

ment (HT) in a group of women with diabetes mellitus type II (DM) on menopause compared with nondiabetic patients.

**Methods:** The analysis included 163 women - 94 without HT (22 DM), and 69 with HT (16 DM), followed-up for two years. The descriptive data were socio-demographic, BMI, dietary habits, alcohol consumption, smoking, menopause symptoms before and after HT, with or without HT. Lab tests were assessed every 6 months combined with a physical exam. HT was estradiol transdermal with dydrogesterone (12 days monthly).

**Results:** Symptoms were similar for DM and nonDM, but in DM patients the urogenital problems were significant higher. The BMI decreased, significantly under HT in the DM vs controls. Triglyceridemia decreased significantly in the DM group. The results were maintained till the end of the 2 years follow-up. HDL-Cholesterol increased at 6 month of treatment in HT, mostly for the DM patients. LDL-Cholesterol and total Cholesterol levels were lower in the HT patients. Glycemia levels decreased under HT in DM patients, and during the follow-up no patient with DM under HT changed on insulin therapy. QoL significant improved under HT for DM and nonDM and maintained during follow-up.

**Conclusions:** HT has positive effects on lipid and glycemic metabolism, mostly for DM patients. Transdermal HT had beneficial effects in DM. The key points of the good results of HT in menopause are strict controlled indications, follow-up, individualization of the dose and natural HT.

**Keywords:** Menopause, diabetes mellitus, HT.

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### HORMONE THERAPY SELF-USE VERSUS PRESCRIPTION PRACTICES OF AMERICAN GYNECOLOGISTS SUBSEQUENT TO THE WOMEN'S HEALTH INITIATIVE STUDY

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**Objectives:** The results of the Women's Health Initiative (WHI) study of postmenopausal women randomized to HT (conjugated equine estrogens plus medroxyprogesterone acetate) or placebo challenged decades of earlier observational findings, leading to a dramatic decline in the number of HT prescriptions. However, subsequent studies in Europe have shown while this is true, self-use of HT in obstetrician-gynecologists and their female partners has remained essentially unchanged. We wished to investigate HT self-use versus HT prescription practices of obstetrician-gynecologists (and their female partners) in New York City.

**Methods:** All 1,797 board-certified obstetrician-gynecologists in New York City were sent a questionnaire concerning attitudes, management strategies, and use of HT.

**Results:** Two hundred seven questionnaires were returned, with 206 questionnaires containing valid data. The majority of physicians (81%; 166/206) had difficulty assessing the advantages and disadvantages of hormone therapy. Sixty percent (122/202) agreed that HT increases the risk of breast cancer, 55% (112/202) agreed that HT does not protect against primary myocardial infarction, and 37% (75/203) agreed that HT does not prevent Alzheimer's dementia. Nearly three quarters of physicians and their female partners (74%; 67/91) who are postmenopausal or who are experiencing menopausal symptoms are currently or have used HT.

**Conclusions:** Obstetrician-gynecologists in New York City are more likely to use HT for themselves than to prescribe it.

**Keywords:** Hormone therapy, self use, obstetrician-gynecologists

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### EFFICACY OF 1 MG ESTRADIOL AND 2 MG DROSPIRENONE IN CLINICAL SYMPTOMS OF MENOPAUSE AND SEXUAL ACTIVITY AT POSTMENOPAUSAL WOMEN

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**Objectives:** In our study we are proved the efficacy of 1 mg Estradiol and 2 mg Drospirenone (Angeliq<sup>®</sup>) for menopausal symptoms and increases sexual act frequency.

**Methods:** Forty-two postmenopausal women were randomized into two treatment groups. 1<sup>o</sup>. thirty-one women treated with 1 mg Estradiol + 2

mg Drospirenone (E<sub>2</sub>/DRSP); 2<sup>o</sup>. eleven women treated with 1 mg Estradiol + 5 mg dydrogesterone (E<sub>2</sub>/DGS). The period of treatment was six months. The efficacy parameters were the individual relative change of that flushes, sweating episodes, sleep problems, nervousness, breast tenderness, sexual activity. Mean age of women was 50.2±5.5 years for E<sub>2</sub>/DRSP vs 53.7±0.5 years for E<sub>2</sub>/DGS. Time since menopause was 3.8±3.7 years for the first group and 5.2±3.0 years for the second. The weight mean was 65.5±1.5 kg vs 71.1±1.5 kg.

**Results:** The mean number of hot flushes per day, sweating episodes and sleep disturbances decreased by 100% under E<sub>2</sub>/DRSP vs 83% under E<sub>2</sub>/DGS. Breast tenderness decreased by 66% only in first group. The mean weight loss was at 8.9 kg under E<sub>2</sub>/DRSP vs 2.8 kg under E<sub>2</sub>/DGS. The positive effect (40%) in sexual activity was probably the result of a reduction of vaginal dryness in the both groups.

**Conclusions:** E<sub>2</sub>/DRSP (Angeliq<sup>®</sup>) was efficacious in the treatment of climacteric symptoms and improved the sexual activity. The good results were obtained in breast tenderness and loss body weight can be explained by drospirenone, a progestine who has potent antiminerlocorticoid activity.

**Keywords:** Menopause, estradiol, drospirenone.

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### HORMONE THERAPY IN RECENT POSTMENOPAUSAL WOMEN: IMPACT OF THE ROUTE AND DOSE OF ADMINISTRATION ON CARDIOVASCULAR RISK FACTORS

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**Objective:** To evaluate the effects of low-dose oral hormone therapy (HT) or non-oral HT on C-reactive protein (CRP) levels, fibrinogen, endothelin-1 and von Willebrand factor and on conventional risk factors in early postmenopausal early women. CRP levels were stratified as low (< 1 mg/L), intermediate (1.0 to 3.0 mg/L) and high cardiovascular (CV) risk (>3.0 mg/L).

**Methods:** Cross-over, randomized clinical trial. Twenty patients received oral estradiol 1 mg and drospirenone 2 mg for 2 months. Another group of 20 patients received 3 mg/day intranasal estradiol and then 200 mg/day vaginal micronized progesterone for 14 days/month for 2 months. At the end of this period, the patients were crossed over for another 2 months. Laboratory evaluations were performed before and during HT.

**Results:** Before treatment 8 (20%), 17 (42.5%) and 15 (37.5%) patients presented low, intermediate and high CV risk according to CRP. While the CV risk, estimated by CRP values, remain unchanged after low-dose oral HT (p=0.4), a significant reduction was found after non-oral HT, in comparison to low-dose oral HT (p=0.037). Total cholesterol and LDL-cholesterol decreased below basal levels in both treatment groups. Triglycerides and Von Willebrand factor decreased significantly only with non-oral treatment. Endothelin-1 and fibrinogen were unchanged with both treatments.

**Conclusion:** Neither treatment induced deleterious effects in the short term on variables related to cardiovascular risk in early postmenopausal women. Further studies of longer duration will be helpful to confirm our findings.

**Keywords:** Menopause; cardiovascular risk; hormone therapy; C-reactive protein.

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### EFFICACY OF TESTOSTERONE THERAPY DELIVERED BY PELLET IMPLANT

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**Objectives:** Determine the efficacy of testosterone therapy delivered by pellet implant in pre and post menopausal females.

**Methods:** As part of a long term IRB approved study on the affect of testosterone pellet implants on the incidence of breast cancer (Dimitrakakis, Glaser) 156 newly enrolled patients were asked to complete a validated

survey, Menopause Rating Scale (MRS), at baseline and after testosterone pellet implant (dose 100-150 mg). Vaginal estrogen-progesterone use was allowed. No systemic estrogen therapy was used.

**Results:** Statistically significant improvement (Wilcoxon test for paired samples, p value <0.0001) was seen in all symptom categories:

- Hot flashes, sweating
- Heart discomfort (heart skipping, racing, tightness)
- Sleep problems (difficulty falling asleep, waking)
- Depressive mood, feeling sad, down, lack of drive, mood swings
- Irritability, feeling nervous, inner tension, feeling aggressive
- Anxiety, inner restlessness, feeling panicky
- Physical exhaustion, decrease in performance
- Mental exhaustion, impaired memory, decrease in concentration, forgetfulness
- Sexual problems, (change in desire, activity and satisfaction)
- Bladder problems (difficulty urinating, frequency, bladder incontinence)
- Dryness of vagina (burning, difficulty with intercourse)
- Joint and muscular discomfort (pain in joints, rheumatoid complaints)

**Conclusions:** Testosterone therapy alone, delivered by pellet implant, is effective in relieving symptoms and improving quality of life in pre-menopausal and menopausal patients. Testosterones' protective affect on breast tissue is an additional benefit to be considered.

**Keywords:** Testosterone, implant, symptoms, pre-menopause, menopause, hormone therapy.

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**ANALYSIS OF HORMONE THERAPY PRESCRIPTION RATES BEFORE AND AFTER THE WHI STUDY USING CLAIMS DATA OF A GERMAN SICKNESS FUND**

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**Objectives:** International figures suggest that the application of hormones has considerably decreased since the publication of the WHI study. The aim of our analysis was to clarify if and how prescription rates have changed in Germany.

**Methods:** In a longitudinal retrospective cohort study using Statutory Health Insurance claims data of 1.5 million beneficiaries, the prescription of hormones among menopausal women was investigated.

**Results:** 134,683 women (mean age 54 years) who were continuously enrolled from 2000 until 2005 could be identified. 38,897 (29%) received in the observation period at least one prescription of a drug approved for hormone therapy (HT). The comparison of women who received prescriptions only before the publication of the WHI study (01/2000 till 07/2002) with women who received HT after WHI (02/2003 till 12/2005) shows a decrease in the number of women treated with hormones by a total of 18.9%. The analysis of incident HT resulted in a decrease in the number of women with prescriptions from n=480 to n=157 p.a., corresponding to 67.3%. Related to the study population (n=38,897) this equals a relative decrease of 0.9%.

**Conclusions:** Although the number of HT prescriptions has decreased in the observation period, after the WHI study in Germany a considerable number of hormone treatments is still undertaken or commenced.

**Acknowledgement:** This study was supported by the BMBF (German Federal Ministry of Education and Research) and accomplished in co-operation with the Robert Koch Institute, Berlin, and the Charité - Universitätsmedizin Berlin.

**Keywords:** Hormone replacement therapy, utilisation, drug prescription, claims data.

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**ADEQUATE TREATMENT DURATION TO ASSESS LONG-TERM EFFICACY OF NON-HORMONAL HOT FLASH THERAPIES**

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**Objective:** To determine if there was evidence to support a minimum duration of placebo-controlled treatment in order to reasonably assess

a non-hormonal compound's long-term efficacy in the treatment of hot flashes.

**Methods:** An electronic database search of MEDLINE, Web of Science, and PsycINFO was performed to identify "target studies" showing a non-hormonal hot flash therapy to be effective at early time points only to become ineffective at later time points (i.e., showing short-term but not long-term efficacy).

**Results:** Three target studies were identified. The compounds Bellergal Retard, soy, and venlafaxine showed time points of 2, 6, and 7 weeks, respectively, when they last demonstrated efficacy before subsequently losing efficacy in a randomized controlled trial (RCT).

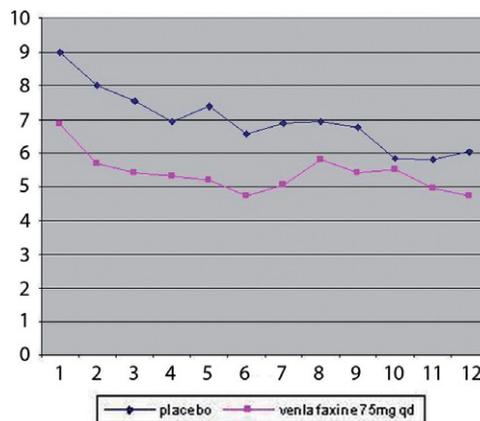


Fig. 1. Daily hot flash frequency by treatment group for venlafaxine. Mean -2.0 treatment effects over first 7 weeks (p=0.05); Mean -1.2 treatment effects over last 5 weeks (p=0.46); Interaction between time and treatment effect (p=0.00516)\*\*.

\*Evans et al., *Obstet Gynecol* 2005;105:161-6.

\*\*Personal communication, Eric Vittinghoff, PhD, University of California, San Francisco.

Daily hot flash frequency treatment effects during final treatment week for non-hormonal therapies studied for at least 8 weeks

Study component (n for treatment + placebo group)	Study treatment length	Treatment effect (Placebo effect - drug effect)	p-value
Gabapentin 300mg tid (n=59) <sup>1</sup>	12 weeks	-1.84	=0.02
Gabapentin 300mg tid (n=281) <sup>2</sup>	8 weeks	-2.10	<0.0001
Oxybutynin ER 15mg qd (n=148) <sup>3</sup>	12 weeks	-3.80	<0.001
Desvenlafaxine 100mg qd (n=222) <sup>4</sup>	12 weeks	-1.56	=0.016

<sup>1</sup>Guttuso T, Jr., et al. *Obstet Gynecol* 2003;101:337-45.

<sup>2</sup>Pandya KJ, et al. *Lancet* 2005;366:818-24.

<sup>3</sup>Simon JA, et al. *Obstet Gynecol* 2007;109:76S.

<sup>4</sup>Speroff L, et al. *Obstet Gynecol* 2008;111:77-87.

**Conclusion:** This analysis supports hot flash RCT treatment duration of at least 8 weeks in order to adequately assess a non-hormonal compound's long-term efficacy. Because this effect was observed among 3 mechanistically unrelated compounds, the minimum 8 week time period is unlikely related to any particular class of therapy and more likely applicable to non-hormonal hot flash therapies, in general.

**Keywords:** Hot flash, clinical trial, methodology, non-hormonal.

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**THE REDUCTION OF BLOOD PRESSURE IN POSTMENOPAUSAL WOMEN USING HRT CONTAINING DROSPIRENONE AND DYDROGESTERONE**

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**Objectives:** This study is to evaluate the effects of Angeliq on blood pressure in postmenopausal Malaysian women within the period of 6 months in comparison with another continuous combined hormone replacement therapy (Femoston-Conti) Significant change in blood pressure was defined as a difference of ±5mmHg.

**Methods:** This randomized control trial involved 40 postmenopausal patients recruited and randomized to receive either HRT containing drospirenone (Angeliq) or dydrogesterone (Femoston-Conti). After a rest of an hour, blood pressure, weight and height measurements were carried