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EFFECT OF INTRAVAGINAL DEHYDROEPIANDROSTERONE IN REDUCING POSTMENOPAUSAL SYMPTOMS

Obstetrics & Gynaecology

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ABSTRACT

BACKGROUND- Dehydroepiandrosterone(DHEA) replacement therapy resulted in a significant improvement in well being and sexuality in women with adrenal insufficiency as a result of direct effect of DHEA on nervous system.DHEA has many of the benefits of estrogen, with no side effects, and helps women with vaginal atrophy to stimulate the cellular growth of the vaginal wall and increases vaginal secretion.

METHOD AND MATERIAL- This study was conducted on 64 postmenopausal women of 40-70 years of age group. A detailed history and thorough systemic and gynaecological examination was done at first visit and then after 12 week of DHEA therapy.Specific investigation- vaginal PH, vaginal cytology for determination of maturation index(MI) and endometrial biopsy. The cases included in the control group were given placebo treatment by vaginal route for a period of 12 week and any change in vaginal symptoms, vaginal pH and smear pattern, maturation index and endometrial histology was observed.

RESULT AND CONCLUSION-It was found that placebo had no significant effect on the desire domain, whereas with 0.5% DHEA , 77% women showed significant improvement ($p<0.05$). When the arousal/orgasm/pleasure domains were observed at the standard 12 week time interval, a significant improvement ($p<0.05$) was observed in study group, when compared with placebo group. A significant decrease in vaginal pH and increase in Maturation Index observed in women treated with DHEA.

KEYWORDS

INTRODUCTION

Dehydroepiandrosterone (DHEA) is a naturally occurring steroid hormone produced by adrenal glanda. It is present in body in two pools "Free" DHEA and the major circulation form, "Sulfated DHEA or DHEAS. DHEA is referred as "Mother Of All Hormone " because it is found in the human body of both sex and it is precursor to nearly all hormone.

DHEA is present in tremendous amount during youth, its peak between age 25-30 and gradually falling as much as 90% by age 60 years and drops to zero in all people just prior to death . After menopause, all estrogens and androgens are made locally from DHEA in peripheral target . Dehydroepiandrosterone replacement therapy resulted in a significant improvement in well being and sexuality in women with adrenal insufficiency as a result of direct effect DHEA on nervous system.

DHEA , a compound with a predominantly androgenic influence, has no deleterious effect on the serum lipid profile, no change in the concentration of cholesterol, its subfraction or triglycerides . Panjari et al (2007) proposed that restoring the circulating levels of DHEA and its sulphate DHEAS to those found in young people may have anti-ageing effects and improve wellbeing and sexual function. In addition, DHEA also improve the four domains of sexual dysfunction i.e. desire, arousal, orgasm and pleasure. Labrie et al (2010). Spark et al (2002) observed the role of DHEA as springboard hormone for female sexuality.

DHEA has many of the benefits of estrogens, with no side effects, and helps women with vaginal atrophy to stimulate the cellular growth of the vaginal wall and increases vaginal secretion. Postmenopausal problems i.e.vaginal atrophy, hot flushes, bone loss, loss of muscle mass and strength, fat accumulation and type 2 diabetes, all these have been found to respond positively to administration of DHEA when used at the proper dose. Currently vaginal atrophy is treated with the intravaginal application of preparations containing estradiol or estriol , with stimulatory effect on endometrial proliferation which further can lead to endometrial carcinoma. It has been proposed that intravaginally administered dehydroepiandrosterone(DHEA) can be used to treat vaginal atrophy(Panjari et al, 2011).

Advantage of dehydroepiandrosterone over estrogen is that it exert its effect in the three layers of the vagina , especially on collagen formation in the lamina propria or second layer without any effect on endometrium. When serum dehydroepiandrosterone decreases in women with age or for any other reason, there is no endogenous compensatory mechanism to increase dehydroepiandrosterone secretion by the adrenals and permit a return of serum dehydroepiandrosterone to normal levels. Consequently, the only possible means of providing postmenopausal women the amount of dehydroepiandrosterone needed to treat their menopausal symptoms is to administer a physiologic amount of exogenous dehydroepi and rosterone, which is metabolized and acts exactly like endogenous dehydroepi and rosterone.

AIMS AND OBJECTIVE

To determine the effect of daily vaginal Dehydroepiandrosterone versus placebo for alleviation of the most bothersome vaginal symptoms (vaginal dryness and /or dyspareunia).

To evaluate the impact of vaginal Dehydroepisterone on sexual dysfunction symptoms i.e. desire, arousal, orgasm and pleasure.

To explore the characteristics of vaginal atrophy and effect of Dehydroepisterone therapy on it.

To evaluate the impact of vaginal Dehydroepiandrosterone on maturation index, vaginal pH and on endometrial histology.

MATERIAL AND METHOD

The present study was conducted on 64 postmenopausal women of 40-70 years of age group attending the outpatient and inpatient, Department of Obstetrics and Gynaecology, Nalanda Medical College And Hospital , Patna, over a period of nine months from june 2019 to March 2020.

Inclusion criteria were-Postmenopausal women between 40-70 years , having at least one moderate to severe symptoms of vaginal dryness and vaginal or vulvar itching. All four aspects of sexual dysfunction i.e. desire , arousal, orgasm, vaginal pain associated with sexual activity. Women having a low maturation index and vaginal $Ph \geq 5$.

Exclusion criteria were- Undiagnosed abnormal genital bleeding, previous diagnosis of cancer, endometrial hyperplasia, use of oral estrogen and progesterone drugs within 6 months before study, hypertension.

A detailed history was taken with special reference to age, parity, habitat, socioeconomic status education, any history of hypertension,

dietary intake of soy i.e.soymilk, and specially for moderate to severe vaginal symptoms, i.e.(vaginal dryness, burning, pruritis, infection, irritation), vasomotor symptoms, about sexual dysfunction(desire, arousal, orgasm, pain at sexual activity), vaginal bleeding and bone pain, history of pelvic surgery, pelvic radiotherapy, utero-vaginal prolapse was also taken.

A thorough systemic and gynaecological examination was done at first visit and then after 12 week of therapy to find out any systemic side effects of DHEA. The following investigations were performed: routine: blood group, Rh, haemoglobin, TLC, DLC, HBsAg, VDRL, HIV-1 & 2, platelet count, fasting & postprandial blood sugar, liver function test, renal function test, coagulation profile, serum lipid profile, complete urine examination.

Specific investigations: vaginal pH, vaginal cytology, vaginal maturation index, endometrial biopsy.

The vaginal pH level was determined by placing pH indicator strip in the pooled vaginal secretion on speculum or against the lateral vaginal wall with a forceps at first visit and then after completion of treatment with dehydroepiandrosterone. The colour was then compared to the colours and corresponding pH value on a standard chart. The best sample for vaginal cytology for determination of maturation index (MI) should be taken with a gentle scrape along the lateral wall of the upper vagina at the level of the cervix. Cellular tissue from this area accurately reflects the hormonal status at the time of collection. The sample was fixed with alcohol and stained with papanicolaous technique. T he collective effect of estrogen(the "estrogen effect") in a woman's body can be estimated through evaluation of the squamous cell layer that lines the vagina in a test known as a maturation index(MI). A MI is a ratio obtained through performing a random count of three major cell types (parabasal cells, intermediate cells and superficial cells) that are shed from the squamous epithelium. MI= % parabasal cells, % intermediate cells, % superficial cells. Maturation value : A 100 cell count was performed to classify cells as : superficial(S) /intermediate(I) /parabasal(P) and were counted and results were expressed as the maturation value of Meisels. The vaginal maturation value (VME) was calculated using the equation (PX0)+(IX0.5)+(SX1). The VME has a range of 0-100. Maturation value 0- 49 indicate low estrogen effect. Maturation value 50-64 indicate moderate estrogen effect. Maturation value 65-100 indicate high estrogen effect. Endometrial biopsy : Curettings from the anterior, posterior and lateral wall of the uterus were taken. They were fixed in formalin and then sent for histology.

These postmenopausal women of study group were given in daily dose of 0.5% dehydroepiandrosterone by intravaginal route for a period of 12 weeks. The changes in the vaginal symptom (vaginal dryness, vaginal and/ or vulvar irritation /itching) were observed after 12 week of treatment with DHEA. Vaginal pH & smear and endometrial biopsy were repeated after 12 week of dehydoepiandrosterone treatment. The cases included in the control group were given placebo treatment by vaginal route for a period of 12 week, and any change in the vaginal symptoms, vaginal pH and smear pattern, maturation index and endometrial histology was observed.

OBSERVATION AND DISCUSSION –

It was found that placebo had no significant effect on the desire domain, whereas with 0.05% DHEA, 77% women showed significant improvement ($p<0.05$). When the arousal/ orgasm/ pleasure domains were observed at the standard 12 week time interval, a significant improvement ($p<0.05$) was observed in study group, when compared with placebo group.

Table -1: Response On Sexual Symptoms After DHEA Treatment

Sexual symptoms	Study group		Control group	
	improved	Not improved	improved	Not improved
	No, %	No,%	No,%	No,%
desire	14/18, 77	4/18, 22	6/23, 20	17/23, 80
arousal	8/12, 66	4/12, 33	5/18, 27	13/18, 72
orgasm	8/12, 66	4/12, 33	5/18, 27	13/18, 72
pleasure	8/12, 66	4/12, 33	5/18, 27	13/18, 72

For vaginal dryness and irritation /itching, a statistically significant difference was also seen in DHEA treated group and placebo group ($p<0.05$).

Table -2: Response After DHEA Treatment On Vaginal Symptoms

Vaginal symptoms	Study group		Control group	
	Improved	Not improved	Improved	Not improved
	No, %	No, %	No,%	No, %
dyspareunia	19/32, 60	13/32, 40	11/32, 34	21/32, 66
Vaginal dryness	11/19, 58	8/9, 42	8/22, 36	14/22, 64
Vaginal irritation	11/19, 58	8/9, 42	8/22, 36	14/22, 64

Dyspareunia, the symptom identified as the most bothersome by most women, remain unchanged in 66% of women in placebo group, whereas it decreased up to 60% in the 0.5% DHEA treated group which was statistically significant($p<0.05\%$).

In present study, 32% women had vaginal pH≤5 and 67% women had pH>5. In study group the percentage of women, with pH≤ 5 increased from 34% to 79% and with pH>5 decreased from 66% to 21% and this difference was found to be statistically significant when compared with placebo group ($p<0.05$).

Maturation value (MV) was calculated before and after 12 week of treatment and it was observed that it increased from 20.75±6.33 on day 1 to 40.75±5.70 after 12 weeks, respectively, in DHEA treated group, while no change was observed in placebo group. This difference between DHEA treated and placebo group was statistically highly significant ($P<0.0001$).

Table-3: Effect Of DHEA On Maturation Index

Study group (n=32)	Maturation value	
	Pre treatment	Post treatment
16	12-20	35-45
16	22-35	35-65
Control group (n=32)	Pre treatment	Post treatment
17	15-20	No change
15	22-30	No change

The endometrial atrophy was seen in all women at the start of treatment remained unaffected by DHEA ovules in study group.

CONCLUSION-

It was concluded from the present study that although estrogens are efficient in correcting the symptoms of vaginal atrophy and vasomotor symptoms, systemic estrogen are not the physiological hormones that permit reduction of symptoms of vaginal atrophy in postmenopausal women who remain asymptomatic throughout their postmenopausal years. Because the only variable source of sex steroids available in postmenopausal women is DHEA secreted by the adrenals and locally transformed in specific cells and tissues into estrogens and/ or androgens . Replacement with DHEA seems to be the only physiological replacement therapy for postmenopausal women experiencing menopausal symptoms. By the local action in the vagina, DHEA applied daily at doses at which serum steroids remain well within normal postmenopausal value exerts relatively potent beneficial effect on all four aspects of sexual dysfunction. The androgenic component of DHEA playa a role in improvement in desire, arousal, orgasm and pleasure. DHEA has many of the benefits of estrogens, with no side effects, and helps women with vaginal atrophy to stimulate the cellular growth of the vaginal wall and increases vaginal secretion, thus restoring the vagina to its youthful condition.

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