ORIGINAL RESEARCH

Effect of Intravaginal Prasterone on Sexual Dysfunction in Postmenopausal Women with Vulvovaginal Atrophy

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ABSTRACT

Introduction. Previous data have shown that intravaginal dehydroepiandrosterone (DHEA, prasterone) improved all the domains of sexual function, an effect most likely related to the local formation of androgens from DHEA.
Aims. To confirm in a placebo-controlled, prospective, double-blind and randomized study the benefits of daily intravaginal DHEA for 12 weeks on sexual function using the Female Sexual Function Index (FSFI) questionnaire.
Methods. Placebo was administered daily to 157 women while 325 women received 0.50% (6.5 mg) DHEA daily for 12 weeks. All women were postmenopausal meeting the criteria of vulvovaginal atrophy (VVA), namely moderate to severe dyspareunia as their most bothersome symptom of VVA in addition to having ≤5% of vaginal superficial cells and vaginal pH > 5.0. The FSFI questionnaire was filled at baseline (screening and day 1), 6 weeks and 12 weeks. Comparison between DHEA and placebo of the changes from baseline to 12 weeks was made using the analysis of covariance test, with treatment group as the main factor and baseline value as the covariate.
Main Outcome Measures. The six domains and total score of the FSFI questionnaire were evaluated.
Results. The FSFI domain desire increased over placebo by 0.24 unit (+49.0%, $P = 0.0105$), arousal by 0.42 unit (+56.8%, $P = 0.0022$), lubrication by 0.57 unit (+36.1%, $P = 0.0005$), orgasm by 0.32 unit (+33.0%, $P = 0.047$), satisfaction by 0.44 unit (+48.3%, $P = 0.0012$), and pain at sexual activity by 0.62 unit (+39.2%, $P = 0.001$). The total FSFI score, on the other hand, has shown a superiority of 2.59 units in the DHEA group over placebo or a 41.3% greater change than placebo ($P = 0.0006$ over placebo).
Conclusion. The present data show that all the six domains of the FSFI are improved over placebo (from $P = 0.047$ to 0.0005), thus confirming the previously observed benefits of intravaginal DHEA on female sexual dysfunction by an action exerted exclusively at the level of the vagina, in the absence of biologically significant changes of serum steroids levels. **Fernand Labrie, Leonard Derogatis, David F. Archer, William Koltun, Andrée Vachon, Douglas Young, Louise Frenette, David Portman, Marlene Montesino, Isabelle Côté, Julie Parent, Lyne Lavoie, Adam Beauregard, Céline Martel, Mario Vaillancourt, John Balser, Érick Moyneur, and Members of the VVA Prasterone Research Group. Effect of Intravaginal Prasterone on Sexual Dysfunction in Postmenopausal Women with Vulvovaginal Atrophy. J Sex Med 2015;12:2401–2412.**

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Key Words. Dehydroepiandrosterone (DHEA); Female Sexual Dysfunction; Desire; Arousal; Female Sexual Function Index (FSFI); Postmenopause; Androgens; Intracrinology; Prasterone

Introduction

Menopause is accompanied by a progressive decrease in sex steroid availability secondary to an age-related decline in serum DHEA, a change which starts at the age of 30 years with an average 60% loss already observed at time of menopause [1]. Most importantly, at menopause, following cessation of estrogen secretion by the ovaries, DHEA becomes the exclusive, but highly variable source of sex steroids while serum estradiol remains at biologically inactive concentrations below the 95th centile of 9.3 pg/mL [2–5].

Sexual dysfunction is a common problem with rates of up to 50% self-reported among women in community studies [6–8]. In the United States, it has been observed that 43% of women have sexual dysfunction of one type or another. The prevalence of sexual dysfunction increases after ovariectomy and with age [9,10] with a higher incidence in postmenopausal women [11–14].

Recent data have indicated the benefits of the local intravaginal action of DHEA on all domains of sexual dysfunction [15,16], while the symptoms of vaginal atrophy were also improved [17]. While it is recognized that estrogens improve the vaginal atrophy symptoms by an action in the most superficial layer of the vagina, intravaginal DHEA improves both vaginal atrophy [17–20] and sexual dysfunction [15,16].

It was then observed that the benefits of intravaginal prasterone on the different domains of sexual dysfunction evaluated by the menopause-specific quality of life (MENQOL) and abbreviated sexual function (ASF) questionnaires are the same in the presence and absence of dyspareunia [16]. It thus appears reasonable to suggest that vulvovaginal atrophy and sexual dysfunction (called VVSD, vulvovaginal sexual dysfunction) are two separate medical entities, which are independently controlled by the sex steroids made locally in the vagina from the precursor DHEA of either endogenous or exogenous origin. An extension of VVA including genitourinary symptoms is referred to the genitourinary syndrome of menopause [21] or midlife gynecological symptoms (Labrie, unpublished data).

Aims

The present data were obtained from a placebo-controlled, randomized, double-blind and prospective clinical trial (ERC–238) where 482 postmenopausal women (intent-to-treat [ITT] population; placebo: N = 157 and 0.50% DHEA: N = 325) having classical VVA symptomatology at baseline have filled the Female Sexual Function Index (FSFI) questionnaire at screening, day 1, week 6 and week 12. Considering the well-recognized value of the FSFI to assess various aspects of sexual dysfunction, the FSFI was evaluated as a secondary objective in study ERC–238 in order to confirm our previous positive data on sexual dysfunction observed after intravaginal DHEA based upon the less often utilized MENQOL and ASF questionnaires [15,16].

Methods

Study ERC–238 was a phase III, placebo-controlled, double-blind, prospective and randomized study (NCT02013544, https://clinicaltrials.gov) to confirm, as primary objective, the efficacy of daily intravaginal administration of 0.50% (6.5 mg) DHEA ovules (suppositories) for 12 weeks on moderate to severe (MS) pain at sexual activity as most bothersome symptom (MBS) of VVA as evaluated by a questionnaire and to evaluate, as secondary objective, the benefits on sexual dysfunction. Women were randomized in a 2:1 ratio between the 0.50% (6.5 mg) DHEA (prasterone) and placebo groups [22].

Independent Ethics Committee or Institutional Review Board (IRB)

The protocol was approved by the IRB Services (Central IRB) for all investigational sites except for the Eastern Virginia Medical School, Department of Obstetrics and Gynecology, Clinical Research Center where a local IRB gave approval before the start of the study.

Informed Consent

A written informed consent was obtained from all subjects prior to the performance of any study-related procedure.