Estrogen Research Abstracts

Safety and efficacy of oestriol for symptoms of natural or surgically induced menopause.

Takahashi K, Okada M, Ozaki T, et al.
Human Reproduction. 2000 May, 15 (5): 1028-1036

From the findings of this study, estriol appeared to be safe and effective for relieving post-menopausal symptoms. The study looked at two groups of women; those who had gone through natural menopause (group 1), and those who had gone through surgically induced menopause as a result of a hysterectomy with bilateral oophorectomy (group 2). All women in the study received a daily dose of 2mg estriol for 12 months. The study showed that this daily dose significantly relieved climacteric symptoms, such as hot flushes, sweating, insomnia and dyspareunia, in both groups of post-menopausal women within one month of starting treatment and over the remaining 9 months of the study. The level of satisfaction with the hormone therapy was also measured throughout this study with both groups of women expressing increased satisfaction as the study time increased. Histological evaluation of the endometrium (group 1), and ultrasound assessment of the breasts (both groups) after 12 months showed normal results for all women indicating that estriol appeared to be safe and effective.

Different effects of oral conjugated equine estrogen and transdermal estrogen replacement therapy on size and oxidative susceptibility of low-density lipoprotein particles in postmenopausal women.

Wakatsuki A, Okatani Y, Ikenoue N, Fukaya T.
Circulation. 2002 Oct; 106(14): 1771-6.

The aim of this study was to investigate whether transdermal estrogen hormone therapy could eliminate the adverse effects of oral estrogen on the size of low-density lipoprotein (LDL) particles in post-menopausal women who had been treated with estrogen either orally (0.625mg conjugated equine estrogen daily) or transdermally (17-β-estradiol patch – 50 µg/daily). This involved measuring the plasma concentrations of lipids, the size of LDL particles and susceptibility of LDL particles to oxidative modification. Transdermal estrogen administration was associated with a decrease in plasma concentration of triglyceride and an increase in size of LDL particles. Overall this suggests that transdermal delivery has the potential to ameliorate the adverse effects caused by oral estrogen hormone therapy on size and oxidative susceptibility of LDL particles, properties which are associated with an increased risk of coronary heart disease.

Differential effects of oral versus transdermal estrogen replacement therapy on C-reactive protein in postmenopausal women.

Vongpatanasin W, Tuncel M, Wang Z et al.
Journal of the American College of Cardiology. 2003 Apr; 41(8): 1358-63.

The aim of this study was to compare the effects of transdermal estrogen and oral estrogen on C-reactive protein (CRP) and inflammatory cytokines in a group of 21 post-menopausal women. Previous studies demonstrate that oral estrogen therapy causes a sustained increase in CRP which suggests a pro-inflammatory effect. Transdermal estradiol (100µg/day), oral conjugated estrogen (0.625mg/day) or a placebo was administered for a period of 8 weeks. Prior to and following the 8-week period, CRP, IL-1-beta, IL-6 and tumour necrosis factor-alpha, IGF-1, and a hepatic-derived anabolic peptide levels were measured. Overall, the study found that oral estrogen increased CRP levels by a first-pass hepatic effect, whereas transdermal estradiol did not. This finding is clinically significant as CRP is an independent predictor of cardiovascular events.

Contrasting Effects of Oral Versus Transdermal Estrogen on Serum Amyloid A (SAA) and High-Density Lipoprotein-SAA in Postmenopausal Women.

Abbas A, Fadel PJ, Wang Z et al.

Arteriosclerosis, Thrombosis and Vascular Biology. 2004 Oct; 24(10):e164-7

This study assessed whether the route of administration of estrogen had an effect on serum amyloid A (SAA) and the SAA content of high-density lipoprotein (HDL-SAA) levels in post-menopausal women. A group of 29 women were randomised to receive transdermal estradiol (100 µg daily), synthetic conjugated estrogen (0.625 mg daily) or a placebo for 8 weeks. There was an increase in total SAA (by 20%) and HDL-SAA (by 10%) levels in the group receiving oral estrogen. This was compared to a significant decrease by 25% in both SAA and HDL-SAA levels for the transdermal estradiol group. The placebo had no effects on these levels. These findings are clinically significant considering that elevated SAA levels interfere with the antiatherogenic, antioxidative and anti-inflammatory properties of HDL. SAA is also a precursor of amyloid fibroid which deposits in the brain of Alzheimer's disease patients. In addition, elevated SAA levels are independently associated with adverse cardiovascular events in women.

Does the route of administration for estrogen hormone therapy impact the risk of venous thromboembolism? Estradiol transdermal system versus oral estrogen-only hormone therapy.

Laliberté F, Dea K, Duh MS, Kahler KH, Rolli M, Lefebvre P. Menopause 2011;18(10): 1052-9.

The aim of this retrospective matched-cohort study was to quantify the magnitude of risk reduction for venous thromboembolism (VTE) events with transdermal estradiol therapy system (ETS) compared to oral estrogen-only hormone therapy. A total of 27,018 ETS users were matched with an equal number of oral estrogen-only users. Overall, both unadjusted and adjusted results of this study consistently indicated a significant risk reduction for VTE associated with ETS compared with oral estrogen-only therapy.

A systematic review of the effects of estrogens for symptoms suggestive of overactive bladder.

Cardozo L, Lose G, McClish D, Versi E.

Acta Obstetricia et Gynecologica Scandinavica 2004;83(10): 892-7.

This paper comprises a systematic review and meta-analysis of the effects of estrogen therapy on symptoms suggestive of overactive bladder (OAB) in post-menopausal women. The researchers identified 11 randomised trials which included a total of 430 participants; 236 individuals received estrogen therapy and 230 were placebo controls. Estrogen therapy included treatment administered systemically or locally as estriol, estradiol, conjugated estrogen, or estradiol and estriol. Overall, the researchers found that estrogen therapies were associated with statistically significant improvements in all outcomes: diurnal frequency, nocturnal frequency, urgency, number of incontinence episodes, first sensation to void, and bladder capacity. Local therapies had statistically significant benefits on all outcomes, whereas systemic therapies only caused significant improvements to incontinence episodes and first sensation to void.

Vaginal administration of estradiol: effects of dose, preparation and timing on plasma estradiol levels.

Santen RJ.

Climacteric 2015;18:121–34

In this review, Santen identified articles that assessed the use of vaginal estrogen as a local therapeutic method to manage symptoms resulting from vulvovaginal atrophy, without increasing plasma estradiol levels. Overall, low-dose vaginal estrogen was found to be effective at increasing plasma estradiol levels during chronic administration but not above the

normal range. Vaginal estrogen was also associated with systemic effects to lower plasma levels of low density lipoprotein (LDL) cholesterol and bone resorption rates.

Effects of ultralow-dose transdermal estradiol on bone mineral density: a randomized clinical trial.

Ettinger B, Ensrud KE, Wallace R, et al.
Obstet Gynecol 2004;104:443–51

This randomised, placebo-controlled, double-blind trial investigated the safety and effectiveness of unopposed, very-low-dose estradiol for preventing bone loss in a group of post-menopausal women, aged 60-80 years with intact uteri and bone mineral density (BMD) z scores of -2.0 or higher. The women were randomised to receive either 0.014mg of unopposed transdermal estradiol daily or a placebo. Both groups of women received calcium and vitamin supplementation. Lumbar spine and total hip BMD change was measured by dual-energy X-ray absorptiometry and endometrial hyperplasia incidence was assessed by endometrial biopsy. Overall, the findings showed that there was an increase in median plasma estradiol in the estradiol group compared to no change in the placebo group. A greater increase in lumbar spine BMD and an increase in mean total hip BMD for the estradiol group was observed in comparison to the placebo group. In addition, osteocalcin levels and bone-specific alkaline phosphatase were lower in the estradiol group, and endometrial hyperplasia developed in one participant from the estradiol group compared to zero in the placebo group.

Estradiol-based postmenopausal hormone therapy and risk of cardiovascular and all-cause mortality.

Mikkola TS, Tuomikoski P, Lyytinen H, et al.
Menopause 2015;22(9):976–83

The aim of this study was to evaluate the risk of death due to coronary heart disease (CHD), stroke, or any disease among female users of estradiol-based hormone therapy (HT) regimens in a nationwide study in Finland. A total of 489,105 women who used hormone therapy from 1994 to 2009 were followed. Overall, the researchers found that the risk of CHD was significantly reduced by 18-54% in HT users and this reduction was positively related to HT exposure time. The risk of stroke was reduced by 18-39% in HT users, but this reduction was not related to HT exposure time. The risk of all-cause mortality was also reduced in HT users by 12-38%, and this reduction was found to have an almost linear relationship with HT exposure time.

Hormone therapy and recurrence of venous thromboembolism among postmenopausal women.

Olie V, Plu-Bureau G, Conard J, et al.
Menopause 2011;18: 488–93

The aim of this study was to assess the impact of the route of estrogen administration on the risk of recurrent venous thromboembolism (VTE). A total of 1,023 consecutive post-menopausal women aged 45-75 years with a confirmed first VTE were studied. The researchers found that recurrent VTE occurred in 77 women, and after adjustment for potential confounders there was no significant association between the use of transdermal estrogen and recurrent VTE versus non-users. However, women in the oral estrogen group had an increased risk of recurrent VTE. The findings suggest that transdermal estrogen delivery may be safer when considering risk of VTE.

Improvement of skin surface texture by topical estradiol treatment in climacteric women.

Masuda Y, Hirao T, Mizunuma H.
J Dermatol Treat 2013;24:312–17

The aim of this study was to determine the effect of topical estradiol hormone replacement therapy on skin surface texture, a major determinant of skin appearance. Estradiol was administered as a daily 1.08mg gel to the upper limbs of menopausal or ovariectomised women for a period of 8 weeks, followed by a lower-dose estradiol 0.54 mg or placebo gel applied for a further 16 weeks. Overall, the study found that there was an increase in fineness of texture by topical HRT observed not only in the forearm, where estradiol was applied, but also in the cheek. This finding suggests that topical HRT can improve the age-associated decline of fineness of skin surface texture.

Estriol: emerging clinical benefits

Emad S Ali, Cheyenne Mangold, Alan N Peiris
Menopause 2017 Sep;24(9):1081-1085

Estriol is the main estrogen in pregnancy, but has received less attention outside gestation. It is well known that pregnancy has an immunosuppressive effect on many autoimmune diseases such as multiple sclerosis, psoriasis, thyroiditis, uveitis, and rheumatoid arthritis. Emerging evidence indicates that estriol has potential immunomodulatory benefits for many disease states including autoimmune, inflammatory, and neurodegenerative conditions. In this review, we discuss emerging roles for estriol in the treatment of menopausal symptoms, osteoporosis, cancer, hyperlipidemia, vascular disease, and multiple sclerosis. Estriol appears to offer a potentially cost-effective approach to a variety of conditions and may offer a wide range of health benefits.