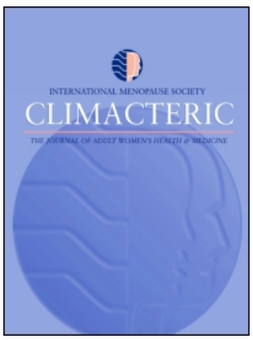

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REVIEW

The effects of dehydroepiandrosterone on sexual function: a systematic review

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ABSTRACT

Objective: Faced with the growing interest about the action of dehydroepiandrosterone (DHEA) and its benefits, as well as the negative impacts that sexual dysfunctions have on people's quality of life, this systematic review was undertaken with the objective of evaluating the effect of DHEA use on aspects of sexual function.

Method: An electronic search was conducted in the databases of PubMed, ISI Web of Science and Virtual Health Library (VHL) combining the terms 'DHEA treatment' and 'DHEA use' with terms such as 'sexual dysfunction', 'sexual frequency' and 'libido'. No limits on time and language were imposed. Clinical studies were considered eligible where individuals for any reason made use of DHEA and if they had any aspect of sexual function assessed. Preclinical studies and systematic reviews were considered ineligible.

Results: The search identified 183 references and 38 were considered eligible. DHEA improved aspects such as sexual interest, lubrication, pain, arousal, orgasm and sexual frequency. Its effect was better in populations with sexual dysfunction, especially in perimenopausal and postmenopausal women.

Conclusion: Considering the studies currently published, DHEA is effective in improving several aspects of sexual function, but this effect did not reach all the populations studied.

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Sexual function; sexual dysfunction; DHEA treatment; DHEA use

Introduction

Sexuality is one of the most important aspects of human life; its role transcends the reproductive function, since sexual satisfaction is closely related to the quality of life[1,2]. Based on an interrelation of psychophysical aspects, men and women possess a sexual response cycle divided into the following three phases: desire, arousal and orgasm. Alterations in any of these phases can be characterized as sexual dysfunction[2,3].

The etiology of sexual dysfunction can be organic or psychological, and, despite the scientific advances in the topic, its prevalence remains extremely high, nearly 50% in men and women in various countries[4–6]. Given the significant proportion of the global population affected by problems related to sexual function, the search for therapeutic assistance is of great importance[4–6].

Dehydroepiandrosterone (DHEA) and its sulfate (DHEA-S) are sexual hormones secreted abundantly in human beings and other primates[7–9]. These indirect precursors of androgen and estrogen are produced primarily by the adrenal glands, gonads and brain, allowing DHEA and DHEA-S to be classified as neurosteroids[10–12]. The production of these hormones is strongly linked to age, peaking at the age range of 25–35 years and gradually declining thereafter. At approximately 70 years, it is expected that hormone production reaches between 10% and 20% of what was produced during the peak years.

Recent decades have seen much speculation regarding the therapeutic potential of DHEA and its capacity to enhance, among other aspects, mood, cognition, life quality and sexual function[13–19]. In fact, many studies have achieved encouraging results regarding the effect of DHEA on sexual function[20–39], although other studies have not observed similar results[40–53].

Based on the preliminary analysis of some works, our hypothesis is that individuals with sexual dysfunction can improve aspects of sexual function through the use of DHEA. Thus, faced with the growing interest in DHEA's function and its benefits and considering the negative effects of sexual dysfunction on quality of life, this systematic review was undertaken with the objective of evaluating the effect of DHEA use on aspects of sexual function.

Methodology

The selection of articles in this review was the result of an electronic search in the databases of PubMed, ISI Web of Science and Virtual Health Library (VHL). The first search occurred in October 2015, and the final search

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Supplemental data for this article can be accessed here.

was in August 2016. As a research strategy in PubMed, the expressions 'DHEA treatment' and 'DHEA use' were combined with the following key words: sexuality, sexual, sexual dysfunction, sexual frequency, sexual appetite, sexual thought, sexual fantasies, sexual interest, sexual activity, sexual problems, sexual potency, sexual drive, sex drive, sexual desire, and libido. For example, one search used DHEA treatment AND sexuality OR DHEA use AND sexuality. The utilized filter was 'Clinical Trial' and limits on time and language were not imposed. Eligible clinical studies included studies in which individuals with or without sexual dysfunction used DHEA for any reason, independently of gender, age, quantity, duration of use and whether they had any aspect of sexual function assessed. Preclinical studies and systematic reviews were considered ineligible.

Two reviewers worked independently during the process of selection, utilizing the following research strategy: database research, exclusion of repeated references, abstract reading and selection of potentially eligible articles; a full reading of potentially eligible articles; final selection of articles. There was no divergence between the reviewers regarding the articles composing this review.

For the extraction of data, a protocol was created and tested on four articles. The following information was identified and analyzed: population, gender, age, study type, posology, manner of administration, time of treatment, assessment tools for sexual function, effects on hormones, effects on sexual function and adverse effects. The risk of bias in this study was evaluated through the Jadad Scale.

Results

Although the database search identified 183 references, only 38 were considered eligible for the current review, and these are presented in Figure 1. Of the 38 selected references, 20 reported positive results, 14 reported negative results and four reported inconclusive results. A study was considered inconclusive if the study was contradictory or unclear regarding DHEA's effect on sexual function.

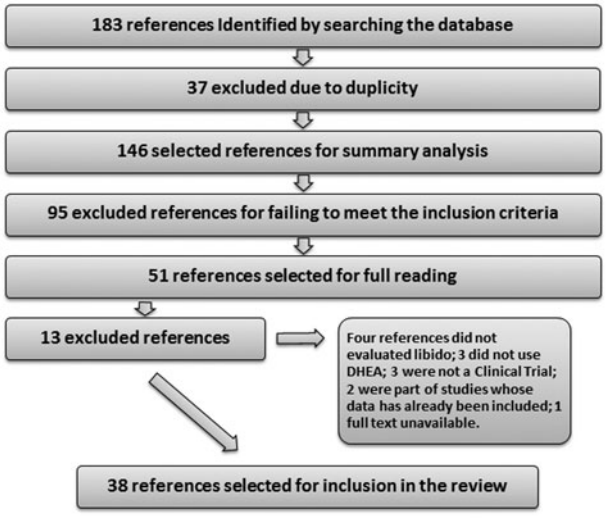

Figure 1. Flow of information through the different phases of the systematic review.

Studies that have found an effect of DHEA on sexual function

Population

DHEA treatment has been shown to be effective predominantly in samples with sexual dysfunction[20–27,29,30,34,35,39]. However, in some studies, aspects of sexuality improved in patients with endocrine disorders, autoimmune diseases, chronic fatigue syndrome and in healthy subjects[28,31–33,36–38].

Gender

Sixteen studies comprised female samples, and only one study had an exclusively male sample[39]. Three studies used heterogenic samples; however, sexual parameters only showed improvement in women.

Age

Excepting a study in which the average age was 39 years[35], the average age for women was over 40, and in 13 studies the average age was more than 50[20–30,33,36]. The average age for men was over 45 years in all studies. In a study in which DHEA improved sexual function in men, the average age was 56.5[39].

Hormonal parameters

Seven studies using oral DHEA that assessed levels of DHEA and DHEA-S observed low baseline levels of these hormones[27,31–34,37,38]. The same was not observed in three studies conducted on healthy individuals[28,33,35]. Studies also showed that DHEA and DHEA-S increased during treatment to values commensurate with those of young adults, including men who were more than 70 years old, although at a slower pace than in men younger than 70 years[36]. A study with an acute dose of 300 mg DHEA observed a significant increase in levels of DHEA-S after 50 min of administration[33], and other studies noted a return to baseline levels after suspension of treatment[31,36]. One study observed that, after cessation of treatment, DHEA-S levels decreased less significantly in men and women older than 70 than in men and women younger than 70[36].

The studies that assessed testosterone (free/total) noted a significant increase in women but not in men[27,28,31,32,34–36,38]. In one study of women treated with 50 mg/day DHEA for 12 months, 10% of the sample exceeded the testosterone levels observed in women during menstruation[36]. Two studies indicated that testosterone levels do not continue after interruption of treatment[31,36].

Few studies measured estradiol and androstenedione although, in all cases, these hormones increased in men as well as in women[27,28,31,32,35,36]. One study measured androsterone and noted a significant increase in men and women ($p < 0.001$, $p < 0.05$, respectively)[27]. Another study of women identified an increase in cortisol during DHEA use[28].

Studies performed with intravaginal DHEA could not identify changes in hormonal parameters from this manner of administration. All steroids measured, including DHEA, DHEA-S, estradiol and testosterone, caused no or minimal increase

in serum sex steroid levels; these remained within the reference range of the studied population's age group after the 12 weeks of treatment[22,54].

Sexual parameters

Using sexual scales, studies on oral DHEA observed an improvement statistically significant in one or more aspects of sexuality, such as sexual thinking, sexual fantasies, sexual arousal, orgasm, sexual desire and vaginal lubrication. Two of those studies indicated an increase in the frequency of sexual intercourse and the quality of relations (including masturbation) during treatment with DHEA[28,36]. Two studies indicated an improvement in sexual aspects only by self-report or direct questioning[31,35], and one study did not specify which sexual aspect increased during treatment[38]. A study of men noted improvement in desire, erection, orgasm, satisfaction with sexual relations and general satisfaction[39].

The use of intravaginal DHEA in women with vulvovaginal atrophy improved several parameters of sexual function[20–26,29,30]. Utilizing the Female Sexual Function Index (FSFI), one of the studies observed an increase in scores of desire (29%), sexual arousal (45%), lubrication (106.5%), orgasm (50%), satisfaction (48.5%) and pain (137%) after 12 weeks of treatment compared with the baseline, a greater improvement than was observed with a placebo ($p < 0.05$)[23]. Another study showed an improvement in all FSFI dimensions after 52 weeks of treatment, highlighting the dimensions of lubrication and pain that improved by 115% and 108%, respectively, compared with the baseline[20]. Other studies showed superior effects (up to 43%) on sexual desire, vaginal dryness and intimacy avoidance, with a significant difference when compared with the placebo ($p \leq 0.0036$)[25,26,29,30] and a reduction of scores on the gravity of dyspareunia greater than 45% when compared with baseline ($p = 0.013$ compared with the placebo)[22]. One hundred men were assessed regarding their perception of their partners' vaginal dryness after 12 weeks of treatment. In this study, the men, responding to a specific questionnaire, reported an improvement of 81% compared with the placebo ($p = 0.0347$) and 59% compared with the baseline.

Other parameters

When compared to the placebo, intravaginal DHEA reduced the percentage of parabasal cells by 45.8% ($p < 0.0001$), increased superficial cells in 4.7% ($p < 0.0001$) and vaginal dryness in 42% ($p = 0.013$) of subjects[22]. Gynecologic evaluation identified an improvement in vaginal secretions, epithelial integrity, thickness of the epithelial surface and vaginal coloration; similar results were not observed in the placebo group[22].

Correlations between hormonal and sexual parameters

In women, correlations were observed between the levels of bioavailable testosterone and sexual cognition ($r = 0.47$), arousal ($r = 0.61$) and orgasm ($r = 0.49$); and DHEA-S was correlated with satisfaction ($r = 0.47$)[27]. In men, correlations were identified between total serum levels of testosterone and arousal ($r = 0.45$), sexual drive ($r = 0.50$) and orgasm ($r = 0.55$); nevertheless, there was not a significant improvement in sexual parameters in men in the present study[27]. In an entire year of randomized study that assessed different types of hormonal replacement therapy on sexual function in 48 postmenopausal women, not only the group that received DHEA (10 mg) but also the group that received oral estradiol (1 mg) plus dehydrogesterone (5 mg) presented improvement on McCoy's total score ($p < 0.001$ and $p < 0.01$, respectively). In this same study, there was an increase in the frequency of sexual relations in groups that received DHEA, estradiol plus dehydrogesterone and in the group that received tibolone (2.5 mg) ($p < 0.01$, $p < 0.05$, $p < 0.01$, respectively). These data indicate that DHEA can be better than other forms of treatment[28].

Posology

Among studies of oral DHEA, eight studies used doses of between 50 and 100 mg/day, two studies used doses of between 10 and 15 mg/day and one study used an acute dose of 300 mg. The majority of studies that reported some sort of effect on sexuality lasted longer than 12 weeks with a low dosage (up to 50 mg/day)[28,31,32,36–38]. However, there was an effect on sexuality in studies up to 12 weeks but with a dosage higher than 50 mg/day[27,33]. Intravaginal DHEA was used with doses between 3.25 and 13 mg for a period of 12–52 weeks. Studies with intravaginal DHEA tested doses of 3.25 mg, 6.5 mg and 13 mg in periods of 12 weeks[26,29,30]. Despite all these tested doses having shown themselves to be superior to placebo ($p < 0.05$), the 6.5 mg dose was the one that showed better results ($p < 0.0001$)[29], therefore being the dose chosen for the studies of 52 weeks of time[25]. In the studies of 12 weeks, the assessments were held during weeks 0, 4, 8 and 12. When analyzing the sexual domain with MENQOL, intravaginal DHEA was shown to be better than placebo starting from the assessment conducted in the fourth week of treatment ($p = 0.096$)[30].

A summary of articles included in this review is presented in Table 1. The percentage of increase in scores of assessment tools used in some of the studies with oral DHEA is presented in Figure 2. A study that only lasted for a day[33] and two studies that only stated that there was an improvement in some aspect of sexual function but did not indicate how much improvement were not included in Figure 2[31,36]. The percentage of increase in scores of assessment tools used in studies with intravaginal DHEA can be observed in Figure 3. The risk of bias in the studies that observed DHEA effect on sexual function can be seen in Table S1 (Supplementary Material, see http://dx.doi.org/10.1080/13697137.2017.1279141).

Studies that did not identify a DHEA effect on sexual function

Population

DHEA did not improve sexual function, particularly in healthy individuals[42,46,47,50–53]. In addition, DHEA did not improve

Table 1. Summary of studies that have found effects of dehydroepiandrosterone (DHEA) on sexual function.

First author (year)	Population	Gender M/F	Age (years) M/F	Daily dose (mg)	Time (weeks)	Evaluation instruments	Results
Reiter (1999)[39]	Erectile dysfunction	40/0	56.5	50	24	IIEF	Improved erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction
Arlt (1999)[37]	Adrenal insufficiency	0/24	42	50	16	VAS	Increased sexual interest degree, as well as sexual thoughts frequency and sexual fantasies
Himmel (1999)[38]	Chronic fatigue syndrome	0/23	44.6	25–100	26	MHAQII	Sexual problems improved 22%
Baulieu (2000)[36]	Healthy elderly	140/140	60–79	50	52	GWB, and Scale of Dupuy	Improved most libido parameters in women >70 years. In women <70 years and in men there was no improvement
Guay (2001)[35]	Perimenopausal women with decreased libido	0/12	39	50–100	>8	Self-report	Improved sexual aspects such as desire, lubrication, arousal and orgasm
Munarriz (2002)[34]	Androgen insufficiency	0/113	43.5	50	16	SDS and FSFI	Improved sexual aspects such as desire, arousal, lubrication, orgasm, satisfaction and pain
Hackbert (2002)[33]	Postmenopausal healthy women	0/16	59.8	300	Single dose	DISF, OFQ and FES	Increased sexual arousal
Nordmark (2005)[32]	Systemic lupus erythematosus	0/37	47.6	10–15	52	McCoy	Improved sexual problems, vaginal dryness and dyspareunia
Brooke (2006)[31]	Hypopituitarism	18/26	48.7/47.8	50	52	Sexual Self-efficacy Scale	Only in women, increased the sexual thoughts frequency
Labrie (2009)[30]	Postmenopausal women with VVA symptoms	0/216	58	3.25–13[a]	12	ASF, MENQOL, and SC	Improved libido and sexual function
Labrie (2011)[29]	Postmenopausal women with VVA symptoms	0/114	58	3.25–13[a]	12	Self-report	Highly effective in reducing pain during sexual intercourse
Genazzani (2011)[28]	Postmenopausal healthy women	0/48	54.5	10	52	McCoy	Improved McCoy's total score and increased sexual intercourse frequency
Bloch (2013)[27]	Hypoactive sexual desire disorder	21/27	45.9/55.8	100	6–12	DISF, FSFI	Improved some sexual function parameters in women, but not in men
Labrie (2014)[26]	Postmenopausal women with VVA symptoms	0/216	58	3.25–13[a]	12	ASF, MENQOL, and SC	Improved sexual function in women with dyspareunia regardless of pain level at beginning of treatment
Labrie (2015)[23]	Postmenopausal women with VVA symptoms	0/435	57.9	6.5[a]	52	VASQ	Improved pain during sexual activity
Labrie (2015)[24]	Postmenopausal women with VVA symptoms	0/100	40–80	6.5[a]	12	Questionnaire directed to partner	Male sexual partner indicated improvement in his perception in relation in vaginal dryness feeling of partner after treatment
Labrie (2015)[25]	Postmenopausal women with VVA symptoms	0/554	59.5	6.5[a]	12	FSFI	Improved all sexual function parameters
Archer (2015)[22]	Postmenopausal women with VVA symptoms	0/255	58.5	3.25–6.5[a]	12	VASQ	Improved pain during sexual activity
Labrie (2016)[21]	Postmenopausal women with VVA symptoms	0/463	59.5	6.5[a]	12	VASQ	Improved pain during sexual activity
Bouchard (2016)[20]	Postmenopausal women with VVA symptoms	0/154	40–75	6.5[a]	52	FSFI	Improved all sexual function parameters

ASF, Abbreviated Sexual Function; DISF, Derogatis Interview Sexual Functioning Inventory; FES, Film Evaluation Scale; FSFI, Female Sexual Function Index; GWB, General Well Being; IIEF, International Index of Erectile Function; McCoy, McCoy's Sex Scale Questionnaire; MENQOL, Menopause-Specific Quality of Life; SC, Sexual Concern questionnaire; MHAQII, Modified Health Assessment Questionnaire-II; OFQ, Orgasmic Functioning Questionnaire; SDS, Sexual Distress Scale; VAS, Visual Analog Scale; VASQ, Vaginal Atrophy Symptoms Questionnaire; VVA, vulvovaginal atrophy

[a], Intravaginal cream (Prasterone)

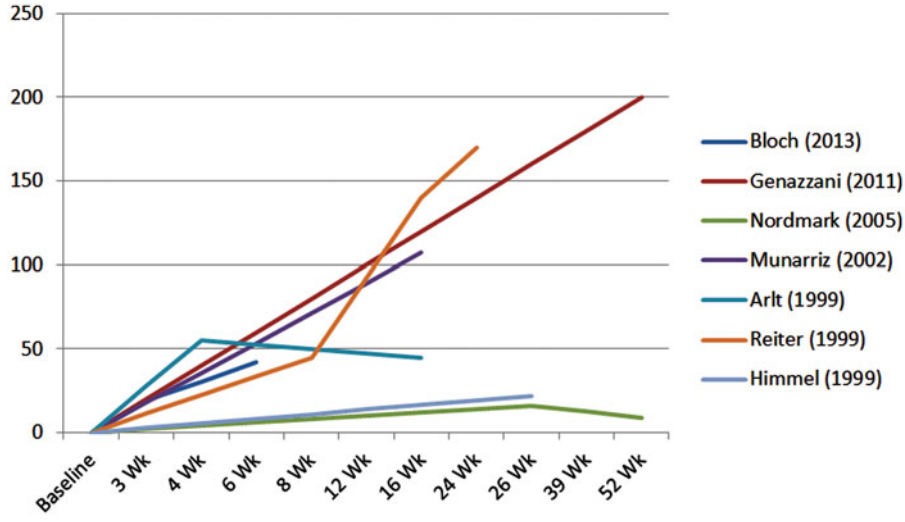

Figure 2. Percentage increase in the score of the assessment tools used in studies where oral DHEA was effective. Bloch[27]: Female Sexual Function Inventory (FSFI) – sexual arousal, scores reported for weeks 0, 3 and 6 ($p = 0.001$); Genazzani[28]: McCoy Female Sexuality Questionnaire (McCoy) – sexual intercourse, scores reported for weeks 0 and 52 ($p < 0.01$); Nordmark[32]: McCoy – score total, scores reported for weeks 0, 26 and 52 ($p < 0.05$); Munarriz[34]: FSFI – sexual arousal, scores reported for weeks 0 and 16 ($p =$ uninformed); Arlt[37]: visual analog scale – sexual interest, scores reported for weeks 0, 12 and 16 ($p = 0.05$); Reiter[39]: International Index of Erectile Function (IIEF) – erectile function, scores reported for weeks 0, 8,16 and 24 ($p < 0.001$); Himmel[38]: Modified Health Assessment Questionnaire-II (MHAQII) – sexual problems, scores reported for weeks 0 and 26 ($p = 0.06$).

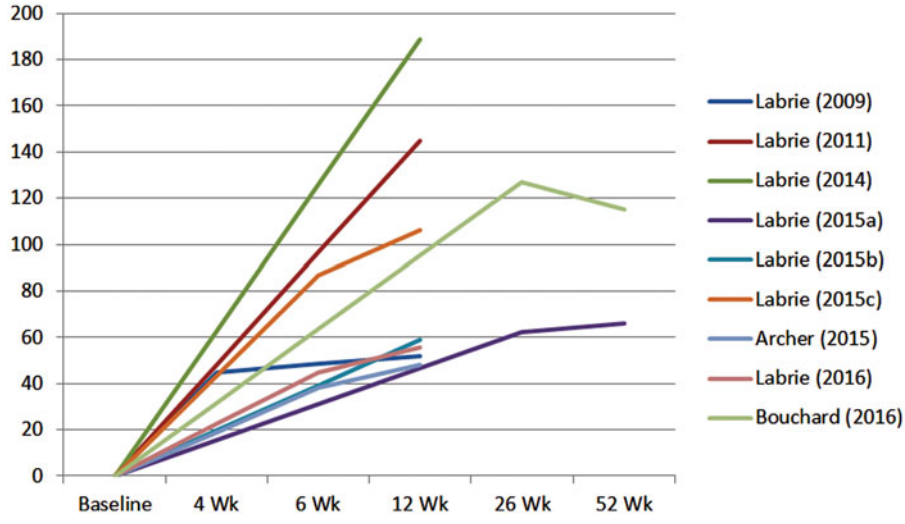

Figure 3. Percentage increase in the score of the assessment tools used in studies where intravaginal DHEA was effective. Labrie[30]: Menopause-Specific Quality of Life (MENQOL) – sexual domain, scores reported for weeks 0, 4 and 12 ($p < 0.0001$); Labrie[29]: vaginal examination – dyspareunia, scores reported for weeks 0 and 12 ($p < 0.0001$); Labrie[26]: Abbreviated Sexual Function (ASF) – arousal/lubrication, scores reported for weeks 0 and 12 ($p < 0.05$); Labrie[23]: vaginal atrophy symptoms questionnaire – dyspareunia, scores reported for weeks 0, 12, 26 and 52 ($p < 0.0001$); Labrie[24]: specific questionnaire – perception of vaginal dryness of partner, scores reported for weeks 0 and 12 ($p < 0.0001$); Labrie[25]: Female Sexual Function Index (FSFI) – lubrication, scores reported for weeks 0, 6 and 12 ($p < 0.0005$); Archer[22]: Vaginal Atrophy Symptoms Questionnaire (VASQ) – dyspareunia, scores reported for weeks 0, 6 and 12 ($p = 0.013$); Labrie[21]: VASQ – pain, scores reported for weeks 0, 6 and 12 ($p < 0.001$); Bouchard[20]: FSFI – lubrication, scores reported for weeks 0, 6 and 12 ($p < 0.0001$).

any other aspect of sexual function in two studies with subjects in conditions that affected their quality of life and in three studies with subjects with endocrine problems[43–45,48,49]. Only two studies showed no improvement with treatment with samples comprising subjects with sexual dysfunction[40,41].

Gender

The majority of these studies had men in their samples, eight in total, with four of them focused solely on men. Six studies had samples exclusively comprising females.

Age

Among men, the average age was greater than 48 years old, except in a study in which the average age was 40[48]. In women, the average age was primarily greater than 46 years old; however, in three studies, the medium age was ≤40 years[46,48,53] and, in one of these studies, the average age was 27 years[46].

Hormonal parameters

Levels of DHEA, DHEA-S, estradiol and androstenedione increased in men and women in all studies that rated these

hormones. Testosterone increased in women in all of the studies; however, in men, testosterone increased in only two studies[40,50]. Cortisol did not change in a study with patients with Addison's disease but decreased in a study of postmenopausal women[49].

Posology

Only oral DHEA was used in these studies. The most common dose was 50 mg/day, used in ten of the 14 studies. Two studies used a 100 mg/day dose[11,50]. One study used a dose of 25 mg/day, and another study used an acute dose of 300 mg/day[46]. Eight studies lasted up until 12 weeks, and six lasted for 16 weeks or more.

A summary of the articles included in this review that did not report any DHEA effect on sexual function is presented in Table S2 (Supplementary Material, see http://dx.doi.org/10.1080/13697137.2017.1279141).

Studies with inconclusive results

Population, gender, age, posology

The studies that presented inconclusive results presented no clear standard. Their samples presented varied characteristics, different ages and both genders. In addition, the dosages used were not consistent among the studies[55–58].

Hormonal parameters

Levels of DHEA, DHEA-S and androstenedione increased in both men and women. Testosterone increased in all women assessed. In a study with a low dose (20–30 mg/day), the level of testosterone increased but did not reach normality[56]. In a study with a high dose (200–500 mg/day), serum testosterone increased in two women on <20 ng/dl to 98 and 134 ng/dl after 8 weeks[57]. In men, testosterone showed a decrease in two studies, yet an increase in most male carriers of Addison's disease, although less expressive than in women[55]. Estradiol was only assessed in one man, and there was an increase[58].

Sexual parameters

In one of the studies, although DHEA use did not lead to improvement in sexuality aspects when compared to the baseline, three of 13 men and one of seven women reported an increase in sex interest following treatment[55]. A study that had a phase controlled by a placebo and another by an open label observed an improvement in sexual relationships only in the open phase ($p = 0.06$)[56]. HIV + individuals witnessed an improvement in libido; however, this improvement was always associated with a mood enhancement, and was not specifically associated with the effect of DHEA on sexual function[57]. In a case report of two patients, an elderly subject complained of loss of libido whilst a younger patient with depression reported an improvement of depression and libido[58].

A summary of the articles included in this review with inconclusive results is presented in Table S3 (Supplementary Material, see http://dx.doi.org/10.1080/13697137.2017.1279141).

Side-effects

In general, the studies included in this review identified only mild and transitional androgenic effects, including studies in which no adverse effects were reported by the subjects[28,39,44,50]. Side-effects were more common: acne, skin and hair oiliness, and an increase in body hair growth. A study that analyzed alterations in prostate volume during treatment with DHEA did not show any alteration[39]. Another study of elderly men analyzed specific antigen increase in the prostate in the DHEA group, but the increase was scarcely greater than in the placebo group and was not statistically significant[42]. During DHEA use, a patient reported paresthesia and numbness of the upper extremity[53], and another patient showed psychiatric alteration (self-harm attempt)[40].

Discussion

Oral DHEA showed significant effects on the psychological and physiological aspects of sexuality in 11 studies, improving factors such as sexual desire, quality, frequency, arousal, orgasm and lubrication. Its effect was clearly better in women; however, a study of men with erectile dysfunction also showed DHEA to be effective[39]. In four other studies, DHEA appeared to cause some type of improvement, although its results were not sufficiently consistent to be classified as positive results[55–58].

Improvement occurred more commonly in the population with sexual dysfunction and treatment was less effective in a healthy population. However, there were studies on subjects with sexual dysfunction who did not demonstrate any improvement[40,41] as well as studies on healthy individuals in which there was an improvement[36]. In fact, elements such as gender and reproductive stage of life appear to be more related to positive results than specific clinical profiles.

The majority of studies with positive results were conducted using women who were perimenopausal or postmenopausal. Although there was a study in which DHEA demonstrated effectiveness in improving erectile dysfunction, other studies on men reported no improvement. This result may be because of the apparent incapacity of DHEA to increase testosterone levels in men with the same efficiency that occurs in women. As a general rule, the use of DHEA increased levels of DHEA-S in men and women[27,40,42,44,48,52]; however, in only a few cases did levels of testosterone increase in men, and the increase did not appear capable of improving male sexual function[40,47,50]. The study that showed improvement in erectile function in men did not assess levels of testosterone, which limits our ability to confirm that the increase in testosterone levels is in fact responsible for improving sexual function among individuals who received oral DHEA[39]. However, when the fundamental role of testosterone in libido and other aspects of sexual function in men and women was specifically considered[59], it was then

considered that, although testosterone is not the only variable responsible for the increase or decrease in sexual function, testosterone is certainly what was indicated by the results of this review.

Among the studies that showed DHEA's effect on sexual function and the studies that did not show this effect, the most commonly used dose was between 50 and 100 mg/day in oral form. However, DHEA also demonstrated its effectiveness in studies with doses starting at 10 mg/day[28–32]. Two similar studies with acute doses of 300 mg DHEA obtained different results: in one study there was no effect of DHEA on sexual arousal, whilst in the other study, there was an effect[33,46]. These results strengthen the idea of the reproductive phase in women as a possible determining response to the use of DHEA: whereas there was an effect in postmenopausal women, there was no effect in premenopausal women.

While most studies with positive effect lasted longer than 12 weeks, studies without effects generally lasted less than 12 weeks. However, the importance of the time factor remains unclear: once the DHEA displayed effects in a short period of time[33], and there were cases in which the effect of DHEA on sexual function took longer to appear[56].

All of the works with intravaginal DHEA were conducted with postmenopausal women with vulvovaginal atrophy and the medication has shown to be efficient in many aspects in all studies included in this review with doses from 3.25 mg/day. Phase-III, multicentric studies of long duration confirmed the security of using this form of application with doses from 6.5 mg after 52 weeks[20,25]. Based on the initial studies included in this review, recently, intravaginal DHEA has become the first product containing DHEA that was approved by the Food and Drug Administration, indicated for treatment of dyspareunia and vulvovaginal atrophy[60].

The low incidence of serious side-effects observed in the current studies (in oral and intravaginal forms) is encouraging. Even long-term studies did not observe significant adverse effects[20,25]. Adverse effects such as psychiatric alterations and paresthesia were reported in one patient among the thousands of patients who have used the medication; thus, the chances of these symptoms arising specifically from the use of DHEA are quite small[40,53]. Another review that assessed the use of DHEA for the treatment of depression reached a conclusion consistent with this review regarding the side-effects of DHEA, and this corroborates the safety of this medication[14].

Limitations

Although most studies with positive DHEA effects on sexual function have had an appropriate methodological application and most were accomplished with samples larger than 100 participants, eight studies had samples of fewer than 50 participants. Of these studies, half had fewer than 30 participants, which may be a bias of this review. However, the primary limitation observed was the diversity of assessment tools for sexuality used in the studies. Some assessment tools even had no proven validation, which to some degree compromises the quality of the assessment's results. Furthermore, there were cases in which the scoring was not described in an objective format, avoiding declarations that DHEA did or did not have an effect on sexual function and thus limiting the capacity to describe the results. This limitation is partially because the assessment of sexuality was not the primary goal of the several studies included in this review.

Conclusion

In the current work, promising results were identified regarding the use of DHEA on sexual function, improving aspects such as sexual interest, quality, frequency, arousal, orgasm, lubrication, and dyspareunia. However, DHEA's effect appears to be more effective in perimenopausal or postmenopausal women than in other populations.

The use of oral DHEA to increase the circulating level of DHEA and DHEA-S in men and women increased testosterone levels in nearly all women but in only a few cases in men. Therefore, more studies that specifically focus on the relation between increased testosterone and improvement in sexual function in individuals who use oral DHEA are required to increase understanding of this effect, particularly in men.

Considering the low prevalence of serious side-effects in the studies included in this review, even in long-term studies, the use of DHEA has been demonstrated to be one more important alternative in the medical arsenal for the treatment of problems related to sexual function, particularly problems that occur with aging.

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