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Efficacy of intravaginal dehydroepiandrosterone (DHEA) for symptomatic women in the peri- or postmenopausal phase

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ABSTRACT

Objective: There is uncertainty whether treatment with dehydroepiandrosterone (DHEA) decreases menopausal symptoms for women in the peri- or postmenopausal phase. A previous systematic review considering this subject suggested that DHEA may slightly improve sexual function compared with placebo (CS. Scheffers, S. Armstrong, AEP. Cantineau, C. Farquhar, V. Jordan Dehydroepiandrosterone for women in the peri- or postmenopausal phase. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No.: CD011066. DOI: https://doi.org/10.1002/14651858.CD011066.pub2). The purpose of this article is to review recent research investigating whether the use of DHEA, and in particular intravaginal DHEA (Prasterone®), improves sexual function.

Methods: We conducted an online search using Medline OVID for recent articles related to DHEA and menopause. We found 48 relevant publications, out of which 14 papers were original research, all related to the development and licensing of intravaginal DHEA. We critically analysed these 14 articles in relation to sexual function.

Results: All the randomised controlled trials assessed the efficacy of vaginal DHEA in women with vulvovaginal atrophy and showed that sexual dysfunction improved with treatment regardless of the level of dyspareunia at baseline. Treatment with DHEA was found to be superior to placebo and at least as efficacious as vaginal oestrogens in improving symptoms.

Conclusion: Intravaginal DHEA appears to be a safe and effective treatment for menopausal vulvovaginal atrophy and dyspareunia in most women. Further studies are required before it can be recommended for women with a history of thrombosis, cardiovascular disease or hormone-sensitive neoplasms.

1. Introduction

In view of growing public enthusiasm and the easy availability of dehydroepiandrosterone (DHEA) food supplements, it has become important to assess the clinical effectiveness and safety of use of DHEA for treatment of menopausal symptoms. Cochrane authors have published 6 reviews since 2006 on the use of DHEA in the treatment of various health conditions such as cognitive function decline, systemic lupus erythematosus, schizophrenia, poor ovarian reserve and symptoms during the peri- or postmenopausal phase [1–6]. The Cochrane review on DHEA for women in the peri- or postmenopausal phase was published in January 2015 and the evidence was current to 3rd June 2014 [1]. It concluded that there was no evidence that DHEA improved the quality of life but found some evidence that it was associated with androgenic side-effects. There was uncertainty whether DHEA decreased menopausal symptoms, but it was suggested that DHEA may slightly improve sexual function compared with placebo. Previous reviews have highlighted a need for further studies to explore the long-term safety and efficacy of DHEA supplementation [1–9]. None of the reviews have so far examined the use of intravaginal DHEA for menopausal symptoms. The aim of this review was to investigate whether further research has been published on the role of DHEA in treatment of sexual dysfunction and other menopausal symptoms in women during menopausal transition and post-menopause.

2. Background

2.1. DHEA – physiology and mechanism of action

Dehydroepiandrosterone sulphate (DHEAS), DHEA,

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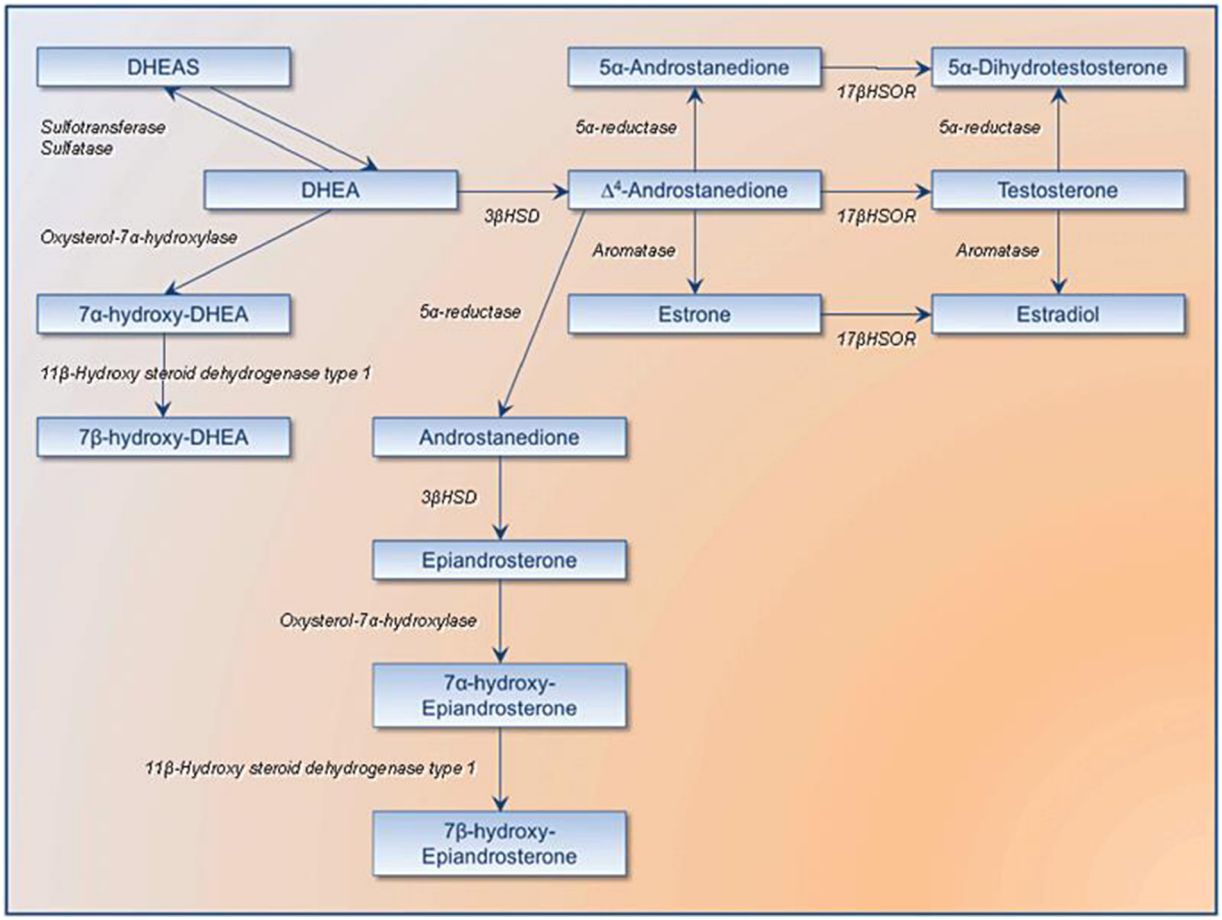

Fig. 1. Shows the biochemical transformations of DHEA into various derivatives.

androstenedione, testosterone and dihydrotestosterone (DHT) are the circulating androgens in both men and women [10]. DHEAS has the highest levels in women but it is a weak androgen. Whilst DHEAS is only produced in the adrenal gland, DHEA is also produced in the ovaries [11–14]. DHEAS can be converted into DHEA and vice versa (Fig. 1). DHEAS has longer half-life than DHEA and is maintained at consistent serum levels throughout a 24-hour period [11]. Serum concentrations of both DHEAS and DHEA decrease with age from 30 years onwards and women in their seventies will have about a fifth of the concentrations in their twenties. DHEA is converted by the body to oestrogens and androgens (Fig. 1), therefore supplementation with DHEA could in theory increase levels of both oestrogen and androgens, and therefore help with menopausal symptoms.

2.2. Androgens and sexual function

The role of androgens and the consequences of androgen deficiency in women during menopausal transition are not well defined. Although overall androgen production will decrease throughout a woman's life, ovarian testosterone production remains relatively constant [15–17]. Hormonal alterations alone may not account directly for changes in sexual function during the menopausal transition. Menopausal symptoms and other life changes that occur at the time of menopause may supersede the effects of hormonal change [8,18–20].

It has been suggested that administering androgen therapy to increase serum concentrations of androgens to the upper limit of normal, can improve female sexual function in selected populations of postmenopausal women [9,21]. Although there are currently no licensed androgen preparations for this purpose for women in the United Kingdom, testosterone gel has recently attracted attention as a viable short-term treatment option. DHEA supplementation has also been shown in some studies to improve sexual interest and satisfaction in women with adrenal insufficiency [1], however evidence of its efficacy in healthy women who are perimenopausal or post-menopausal is lacking Therapeutic use of testosterone can achieve supra-physiologic levels of the hormone in the body but has the potential to cause side-effects such as acne and hirsutism [21]. The long-term consequences of maintaining such levels of androgens are unknown. For vaginal symptoms during menopausal transition (such as vaginal dryness and dyspareunia), intravaginal administration of hormones has the advantage of local action on peripheral target tissues whilst reducing systemic absorption [20,22]. Intravaginal administration of DHEA has the potential to provide oestrogens and/or androgens only to the cells/tissues which possess the required enzymes to transform DHEA, and hence avoid systemic effects [19].

3. Methods

A literature search was undertaken using Medline OVID with the following search criteria: DHEA, dehydroepiandrosterone, diandron, diandrone, fidelin, prestara, psicosterone, trans dehydroandrosterone AND climacteric, menopause AND sexual function, low libido.

All literature published between 1st June 2014 to 31st May 2017 was included. Limits were set such as the publication needed to be in English language and that the research was conducted in human subjects. The publications identified were then weeded and editorials, case reports and letters were excluded. Only original studies and review articles were included.