeštjen[2], Elko Borko[1], Wolfgang Koenig[3]

[1] Klinični oddelek za ginekologijo in perinatologijo, Učna bolnišnica Maribor, Ljubljanska 5, 2000 Maribor
[2] Klinični oddelek za žilne bolezni, Klinični center, Zaloška 7, 1525Ljubljana
[3] Oddelek za interno medicino II – kardiologija, Medicinski center univerze v Ulmu, Ulm, Nemčija

Ključne besede: *nadomeščanje estrogenov; označevalci vnetja; koagulacija in fibrinoliza*

Izvleček – Izhodišča. *Hormonsko nadomestno zdravljenje povezujejo s povečanim tveganjem za srčno-žilne bolezni v prvem letu po začetku zdravljenja. V randomizirani raziskavi smo primerjali vpliv peroralnega in transdermalnega nadomeščanja estradiola na kazalnik vnetja, na koagulacijo in fibrinolizo.*

Metode. *Triinštirideset zdravih preiskovank smo 6 tednov po kirurško povzročeni menopavzi naključno razdelili v dve skupini. V prvi skupini smo preiskovankam estradiol nadomeščali peroralno, v drugi pa transdermalno. Na začetku, 6 tednov po operaciji in po 28 tednih peroralnega ali transdermalnega nadomeščanja estradiola smo opravili klinični pregled in laboratorijske krvne analize.*

Rezultati. *Med fibrinolitičnimi parametri se je po peroralnem nadomeščanju skrajšal čas evglobulinske lize (p<0,05), znižala raven t-PA (p = 0,001), zmanjšala aktivnost PAI-1 (p<0,05). Med koagulacijskimi parametri se je po obeh oblikah nadomeščanja estradiola znižala raven fibrinogena (p = 0,002 za peroralno nadomeščanje in p = 0,007 za transdermalno nadomeščanje). Med označevalci vnetja je prišlo do pomembnega porasta ravni CRP samo po peroralnem nadomeščanju z 2,15 (0,71–4,05) na 3,41 (1,12–5,92) mg/l (p = 0,04). Ravni serumskega amiloida A, interlevkina-6 in faktorja tumorske nekroze alfa se niso pomembno spremenile po nobeni od obeh oblik nadomeščanja. Peroralno nadomeščanje estradiola je pomembno izboljšalo lipidni profil, vpliv transdermalnega nadomeščanja je bil manjši. Obe obliki nadomeščanja sta pomembno znižali raven krvnega sladkorja.*

Zaključki. *V naši raziskavi je peroralno nadomeščanje estradiola kazalo provnetni učinek, po drugi strani je izboljšalo fibrinolizo in ni imelo prokoagulantnega učinka. Ugodno je delovalo tudi na krvne lipide in lipoproteine. Transdermalno nadomeščanje estradiola ni vplivalo na označevalce vnetja, koagulacijo in fibrinolizo, vendar je prišlo do ugodnega znižanja ravni fibrinogena.*

Key words: *estrogen replacement therapy; markers of inflammation; coagulation and fibrinolysis*

Abstract – Background. *Estrogen replacement therapy (ERT) has been found to be associated with increased cardiovascular risk in the first year after initiation of ERT. We compared the effects of oral and transdermal estradiol (E2) replacement therapy on markers of inflammation, coagulation and fibrinolysis in a randomized double-blind trial.*

Methods. *Fortythree healthy women were randomized six weeks after surgically induced menopause to receive treatment with either oral or with transdermal E2 over a period of 28 weeks. At baseline and after 28 weeks, levels of serum lipids and lipoproteins, and markers of coagulation, fibrinolysis, and inflammation were determined.*

Results. *Among fibrinolytic parameters, oral E2 shortened euglobulin clot lysis time (p<0.05), reduced tissue type plasminogen activator antigen (p = 0.01), and plasminogen activator inhibitor activity (p<0.05). Among coagulation parameters, both routes of E2 replacement decreased fibrinogen levels (p = 0.002 for oral and p = 0.007 for transdermal E2). Oral E2 resulted in an increase in C-reactive protein from 2.15 (0.71–4.05) to 3.41 (1.12–5.92) mg/l (p = 0.04), while transdermal E2 showed no effect. Levels of serum amyloid A, IL-6 and TNF-á did not change significantly after oral and transdermal E2.*

Conclusions. *Oral E2 significantly improved the lipid profile, while transdermal E2 had a less pronounced effect. Both oral and transdermal E2 significantly reduced fasting glucose. Oral E2 was associated with a pro-inflammatory response, but at the same time improved fibrinolytic capacity, showed no pro-coagulatory effects, and acted beneficially on lipids and lipoproteins. There was no influence of transdermal E2 on markers of coagulation activation, fibrinolysis and inflammation, but it decreased fibrinogen levels significantly. Further studies are needed to explore the clinical relevance of these observations.*