Towards Self-adjusted Postmenopausal Hormone Replacement Therapy:
Biochemical and Clinical Parameters Associating with Percutaneous Treatment

Tarja Vihtamäki, University of Tampere, Finland

This thesis was undertaken to evaluate the factors affecting the use and compliance of hormone replacement therapy (HRT) in Finland and to examine the applicability and effectiveness of percutaneous estrogen therapy carried out by a woman with a novel self-adjusted method. In addition, the different factors, producing variations in serum estradiol (E_2) concentrations during topical HRT (E_2 gel) were investigated. Results: Prevalence of HRT has increased in Finland during the last 15 years but compliance with HRT is poor. Approximately 30 % of users discontinue the therapy within 6 months and almost half within one year, mostly because of side-effects related to the therapy. Also current users (20 %) are reporting continuous side-effects from the therapy. In our study, the women tailored individual estrogen (17ß-E_2) doses for themselves based on the disappearence of climacteric symptoms. The E_2 dose in which symptom control was achieved varied inter-individually from 1 mg/day to 6 mg/day. Compared with the dose recommended by the pharmaceutical manufacturer of the product, 29 % of the women managed with lower doses (1 mg E_2 per day), 52 % became symptom-free with the recommended dose (1.5 mg E_2 per day), and 19 % needed greater doses. The initial symptom scores (Kupperman index = KI) had no correlation with the final self-adjusted treatment doses, but there was a positive correlation between KI and serum follicle stimulating hormone (FSH). After three months, with self-adjusted E_2 doses, serum E_2 was at a postmenopausal level (<50 pg/ml) in 22 % of the women. In all, 45 % showed serum E_2 remaining under 60 pg/ml, 29 % had serum E_2 levels of 60 - 100 pg/ml, and 26 % showed E_2 of more than 100 pg/ml. A negative correlation was observed between serum E_2 and FSH, and a positive correlation between serum E_2 and sex hormone binding globulin (SHBG), indicating a minor induction in SHBG production. The effects of ascorbic acid (AA) supplementation on serum E_2 were studied in women on self-adjusted percutaneous E_2 with stable serum E_2 concentrations. One month of treatment with 1000 mg AA daily increased serum E_2 by 21 %. A greater responses were seen in two subgroups with the lowest initial blood concentrations of either AA (55 % increase)or E_2 (100 % increase). We also studied the effect of skin contamination by E_2 gel on circulating E_2 levels. Skin contamination by the gel significantly affected serum E_2 levels by producing highly fluctuating values. In non-contaminated samples serum E_2 intra-individual fluctuation was slight. Conclusions: Self-adjusted method of percutaneous estrogen therapy provides good control of menopausal symptoms with the lowest possible estrogen dose. Side-effects of the treatment are also minimized. As with self-adjusted doses, serum E_2 concentrations may remain at a postmenopausal level in some women, it may be worthwhile investigating whether the achieved E_2 concentrations also ensure longer-term benefits of HRT. Intra-individual fluctuation in serum E_2 concentrations during percutaneous estrogen therapy is minimal when the source of error, caused by skin contamination by E_2 gel is eliminated.

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e-mail:tarjavi@sgic.fi

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