Effect of Hormone Replacement Therapy on Sexual Dysfunction in Postmenopausal Women

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The menopause raises existential, physiological, sexual, psychological, socio-professional issues for women. To eliminate the fears of postmenopausal women, the hormone replacement therapy represents a way to preserve their life quality.

Abstract

Objectives: *In our study, we proved the efficacy of 1 mg Estradiol and 2 mg Drospirenone for menopausal symptoms and increasing sexual act frequency.* ***Methods:*** *Forty-two postmenopausal women were randomized 3:1 into two treatment groups. 1. thirty-one women treated with 1 mg estradiol + 2 mg Drospirenone (E2/DRSP); 2. eleven women treated with 1 mg estradiol + 5 mg dydrogesterone (E2/DGS). The period of treatment was six months. The efficacy parameters were the individual relative change of hot flushes, sweating episodes, sleep problems, nervousness, breast swelling, sexual activity.* ***Results:*** *Sexual life, judged by the increase in the number of intercourses/month, has registered a high increase after a six months treatment for both groups, while the difference between the response to the two therapies has been insignificant. The other symptoms of menopause have significantly improved under both treatments. Body weight and breast swelling have registered significant changes only under E2/DRSP.* ***Conclusions:*** *E2/DRSP and E2/DGS were effective in the treatment of climacteric symptoms and improved the sexual activity.*

Keywords: *menopause, estradiol, drospirenone*

Rezumat

Obiective: *Studiul nostrul îşi propune să evalueze eficacitatea a 1 mg estradiol cu 2 mg drospirenone asupra simptomelor menopauzei şi a îmbunătăţirii activităţii sexuale.* ***Metode:*** *Patruzeci şi două de femei în postmenopauză au fost randomizate 3:1 în două grupe: 1 - treizeci şi una femei au primit 1 mg estradiol + 2 mg drospirenone (E2/DRSP); 2 - unsprezece femei au fost tratate cu 1 mg estradiol + 5 mg dydrogesterone (E2/DGS) pe o perioadă de 6 luni. Eficacitatea terapiei s-a apreciat prin modificarea individuală a următorilor parametri: valuri de căldură, episoade de transpiraţie, tulburări de somn, nervozitate, turgescenţa sânilor, activitate sexuală.* ***Rezultate:*** *Rezultatele au arătat o creştere semnificativă a numărului raporturilor sexuale după şase luni în ambele grupe.* ***Concluzii:*** *Simptomele menopauzei s-au ameliorat la toate femeile tratate, greutatea şi turgescenţa sânilor s-au modificat doar la cele tratate cu E2/DRSP. În concluzie medicamentele care îmbunătăţesc simptomele menopauzei cresc şi activitatea sexuală.*

Cuvinte-cheie: *menopauză, estradiol, drospirenone*

Introduction

We move towards aging since the day we are born. Our society hardly accepts aging and all the resources of modern technologies are directed against it. An accidental trouble in the sexual field is an occasion to remind us of our sexual identity. The menopause raises this issue to women - it is a real crisis - the problem is existential, physiological, sexual, psychological, socio-professional.

The epidemiologic studies show that the world population is increasing. If in the XVIIth century 30% of women get to the menopause age, today this percentage is 90%[1] . The global trend of increasing the hope for life also increases the number of aged persons, in 2025 the population over 65 years being estimated to 1.555 millions. In these conditions, the studies on the healthy old population are of great value, to see if they are sexually active. The epidemiologic studies show that while over 45% of men aged 50-70 years continue their sexual life, only 33% of women have sexual activity over 50 years[1].

During menopause, women report changes in sexuality:

- decrease of sexual intercourse number;
- diminishment of pleasure;
- increase of dyspareunia frequency (15%)[2];
- pain (17%)[2].

Menopause can influence the life of a couple:

- in couples with long term sexual disturbances, these will aggravate post-menopause;
- in couples with satisfactory sexual activity, the first difficulty can appear.

Against the physical and psychological changes in postmenopausal woman, the partner can present multiple difficulties: erectile problems, libido decrease; 25% of sexual difficulties at menopause are caused by the partner[3]. The postmenopausal difficulties of women should take into consideration the possible difficulties of the partner and treat these as priority[3].

Why do we speak today increasingly often about the postmenopausal sexuality, the third age sexuality? Becau-

se the sexual health is considered crucial for the well-being of women in the second half of their lives. It is well-known that sexuality represents an important aspect of the quality of life for all people at every age[4,5,6]. "Postmenopausal sex" depends on each woman; she can choose to have a positive look on menopause and enjoy the sexual partner, or she can be afraid of menopause and this will bring the end of her sexuality.

Female sexual dysfunction (FSD) means: decrease of sexual energy; aversion to sexual life; sensorial difficulties; incapacity to reach orgasm; pain during the intercourse[7]. FSD prevalence in the average population is controversial[8]; the sexual desire decrease goes from 5%[9] to 55%[10]. FSD assessment implies standardization of the measurement method.

The FSD cure at menopause implies two big alternatives: hormone replacement therapy or androgen treatment[14,15]. In hormone replacement therapy (HRT), the progestin effect depends on the molecule from which it derives. Drospirenone, derived from 17 α spironolactone, has anti-mineralocorticoid potential and antiandrogen.

DROSPIRENONE

- antimineralocorticoide potential
- antiandrogen

↓

reduces water retention

↓

effect on blood pressure by extra cellular volume decrease

↓

weight loss

The new product entry on the drug market, that contains Estradiol + Drospirenone, allowed us to perform a randomized clinical study (3:1) in which the answer on postmenopausal symptoms and sexual dysfunction was tracked.

Material and methods

We have performed a randomized prospective study regarding the efficacy, security and tolerance of a new drug used for treating menopause disorders with 1 mg estradiol + 2 mg drospirenone as compared to a drug whose efficacy was already known (1 mg estradiol + 5 mg dydrogesterone). We have tracked the effects of the replacement therapy on sexual dysfunction for menopausal women.

The patients tracked by the study have been selected based on a simple questionnaire filled in by the attending physician and they have been informed about the development of the study and its content.

The questionnaire comprised two parts: general data and data regarding disorders related to menopause and the woman's sexual life.

The general data consisted of: age, date of the installation of menopause (natural or surgical), weight, arterial hypertension antecedents, cardiac pathology, thromboembolic disease, gynecological or mammary pathology, hormone replacement therapy.

The second part of the questionnaire has quantified the presence of menopause disorders and its effect on the sexual life. The following have been tracked: hot flashes intensity and duration; sweating: number/24 h and duration; sleep disorders, nervousness, breast swelling; sexual activity: number of intercourses/month.

The clinical exam of the patients has been performed both at the beginning and at the end of the study: e.g. gynecological and pelvic echography (and mammary if such was the case), hormonal exams for confirming menopause.

The inclusion criteria were: normal endometer, 12 months amenorrhea or over 3 months amenorrhea with plasmatic level E2 ≤ 20 pg/mL and FSH ≥ 40 U/L.

Exclusion criteria: gynecological or mammary pathology present, arterial hypertension uncontrolled by drugs, antecedents of thrombotic disease, cardiac pathology, age over 56 years, postmenopausal period over 10 years, surgical menopause.

The patient enrollment period was 3 months. The patients fulfilling the inclusion criteria received hormone replacement therapy and this was randomly given 3:1 by the attending physician: - (3 patients - therapy with 1 mg estradiol + 2 mg drospirenone (E2/DRSA) test group; 1 patient - treatment with 1 mg estradiol + 5 mg dydrogesterone (E2/DGS) control group. 45 patients were enlisted in the study, out of these 33 were treated with E2/DRSP and 12 with E2/DGS. The tracking period was of 6 months. At the end of the 6 months, the patients have again completed the same questionnaire. 2 patients treated with E2/DRSP and 1 treated with E2/DGS have quit the study. The treatment interruption after 2-3 months was deliberate (without signs of unwanted therapy effects). At the end of the study, there were 31 patients from the E2/DRSP group and 11 patients from the (E2/DGS) control group left.

The average age of the patients in the test group was of 50.2±5.5 years, as compared to the average age of the patients from the control group, which was 53.2±3,0 years. The postmenopausal period was 3.8±3.7 years for the test group and 5.2±3.0 years for the control group. The average weight of the patients in the test group was 65,5±1.5 kg and 71.1±1.5 kg for those in the control group.

Statistical analyses

For the statistical processing of data, the statistical functions MS-Excor were used. The paired t-test was used for each sample, including the control sample and test sample and the unpaired t-test was used for comparing the statistic parameters of the two samples. The results are highlighted by the value of the parameter p.

Results

Analyzing the vasomotor disorders on patients treated with 1 mg estradiol + 2 mg drospirenone before and after 6 months, a significant change (S) or highly significant change (IS) under treatment was seen (table 1).

Thus, the duration of sweating episodes, sleep and nervousness have registered highly significant changes under both treatments, but there was an insignificant change between the two groups regarding the sweating episodes/day

Table 1 Postmenopausal symptoms variation under the treatment 1 mg estradiol + 2 mg drospirenone (E2/DRSP) test group - statistical analyses

Before treatment											After treatment							
np	vs	ikg	ivc	inrt	idt	its	inv	iturs	inrass	inrasl	dkg	dvc	dnrt	ddt	dts	dnv	dturs	dnrasl
VT	51	70.0	2.00	4.00	4.00	1	1	1		1	70.0	1.00	1.00	2.00	0.00	0	0	3
AN	50	56.0	2.00	4.00	4.00	1	2	0		2	55.0	0.00	1.00	2.50	1.00	1	0	4
VT	45	59.0	3.00	5.00	4.00	2	1	2		3	58.5	1.00	2.00	2.50	1.00	0	0	6
AV	46	49.0	2.00	4.00	2.50	2	2	1		3	49.0	1.00	2.00	2.50	1.00	0	0	6
TA	55	67.0	2.00	4.00	4.00	1	2	3		1	67.0	5.00	1.00	2.00	0.00	1	0	3
NB	51	65.0	2.00	4.00	3.50	1	1	3		0	64.0	5.00	2.00	2.00	0.00	0	0	1
MM	54	71.0	1.00	0.00	3.50	1	1	0		1	70.5	0.00	0.00	0.00	1.00	0	0	3
NL	49	70.0	2.00	4.00	4.00	2	2	2		3	70.0	0.00	2.00	1.50	1.00	2	1	6
MN	50	53.0	2.00	4.00	4.00	2	2	0		2	53.0	0.00	0.00	0.50	1.00	1	0	5
VR	48	59.0	3.00	5.00	5.00	2	3	1		3	59.0	2.00	3.00	1.50	1.00	1	0	6
MC	48	61.0	3.00	5.00	4.50	3	2	2		3	60.0	1.00	2.00	1.00	2.00	1	1	6
MCC	47	55.0	4.00	7.00	9.00	2	2	2		4	55.0	2.00	5.00	2.50	1.00	1	0	10
TT	52	60.0	2.00	4.00	4.50	2	1	0		1	60.0	1.00	1.00	1.50	1.00	0	0	3
IC	53	63.0	2.00	4.00	3.50	2	1	0		0	62.0	0.00	1.00	1.00	0.00	0	0	1
CC	50	61.0	2.00	2.00	3.50	1	1	1		2	61.0	0.00	1.00	0.50	0.00	0	0	5
VZA	54	74.0	2.00	1.00	3.50	1	0	1		2	73.0	0.00	0.00	0.00	0.00	0	0	4
MO	51	55.0	2.00	1.00	5.50	2	1	1		1	53.0	1.00	0.00	0.00	0.00	0	0	3
JP	51	63.0	2.00	4.00	3.50	2	0	1		1	63.0	5.00	0.00	0.00	0.00	0	1	3
VA	44	70.0	4.00	7.00	7.50	2	2	2		4	72.0	1.00	4.00	2.50	1.00	1	1	10
PP	53	89.0	2.00	1.00	3.00	1	0	3		1	87.0	0.00	0.00	0.00	1.00	0	0	3
DE	45	70.0	3.00	6.00	4.50	2	2	2		2	72.0	5.00	5.00	2.00	0.00	0	1	4
ID	52	63.0	2.00	3.00	2.50	1	0	0		2	63.0	0.00	2.00	2.00	0.00	0	0	4
VC	52	71.0	2.00	2.00	3.50	1	0	1		1	71.0	0.00	1.00	1.00	0.00	0	0	3
VA	47	57.0	2.00	4.00	4.00	1	1	2		3	57.0	0.00	1.00	0.50	0.00	1	0	10
AA	53	76.0	1.00	2.00	3.50	1	1	0		0	75.0	0.00	0.00	0.00	0.00	1	0	2
BC	51	81.0	2.00	2.00	3.50	1	1	0		2	80.0	5.00	0.00	0.00	0.00	0	0	4
BE	48	83.0	3.00	6.00	5.50	1	2	1		2	82.0	1.00	4.00	1.00	1.00	1	0	6
CR	49	73.0	3.00	6.00	6.00	1	2	2		2	72.0	1.00	4.00	1.50	1.00	1	0	5
CE	54	75.0	2.00	5.00	3.50	1	1	0		1	75.0	5.00	2.00	1.50	1.00	0	0	2
SB	50	63.0	3.00	5.00	5.50	1	1	1		2	63.0	1.00	2.00	1.50	0.00	0	0	4
GG	54	79.0	2.00	4.00	5.50	1	1	3		1	78.0	0.00	1.00	0.50	1.00	0	0	3
ttest(ikg\dkg)					p =	0.030124211		s										
ttest(ivc\dvc)					p =	0.016561374		s										
ttest(idt\ddt)					p =	3.19139E-13		is										
ttest(its\dts)					p =	2.1526E-09		is										
ttest(inv\dnv)					p =	6.08882E-09		is										
ttest(iturs\dturs)					p =	1.65016E-06		is										
ttest(inrt1\dnrt)					p =	1.94082E-13		is										
ttest(inrasl\dnrasl)					p =	1.47325E-11		is										

Abbreviations:

np	*= patient*	*ivc*	*= hot flashes*	*inv*	*= nervousness*	*i*	*= significant change*
vs	*= age*	*inrt*	*= sweating (number)*	*iturs*	*= breast swelling*	*is*	*= highly significant change*
ikg	*= weight*	*idt*	*= sweating (duration)*	*inrass*	*= sexual activity/week*		
		its	*= sleep disorders*	*inrasl*	*= sexual activity/month*		

Table 1a Change in sexual activity under E2/DRSP depending on the period from the menopause

Group test: E_2/DRSP			
No. of persons	Postmenopausal period (years)	No. of intercourses	
		Before treatment	After treatment
8	1	2-3/month	8-12/month
10	2-3	2/month	> 3/month
10	4-5	1/month	2-3/month
3	>5	0/month	1/month

Table 2 Postmenopausal symptoms variation under the treatment 1 mg estradiol + 5 mg dydrogesterone (E2/DGS) control group - statistical analyses

Before treatment											After treatment							
np	vs	ikg	ivc	inrt	idt	its	inv	iturs	inrass	inrasl	dkg	dvc	dnrt	ddt	dts	dnv	dturs	dnrasl
MV	54	64.0	2.00	5.00	4.00	1	2	0		3	64.0	1.00	1.00	2.50	1.00	0	0	4
BN	53	70.0	2.00	5.00	5.00	1	1	0		2	69.0	0.00	1.00	2.00	0.00	0	0	4
MN	54	71.0	2.00	5.00	3.50	1	1	1		2	71.0	1.00	1.00	1.50	0.00	0	1	3
GC	55	57.0	2.00	5.00	3.00	1	2	1		2	57.0	1.00	1.00	1.00	1.00	1	1	3
CN	52	55.0	3.00	6.00	6.00	2	2	1		3	54.0	1.00	3.00	2.50	1.00	1	1	5
CP	49	88.0	3.00	7.00	5.50	2	2	2		4	89.0	1.00	2.00	2.50	0.00	0	1	5
PC	56	66.0	2.00	5.00	4.00	2	1	1		4	65.0	0.00	1.00	1.50	0.00	0	1	7
IG	56	72.0	1.00	3.00	3.50	1	1	0		2	71.5	0.00	1.00	1.50	0.00	0	0	3
AF	55	65.0	1.00	2.00	3.50	1	2	0		2	65.5	0.00	1.00	2.50	0.00	0	0	3
CB	55	68.0	1.00	3.00	2.50	2	1	1		0	66.8	1.00	1.00	2.50	1.00	1	1	1
MF	52	65.0	2.00	5.00	3.00	1	1	1		1	64.0	1.00	1.00	1.00	0.00	0	1	2
ttest(ikg\dkg)					p =	0.11366661		ns										
ttest(ivc\dvc)					p =	6.65918E-05		is										
ttest(idt\ddt)					p =	4.30607E-05		is										
ttest(its\dts)					p =	0.0003766		is										
ttest(inv\dnv)					p =	6.89541E-05		is										
ttest(iturs\dturs)					p =	0.340893132		ns										
ttest(inrt1\dnrt)					p =	3.23235E-06		is										
ttest(inrasl\dnrasl)					p =	5.31018E-05		is										

Abbreviations:

np	*= patient*	*ivc*	*= hot flashes*	*inv*	*= nervousness*	*i*	*= significant change*
vs	*= age*	*inrt*	*= sweating (number)*	*iturs*	*= breast swelling*	*is*	*= highly significant change*
ikg	*= weight*	*idt*	*= sweating (duration)*	*inrass*	*= sexual activity/week*	*ns*	*= insignificant change*
		its	*= sleep disorders*	*inrasl*	*= sexual activity/month*		

Table 2a Change in sexual activity under E2/DGS depending on the period from the menopause

Group control: E_2/DGS			
No. of persons	Postmenopausal period (years)	No. of intercourses	
		Before treatment	After treatment
4	1	2-3/month	3-4/month
5	2-3	2/month	3/month
1	4-5	1/month	2/month
1	>5	0/month	0-1/month

Table 3 Postmenopausal symptoms variation. Statistical analyses between test group and control group

ttest(mkg\dkg)	p =	0.793084685	ns
ttest(mvc\dvc)	p =	0.040636347	s
ttest(mdt\ddt)	p =	0.009274559	is
ttest(mts\dts)	p =	0.325353451	ns
ttest(mnv\dnv)	p =	0.407504765	ns
ttest(mturs\dturs)	p =	0.012601049	is
ttest(mnrt1\dnrt)	p =	0.312455612	ns
ttest(mnrasl\dnrasl	p =	0.218417307	ns

Abbreviations:

s = significant change
is = highly significant change
ns = insignificantly change

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in favour of the E2/DRSP therapy and the sweating episodes duration has also registered a highly significant change in favour of E2/DRSP. As for sleeping disorders and nervousness, the difference between the two types of treatment was insignificant. Breast swelling has registered highly significant changes under E2/DRSP and insignificant changes under E2/DGS (table 2); and the difference in response between the two groups was highly significant. Sexual life judged by the increase in the number of intercourses/month has registered a high increase after a six months treatment for both groups (table 1a and 2a), while the difference between the response to the two therapies has been insignificant (table 3).

Body weight changed under E2/DRSP (-8,9 kg) and insignificantly under E2/DGS (-2.8 kg). Weight loss was insignificant between the two groups.

Comparing the results obtained among the two groups, we notice that the weight change is not significant, while breast swelling is still in favour of the E2/DRSP group. The change in sexual activity is insignificant between the test group and the control group. Statistics show that the change in hot flashes is significant in favour of the E2/DRSP therapy vs E2/DGS.

Discussions

The improvement of sexual performances noticed on both treatment groups can be explained by a better vagina lubrication which gives comfort during the intercourse to the postmenopausal women. Our study confirmed the benefic effects of HRT on precocious symptoms of menopause for both groups. Additionally, we noticed the decrease of their anxiety to the pain and fear of failure of an intercourse. It is known that over 50% of menopausal women have difficulties when communicating to the partner their sexual preferences and insatisfaction(16). The urogenital comfort is essential for sexual life satisfaction and for the quality of women's life. Additionally, for the group treated with E2/DRSP, we noticed a decrease of systolic blood pressure with 1.5 - 5 mmHg, phenomenon that was not noticed for the group treated with E2/DGS. Also, for the test group there was a decrease of breast swelling and a higher weight loss than for group control. This phenomenon can be the result of progestin effect within the used drug, drospirenone derived from spironolactone, with known anti-mineralocorticoid effect.

The severity of menopausal symptoms was positive correlated with the decrease of sexual function in women[17,18,19]. Sleep disorders at menopause will also affect the women's life quality. These disorders are related to the plasmatic level of estradiol and become severe when estradiol is lower than 30 pg/mL[20].

Women undergoing a hormone replacement treatment at menopause have improved their sleep when compared with women with no HRT[22,23]. HRT proved to be efficient for the precocious symptoms of menopause. Eliminating vaginal dryness makes the woman more responsive to sexual life.

Conclusions

Sexuality is considered an important factor in the quality of life. Menopause associates physiological and psychological changes that can have an important influence on women sexuality.

In treating postmenopausal female sexual dysfunctions, HRT is of utmost importance. This increases sexual desire, maintains vaginal lubrication, increases pelvic blood flow, decreases atrophy, eliminates dyspareunia and pain. Also, HRT quickly improves postmenopausal symptoms, prevents osteoporosis and gives security to the women and quality to their lives. ■

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