Effect of intravaginal dehydroepiandrosterone (Prasterone) on libido and sexual dysfunction in postmenopausal women

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Abstract
Objective: The objective of this study was to provide evidence that the transformation of DHEA into both androgens and/or estrogens locally in cells of the three layers of the vagina (epithelium, lamina propria, and muscularis) would have effects of greater impact, including effects on sexual function, than only effects on superficial epithelial cells as achieved with estrogens.

Methods: This prospective, randomized, double-blind, and placebo-controlled phase III clinical trial has evaluated the effect of daily local intravaginal application of Prasterone (dehydroepiandrosterone; DHEA) for 12 weeks on the domains of sexual dysfunction, namely, desire/interest, arousal, orgasm, and pain at sexual activity, in 216 postmenopausal women with moderate to severe symptoms of vaginal atrophy.

Results: A time- and dose-dependent improvement of the four domains of sexual function was observed. At the 12-week time interval, the 1.0% DHEA dose led, compared with placebo, to 49% ($P = 0.0061$) and 23% ($P = 0.0257$) improvements of the desire domains in the Menopause Specific Quality of Life and Abbreviated Sex Function questionnaires, respectively. Compared with placebo, the Abbreviated Sex Function arousal/sensation domain was improved by 68% ($P = 0.006$), the arousal/lubrication domain by 39% ($P = 0.0014$), orgasm by 75% ($P = 0.047$), and dryness during intercourse by 57% ($P = 0.0001$).

Conclusions: By a local action in the vagina, DHEA applied daily at doses at which serum steroids remain well within normal postmenopausal values exerts relatively potent beneficial effects on all four aspects of sexual dysfunction. Such data indicate that combined androgenic/estrogenic stimulation in the three layers of the vagina exerts important beneficial effects on sexual function in women without systemic action on the brain and other extravaginal tissues.

Key Words: Dehydroepiandrosterone – Prasterone – Libido – Sexual dysfunction – Postmenopause.

Sexual dysfunction, especially low libido, is a common problem with rates of up to 50% self-reported among women in community studies using questionnaires.1,3 In the United States, it has been observed that 43% of women have sexual dysfunction of one type or another.5 More recently, it has been found that more than 40% of women reported sexual problems, with 25% having sexual dysfunction.5 Overall, in another study, approximately 42% of women complained of one or more sexual problems compared with 30% of men.7 The prevalence increases after oophorectomy and with age.5,8 As indicated in the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (1994) of the American Psychiatric Association,9 the general categories of female sexual dysfunction (FSD) include desire disorders (hypoactive sexual desire disorder), arousal disorders, orgasmic disorders, and sexual pain disorders. These disorders can occur individually or in any combination. The common problem of sexual dysfunction is believed to be a composite of biological, psychological, and interpersonal components.10 Although psychological factors are believed to play an important role in the loss of sexual desire/interest and arousal, many studies have reported a beneficial effect of androgens.
on sexual function in women.\textsuperscript{11-20} These observations have resulted in an increased use of testosterone for this indication,\textsuperscript{21,22} although some controversy about the efficacy of androgens on sexual dysfunction still persists.\textsuperscript{23,24}

Persistent controversial data relate to the search for a potential correlation between desire and serum testosterone in healthy women.\textsuperscript{25-27} In fact, most studies have found no correlation between serum testosterone and arousal.\textsuperscript{26} It is important to indicate that this lack of correlation can be fully explained by the finding that serum testosterone is clearly not a valid parameter of androgenic activity in women.\textsuperscript{28}

The finding that women make approximately 50% as much androgens as men has important implications for the design of the most appropriate hormone therapy for women at menopause and postmenopause. This issue is particularly important because approximately 60% of the androgens present at the age of 30 years in women are already lost at time of menopause in parallel with the decrease in serum dehydroepiandrosterone (DHEA; Prasterone).\textsuperscript{28,29}

The important clinical health issues facing women at menopause pertain to vaginal atrophy, hot flashes, bone loss, loss of muscle mass and strength, fat accumulation, and type 2 diabetes. It is of particular interest that all these medical problems have been found to respond positively to androgens and, in most cases, to the administration of DHEA when used at the proper dose and appropriate experimental conditions\textsuperscript{14,30-32} (see review of Labrie\textsuperscript{33}).

Considering the clinical evidence mentioned above strongly suggesting a role of androgens in sexual dysfunction\textsuperscript{1-20} and our recent preclinical findings of beneficial effects of DHEA in the three layers of the vagina,\textsuperscript{34} it seemed particularly important to study the effect of DHEA applied locally in the vagina on the various domains of sexual dysfunction. Such a study would also provide evidence for the relative role played by the brain and the genital organs in the four domains of defective sexual function, namely, desire/interest, arousal, orgasm, and pain at sexual activity. It is important to indicate that intravaginal or systemic administration of estrogens has not been found to have significant effects on libido and coital frequency.\textsuperscript{15,35,36}

The changes in the sexual dysfunction parameters (desire/interest, arousal, orgasm, and pain at sexual activity) were analyzed at screening, at day 1, and at weeks 4, 8, and 12 in 216 postmenopausal women who have vaginal trophy and are randomly treated daily with 0% (placebo), 0.25%, 0.5%, and 1.0% DHEA intravaginal ovules. The validated questionnaires used were the Abbreviated Sexual Function (ASF)\textsuperscript{37,38} and the Menopause-Specific Quality of Life (MENQOL)\textsuperscript{39} questionnaires. Quality of life was evaluated with the Psychological General Well Being (PGWB) questionnaire.\textsuperscript{40}

**METHODS**

This study was a phase III, prospective, multicenter, randomized, placebo-controlled, and double-blind trial planned for 50 participants per arm (for a total of 200 participants to complete the study). Two hundred eighteen postmenopausal women (216 women in the intent-to-treat [ITT] analysis) were thus randomized to receive a daily ovule of the following DHEA concentrations: 0.0% (53 women), 0.25% (3.25 mg DHEA; 53 women), 0.5% (6.5 mg DHEA; 56 women), or 1.0% (13 mg DHEA; 54 women) applied intravaginally with an applicator at bedtime and were part of the ITT analysis. The median range age of women was 58 (49-70), 57 (42-72), 58 (50-74), and 59 (46-69) years in the four groups. The DHEA ovules or suppositories containing Prasterone in a lipophilic base were manufactured by Recipharm (Karlskoga, Sweden). The study was divided into two phases, namely, the screening phase where all the required tests were done to make sure that all inclusion and exclusion criteria were met, followed by the treatment phase of 12 weeks. The protocol was approved by the institutional review board of the Centre Hospitalier de l’Université Laval, Quebec City, QC, Canada; McGill University, Montreal, QC, Canada; Ethica, Montreal, QC, Canada; Eastern Virginia Medical School, Norfolk, VA; and the Western Institutional Review Board, Los Angeles, CA.

Inclusion/exclusion criteria were described in detail in an accompanying article.\textsuperscript{41} The main inclusion criteria were the following:

- Postmenopausal women
- Women having self-identified at least one moderate to severe of the following symptoms
  - Vaginal dryness (none, mild, moderate, or severe)
  - Vaginal and/or vulvar irritation/itching (none, mild, moderate, or severe)
  - Vaginal pain associated with sexual activity (none, mild, moderate, or severe)

The main exclusion criteria were the following:

- Undiagnosed abnormal genital bleeding
- Previous diagnosis of cancer, except skin cancer (non-melanoma)
- Endometrial hyperplasia at biopsy performed at screening or endometrial cancer
- Use of estrogen-alone injectable drug therapy or progestin implant within 3 months before study entry (screening visit)
- Use of estrogen pellet or progestin injectable drug within 6 months before study entry (screening visit)
- Use of oral estrogen, progestin, or DHEA exposure or intruterine progestin therapy in the 8 weeks before baseline assessments (screening visit)
- Use of vaginal hormonal products (rings, creams, or gels) or transdermal estrogen alone or estrogen/progestin products in the 4 weeks before baseline assessments (screening visit)

**Informed consent**

Written informed consent was obtained from all participants before the performance of any study-related procedure. The participants had a medical history, a medical examination, and a complete gynecological examination (including...
women were asked, as a secondary objective, to answer questionnaires related to libido, sexual function, and quality of life at postmenopause. At screening, at day 1, and at weeks 4, 8, and 12, the ASF, the MENQOL, the SC, and the PGWB questionnaires were completed.

Of 171 women who reported one of the three symptoms of vaginal atrophy, namely, vaginal dryness, irritation/itching, and vaginal pain at sexual activity, as being severe, most women (110; 64%) indicated vaginal pain at sexual activity, whereas 48 (28%) and 13 (8%) reported vaginal dryness and irritation/itching, respectively.

Because vaginal pain is most closely associated with loss of libido and sexual dysfunction, it is of major interest to see that at the standard 12-week interval, treatment with 0.25% DHEA decreased the score of the sexual domain of the MENQOL questionnaire by 2.85 ± 0.282 (P = 0.0001 vs placebo). On the other hand, decreases of 1.92 ± 0.289 (P = 0.0036 vs placebo) and 2.50 ± 0.267 (P < 0.0001 vs placebo) were achieved with the 0.5% and 1.0% DHEA doses, respectively (Fig. 1). In fact, the sexual domain score was improved at 12 weeks by 54%, 43%, and 53% with the three increasing doses of DHEA, whereas the placebo effect was 32%.

The three questions covered by the sexual domain of MENQOL are change in your sexual desire, vaginal dryness during intercourse, and avoiding intimacy. The question most directly related to libido, namely, sexual desire, was improved by 55% (P < 0.0001 vs baseline), 32% (P = 0.0006 vs baseline), and 49% (P < 0.0001 vs baseline) in the 0.25%, 0.5%, and 1.0% DHEA groups, respectively. The placebo effect was a reduction of 23% (P = 0.0187 vs baseline; Fig. 2).

As can be seen in Fig. 3, the score “avoiding intimacy” decreased by 46% (P = 0.105 vs placebo), 53% (P = 0.043 vs placebo), and 51% (P = 0.0056 vs placebo) for the 0.25%, 0.5%, and 1.0% DHEA doses, respectively, whereas a decrease of 26% from baseline was observed in the placebo group (P = 0.0079 vs baseline; Fig. 3).
The third question of the sexual domain of the MENQOL questionnaire is vaginal dryness during intercourse. As can be seen in Fig. 4, treatment with the 0.25%, 0.5%, and 1.0% DHEA doses led, at 12 weeks, to 58% \((P = 0.0001\text{ vs placebo})\), 53% \((P = 0.0042\text{ vs placebo})\), and 57% \((P = 0.0001\text{ vs placebo})\) decreases in the severity score of vaginal dryness at intercourse, whereas the placebo effect was 28% \((P = 0.0003\text{ vs baseline})\).

Although no significant effect was noticed on the psychological and physical domains of MENQOL, the particularly strong effect described above on the sexual domain (Fig. 1) led to a significant effect on the global MENQOL score (Fig. 5). The MENQOL summary (total) score decreased at 12 weeks by 0.28 ± 0.13 (9.5%; \(P = 0.03\text{ vs baseline}\)), 0.83 ± 0.131 (27%) in the 0.25% group \((P = 0.001\text{ vs placebo})\), 0.48 ± 0.096 (17.5%) in the 0.5% DHEA group \((P = 0.07\text{ vs placebo})\), and 0.64 ± 0.103 (21%) in the 1.0% DHEA group \((P = 0.03\text{ vs placebo};\ Fig. 5)\).

An important questionnaire related to libido and sexual dysfunction is the ASF questionnaire. When the data of this questionnaire were analyzed, it was found that although placebo had no significant effect on the domain desire, the 0.25% DHEA dose improved the score by 3.40 ± 0.786 \((P = 0.034\text{ vs placebo};\ Fig. 6)\), whereas the increase in the 0.5% DHEA group did not reach statistical significance, and treatment with the 1.0% DHEA ovules increased the desire score at 12 weeks by 23% \((P = 0.0257\text{ vs placebo})\).

When the arousal/sensation domain was examined at the standard 12-week time interval, a highly significant effect of the three DHEA doses was observed versus baseline with \(P\) values equal to 0.0004 and less than 0.0001, whereas placebo has no significant effect \((P = 0.56;\ Fig. 7)\). At 12 weeks, a
statistically significant difference from placebo was observed with the 1.0% DHEA dose ($P = 0.006$ vs placebo; Fig. 7). Even greater beneficial effects were also observed at 12 weeks on the domain arousal-lubrication, with improvements of 169% ($P < 0.0001$ vs baseline), 162% ($P < 0.0001$ vs baseline), and 139% ($P < 0.0001$ vs baseline), whereas the placebo effect was 49% ($P = 0.02$; Fig. 7). At 12 weeks, all three doses have shown a statistically significant difference from placebo.

With this test, at the standard 12-week interval, the score increased by $2.13 \pm 0.352$ ($P = 0.0325$ vs placebo) in the women treated with 0.25% DHEA (Fig. 8). For the women treated with 0.5% DHEA, the score increased by $2.25 \pm 0.31$ ($P = 0.0146$ vs placebo), whereas an increase of $2.62 \pm 0.37$ ($P = 0.0014$ vs placebo) was observed in the group of women treated with 1.0% DHEA.

For the orgasm domain of the ASF questionnaire, at the 12-week time interval, as can be seen in Fig. 9, improvements of $1.88 \pm 0.628$ (NS vs placebo) from $2.87 \pm 0.502$ to $4.86 \pm 0.69$ ($P = 0.047$ vs placebo) were observed for the groups treated with the 0.25%, 0.5%, and 1.0% DHEA doses, respectively. The changes observed from baseline were $65\%$ ($P = 0.004$), $56\%$ ($P = 0.001$), and $75\%$ ($P < 0.0001$) for the three increasing doses of DHEA, whereas the placebo effect was $31\%$ ($P = 0.096$).

FIG. 6. Effect of daily intravaginal application of 0.0%, 0.25%, 0.5%, and 1.0% dehydroepiandrosterone (DHEA; Prasterone) for 4, 8, and 12 weeks on the score of the desire domain of the Abbreviated Sexual Function questionnaire in postmenopausal women. Data are expressed as means ± SEM; the P values are comparisons with placebo at all time intervals except for the placebo group at 12 weeks, which is compared with baseline.

FIG. 7. Effect of daily intravaginal application of 0.0%, 0.25%, 0.5%, and 1.0% dehydroepiandrosterone (DHEA; Prasterone) for 4, 8, and 12 weeks on the score of the arousal-sensation domain of the Abbreviated Sexual Function questionnaire in postmenopausal women. Data are expressed as means ± SEM; the P values are comparisons with placebo at all time intervals except for the placebo group at 12 weeks, which is compared with baseline.

FIG. 8. Effect of daily intravaginal application of 0.0%, 0.25%, 0.5%, and 1.0% dehydroepiandrosterone (DHEA; Prasterone) for 4, 8, and 12 weeks on the score of the arousal-lubrication domain of the Abbreviated Sexual Function questionnaire in postmenopausal women. Data are expressed as means ± SEM; the P values are comparisons with placebo at all time intervals except for the placebo group at 12 weeks, which is compared with baseline.

FIG. 9. Effect of daily intravaginal application of 0.0%, 0.25%, 0.5%, and 1.0% dehydroepiandrosterone (DHEA; Prasterone) for 4, 8, and 12 weeks on the score of the orgasm domain of the Abbreviated Sexual Function questionnaire in postmenopausal women. Data are expressed as means ± SEM; the P values are comparisons with placebo at all time intervals except for the placebo group at 12 weeks, which is compared with baseline.
The three questions of the orgasm domain were the following: “Over the last 4 weeks, how often did you have an orgasm when you took part in sexual activity (may be with or without a partner)?”, “Over the last 4 weeks, in general, how pleasurable were the orgasms that you had?” and “Over the last 4 weeks, in general, how easy was it for you to reach orgasm?”

As can be seen in Fig. 10, the 0.25%, 0.5%, and 1.0% doses of DHEA improved the summary score of the ASF questionnaire at 12 weeks compared with baseline by 55%, 42%, and 50% (all \( P < 0.0001 \) vs baseline and \( P = 0.0508, 0.0879, \) and 0.0043 vs placebo).

Concerning the more general PGWB, the summary score increased from day 1 to 12 weeks by 0.67 ± 1.936 (1%; \( P = 0.73 \) vs baseline) in the 0% DHEA (placebo) group, 7.40 ± 1.69 (9.3%; \( P < 0.0001 \) vs baseline) in the 0.25% DHEA group, 2.92 ± 1.54 (3.5%; \( P = 0.064 \) vs baseline) in the 0.5% DHEA group, and 3.06 ± 1.909 (3.9%; \( P = 0.115 \) vs baseline) in the 1.0% DHEA group.

When the six domains of the PGWB questionnaire are looked at individually, the positive well-being domain at 12 weeks improved by 1.56 ± 0.37 (12%; \( P = 0.0001 \) vs baseline) in the 0.25% DHEA group, 0.73 ± 0.341 (5.4%; \( P = 0.04 \) vs baseline) in the 0.5% DHEA group, and 0.61 ± 0.397 (4.6%; \( P = 0.013 \) vs baseline) in the 1.0% DHEA group. In the placebo group, the improvement of 0.15 ± 0.355 was not statistically significant.

Although some positive effects were observed in the more general PGWB questionnaire, the major effects revealed by the questionnaires were clearly those observed on libido and sexual function in the ASF and MENQOL questionnaires.

**DISCUSSION**

The present data show for the first time that local intravaginal treatment with DHEA, a compound inactive by itself that acts as precursor for the cell-specific local formation of all androgens and/or estrogens after menopause, causes a marked improvement of all four aspects of women’s sexual dysfunction, namely, desire/interest, arousal, orgasm, and pain at sexual activity.

Although the role of psychological, biological, and interpersonal factors in sexual function is a matter of debate, the data described above clearly show that local intravaginal changes induced by sex steroids can exert marked influences on all aspects of sexual function, including desire/interest, a characteristic component of brain function. It thus seems that increased favorable sensitive outputs from a more healthy vaginal area influence the brain to feel increased desire/interest without the need for a direct action of hormones on the brain. The present findings also indicate that there is a highly efficient bidirectional interplay between the genital area and the brain. Most importantly, these benefits are achieved by an exclusive peripheral action of Prasterone, with no or minimal changes in the serum levels of \( E_2 \) and testosterone which remain within the values observed in normal postmenopausal women.

Several studies have reported diminished sexual desire or interest, decreased sexual receptivity, and decreased sexual responsiveness in postmenopausal women. Low sexual desire is strongly associated with a decrease in the other aspects of the sexual response, namely, arousal, orgasm, and pleasure.

The definition of women’s sexual dysfunction has been revised recently. The disorder of the sexual desire/interest domain is illustrated by absent or diminished feelings of sexual interest or desire. In this situation, the incentive/motivation to become sexually aroused is scarce or absent.

The disorders of the arousal domain require the presence of a normal vasocongestive response of the genitalia after erotic sexual stimulation. The disorders of the sexual arousal domain can be divided into (1) subjective sexual arousal disorder (lack of pleasure after sexual stimulation), whereas the vaginal lubrication and other signs of physical response still occur, and (2) genital sexual arousal disorder illustrated by minimal vaginal lubrication and sexual sensations, whereas the subjective (psychological) sexual excitement is present. Orgasm will not occur or occurs with low intensity with loss of sexual excitement and pleasure. A combination of the subjective and genital arousal disorders occurs. The women’s orgasmic disorder, on the other hand, is either the lack of orgasm, markedly diminished orgasmic sensations, or a marked delay in orgasm.

With the present data showing a parallel effect on desire/interest, arousal, orgasm, and pain at sexual activity, it is unlikely that the linear model of desire leading to sexual arousal and orgasm is correct, as already mentioned. The present data clearly show that beneficial effects induced by DHEA at the level of the vagina have parallel effects on desire/interest and arousal and also similar beneficial effects on orgasm and decreased pain at sexual activity. In other words, the present study shows that all aspects of women’s sexual dysfunction can be successfully treated by local intravaginal DHEA therapy.

**FIG. 10.** Effect of daily intravaginal application of 0.0%, 0.25%, 0.5%, and 1.0% dehydroepiandrosterone (DHEA; Prasterone) for 4, 8, and 12 weeks on summary score of the Abbreviated Sexual Function questionnaire in postmenopausal women. Data are expressed as means ± SEM; the *P* values are comparisons with placebo at all time intervals except for the placebo group at 12 weeks, which is compared with baseline.
The current therapeutic recommendations for sexual dysfunction in women are diverse but are generally deceptive. For low sexual desire and arousal (combined and subjective), cognitive-behavioral approaches, sex therapy, and psychodynamic therapies are recommended. Systemic estrogens combined with progestins are also used with the known risks of such therapy for the breast and uterus.

In general, androgens have been reported to increase desire in postmenopausal women, although some data have been controversial. In fact, starting in the 1940s, testosterone was found not only to eliminate menopausal symptoms but also to restore libido. Sexual function has been found to be improved in many studies by adding methyltestosterone to estrogens. Similar findings have been reported, and high doses of testosterone enanthate by intramuscular injection alone or in combination with estrogens have resulted in sexual desire, fantasies, and arousal increase more than placebo or estrogen alone in ovariectomized women. On the other hand, an improvement in sexual activity but not in desire was observed. Sexual arousal was not found to be modified by estrogens plus methyltestosterone in another study. Testosterone in association with repeated erotic stimuli led to increased arousal after a delay, whereas no subjective increase in arousal was observed after testosterone administration and one episode of erotic stimulus.

A recent large-scale study of a population of 483 spontaneous postmenopausal women with hypoactive sexual desire who received 300 µg testosterone or placebo patches twice a week for 24 weeks in addition to oral estrogens or estrogens + progestin therapy. The number of satisfying episodes and desire were significantly increased by 73% and 48%, respectively, in the testosterone group, compared with 19% and 20% in the placebo group. The same dose of testosterone has shown improvement of hypoactive sexual desire disorder in surgically induced menopausal women.

Few data are available for DHEA: systemic therapy (50 mg/d for 4 mo) with DHEA in women with adrenal insufficiency improved the frequency of sexual thoughts or fantasies and sexual interest, and measurable improvements were made in both mental and physical satisfaction. Increased sexual thoughts and fantasies were apparent within 1 mo of starting DHEA. Three small randomized, placebo-controlled studies of DHEA replacement (20-50 mg/d) in women with hypopituitarism reported improvement in quality of life, whereas improved sexual function was reported by those who found improved mood.

In postmenopausal women with normal adrenal function, an increase in sexual excitement and libido was reported at 6 months of DHEA administration. In other studies, DHEA has been reported to improve sexual and mood disorders. DHEA has also been observed to improve psychological and physical well-being in postmenopausal women.

Some other studies, however, have not reported a beneficial effect of DHEA on sexual function. Two studies in women with adrenal insufficiency found no improvement in well-being or sexual function after DHEA administration. In another study in Addison disease, a significant improvement in sexuality was not observed after 12 weeks of treatment with the same DHEA dose. An improvement in mood and spatial cognition was observed in androgen-deficient women with anorexia nervosa who received DHEA, some of whom were depressed.

We believe that the androgenic component of DHEA action plays a so-far unrecognized role in the physiology of the vagina. In fact, our recent preclinical data have shown an important effect of DHEA on all three layers of the vaginal wall, including the collagen fibers of the lamina propria and the muscularis. It is expected that such a previously unknown global action of DHEA on the vagina exerts benefits not previously observed on the signs of vaginal atrophy which can include a reduction in the length and diameter of the vagina, the loss of vaginal rugal folds, and the disappearance of vaginal fornices. All these atrophic changes are accompanied by decreased vascularization, decreased vaginal secretions, and more susceptibility to trauma and pain. The specific androgenic effect on collagen formation could play a major role in the particularly positive results obtained in the present study.

Most importantly, the present data clearly show that intravaginal DHEA is a very efficient treatment for FSD without significant systemic exposure to a drug because all steroids remain within the postmenopausal range. The other advantage is that the drug used is already present in women at a relatively high level, thus practically eliminating the risk of an unexpected secondary effect at any site.

It should be mentioned that no women were excluded from the trial on the basis of other medications potentially affecting FSD, except sex hormones which could have affected vaginal atrophy. Another important aspect of the present study is that women were not selected on the basis of personal distress or desire to see improved sexual function. In fact, approximately 50% of women indicated that they desired improved sexual life, thus suggesting that interest in sexual life is not a prerequisite to achieve an improvement in the four domains of sexual function in that population of women.

The Food and Drug Administration Guideline for Industry in FSD recommends that “the endpoints be based on the number of successful and satisfactory sexual events or encounters over time.” The present data not only show a significantly increased number of successful and satisfactory events compared with placebo (Fig. 10) but also show that all four components of FSD are highly statistically (P < 0.01 or more) improved compared with placebo.

CONCLUSIONS

The new knowledge gained about intracrinology in women clearly indicates that the appearance of symptoms of vaginal atrophy in postmenopausal women is due to a lack of DHEA and/or insufficient transformation of this precursor into active androgens and/or estrogens in the vagina. Most interestingly, the present data show that in addition to very
rapidly and efficiently correcting the symptoms and signs of vaginal atrophy,\textsuperscript{11} the local application of DHEA in the vagina has a marked influence on all aspects of sexual function, thus indicating the role of an androgenic component of DHEA transformation on vaginal health, which permits improvement in desire, arousal, orgasm, and pleasure.

The present beneficial effects of intravaginal DHEA on sexual dysfunction in women, including orgasm, can be compared to the success of oral therapy for erectile dysfunction in men. A marked difference, however, between the treatment of erectile dysfunction in men and the present treatment of sexual dysfunction in women is that local treatment with DHEA achieves its beneficial effects without significant systemic exposure to a drug, thus avoiding potential systemic risks.

REFERENCES


