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THE EVALUATION OF THE EFFECTIVENESS OF PHYTOESTROGENS IN IMPROVING, REDUCTION OR SUPPRESSION OF THE CLIMACTERIC SYMPTOMATOLOGY

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ABSTRACT. Although menopause is a physiological event that occurs in the life of every woman, endocrine changes associated with it can cause major changes in the health status and psychosocial life in a significant number of women. This study evaluates the effectiveness of the phytoestrogens administered as OTC preparations available in pharmacies, concerning the specific menopausal symptoms and is conducted on a total of 230 postmenopausal women randomized into two study groups, group 1-124 women who received different preparations OTC containing phytoestrogens derived from soy, red clover, *Cimicifuga racemosa* or combinations of plants in various doses recommended by the practitioner and group 2-106 women who received no preparation. The assessment of the symptoms was made based on MRS questionnaire (The Menopausal Rating Scale). From the comparative analysis of the two groups, it was found that phytoestrogens facilitate symptom relief and even their extinction, particularly in the first 6 months.

Keywords: phytoestrogens, climacteric symptoms, MRS, Questionnaires

INTRODUCTION

Menopause is a physiological stage in a woman's life that marks the end of the reproductive stage and is characterized by the permanent cessation of menstruation. Menopause is determined by the reduction of the ovarian function and decreased production of estradiol, leading to depletion of the ovarian follicles (Kopper et al 2008, Blake 2006, Al-Eassa 2012). Depriving the body of estrogen determine the appearance of specific symptoms such as the vasomotor, psychological and urogenital and more generalized physical changes such as weight gain, skin and hair thickness and general tiredness, dizziness etc. (Burger et al, 2002, Perez 2011). Approximately 75-80% of women experience menopausal symptom, almost half of them considers the symptoms painful, while 20-30% has severe symptoms (Palacios, 2003, Burger 1996). As a result, their quality of life is affected physically and psychologically, as well as socially.

Hormone replacement therapy, although effective in treating symptoms associated with menopause, standard doses may be associated with numerous adverse effects, of which the most serious are: breast cancer, venous thromboembolism and stroke (Wells et al 2002). Thus, the early 21st century, prescription and use of HT is still controversial (Garefalakis, 2008).

Therefore, alternative therapies that can be used to treat the same symptoms but with fewer side effects are welcome. Numerous studies in this area have brought into attention phytoestrogens, phytochemicals with estrogenic action (Daley 2006). Estrogenic action of these compounds is due to the fact that it has a structural similarity with the 17-beta-estradiol, female sex hormone. Several compounds belonging to

phytochemical classes interact with estrogen receptors. Thus there are three main groups of phytoestrogens: flavonoids and isoflavones, coumestani, with chemical structures close to isoflavones and lignans. Estrogenic isoflavones (genistein, daidzein and their glycosides), are found mainly in leguminous such as soybeans and red clover. Flaxseed are the richest source of lignans, estrogen (enerodiol and enterolactone) and coumestani (coumestrol) derived mainly from soy (Kreijkamp-Kaspers, 2004). Phytoestrogens compete with estradiol for binding and activation of the ER receptor, reducing the effect of estradiol in vivo, in certain circumstances. The effect depends on the dose (both phytoestrogens and estradiol) (Gail, 2001; <http://www.elsevierhealth.com>.)

The main objective of this study is to assess the effects of phytoestrogens available as OTC preparations on menopausal symptoms.

MATERIALS AND METHODS

This study is a prospective one that evaluates, using statistical methods, the effectiveness of phytoestrogens on menopausal symptoms.

We have studied 230 women with menopause characteristic symptoms. Symptomatic progression was monitored for one year, performing the following evaluations: initially at 3 months, at 6 months and at 12 months. The age of the patients ranged between 34-58 years, mostly originating from urban areas (68,70 %).

Inclusion criteria were: naturally menopausal women over 1 up to 5 years and symptoms of moderate to severe without hormone replacement therapy. Exclusion criteria are: women with induced menopause (surgical, chemotherapy or radiotherapy) menopause lasting for over 5 years and naturally menopausal

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women with duration between 1 and 5 years, without associated symptoms or mild symptoms.

Patients were randomized into two study groups, group 1-124 women who received different OTC preparations that contain phytoestrogens derived from soy, red clover *Cimicifugacemosa* or plant combinations, in different doses recommended by the practitioner and group 2 - 106 women who received no preparation.

Symptomatology evaluation was based on MRS questionnaire (The Menopausal Rating Scale). The questionnaire contains three items: somatic-vegetative symptoms, psychological symptoms and urogenital symptoms (Klaas H, 2004).

The distribution of the patients in the two groups, depending on the intensity of symptoms is presented in table 1.

Table 1. The distribution of the cases according to the severity of initial symptom

	Group 1		Group 2	
	No	%	No	%
Somatic-vegetative symptoms				
Light	28	22,58	22	20,75
Moderated	38	30,65	32	30,19
Severe	58	46,77	52	49,06
Psychological symptoms				
Light	24	19,35	20	18,87
Moderated	36	29,03	26	24,53
Severe	64	51,61	60	56,60
Urogenital symptoms				
Light	24	19,35	20	18,87
Moderated	46	37,10	42	39,62
Severe	54	43,55	44	41,51

Initially, there were no significant differences between the two groups in terms of somatic vegetative

($p = 0.871$), physiological ($p = 0.528$) and of the urogenitalsymptoms ($p=0,782$).

In both groups were predominant the patients with moderate or severe symptoms, regardless of the type of symptoms (Figure 1).

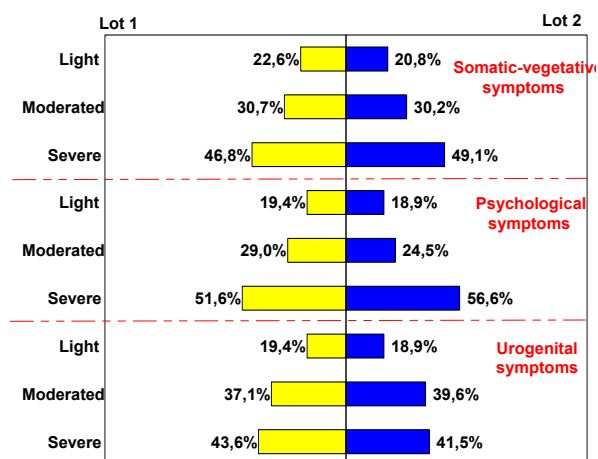


Fig.1. The distribution of the cases according to the severity of symptoms at the initial assessment

Study Design

The treatment with phytoestrogens was started immediately after randomization and was administered for a period of six months. Subjects were administered phytoestrogens as dietary supplements based on extracts of soy, red clover, *Cimicifuga racemosa* or as combinations of various plants. The evaluation was achieved initially at three months, at six months, six months after treatment cessation respectively 12 months after the onset of the study.

RESULTS AND DICUSSIONS

The evaluation of the treatment efficiency was performed by subjective assessment of the individual patient with the questionnaire.

The evolution of the somatic-vegetative symptoms (hot flashes, heart complaints, sleep disorders, joint and muscle pain) during treatment and at 6 months thereafter, at the 2 studied groups, are presented in Table 2.

Table 2. Somatic-vegetative symptoms evolution

	Initially		At 3 months		At 6 months		At 12 months	
	No.	%	No.	%.	No.	%	No.	%
Group 1								
Asymptomatic			16	12,90	44	35,48	54	43,55
Light	28	22,58	30	24,19	30	24,19	20	16,13
Moderated	38	30,65	42	33,87	28	22,58	30	24,19
Severe	58	46,77	36	29,03	22	17,74	20	16,13
Group 2								
Asymptomatic			4	3,77	26	24,53	38	35,85

Light	22	20,75	26	24,53	24	22,64	12	11,32
Moderated	32	30,19	32	30,19	16	15,09	24	22,64
Severe	52	49,06	44	41,51	40	37,74	32	30,19

The absence of the somatic-vegetative symptoms was recorded from the third month, in both groups. The percentage of the patients without somatic vegetative symptoms is significantly higher in group 1, at the evaluation at 3 months (12.90% versus 3.77%, p

<0.001) and 6 months (35.48% versus 24.53%, p = 0.011), but not significant at 12 months (43.55% versus 35.85%, p = 0.108), after 6 months after treatment cessation (figure 2).

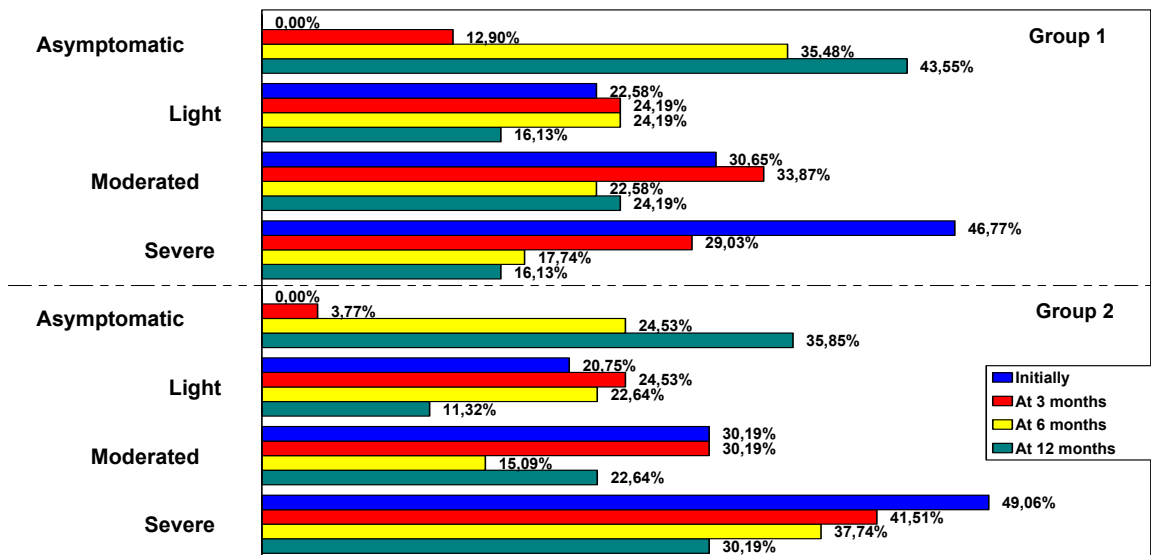


Fig.2. Somatic-vegetative symptom evolution

Psychological symptoms evaluated in the MRS are: depression, irritability, anxiety. Their evolution was

monitored throughout the study and is presented in Table 3.

Table 3. Psychological symptom evolution

	Initially		At 3 months		At 6 months		At 12 months	
	No.	%	No.	%	No.	%	No.	%
Group 1								
Asymptomatic			10	8,06	38	30,65	56	45,16
Light	24	19,35	40	32,26	34	27,42	30	24,19
Moderated	36	29,03	34	27,42	28	22,58	18	14,52
Severe	64	51,61	40	32,26	24	19,35	20	16,13
Group 2								
Asymptomatic			6	5,66	28	26,42	40	37,74
Light	20	18,87	34	32,08	18	16,98	14	13,21
Moderated	26	24,53	14	13,21	14	13,21	10	9,43
Severe	60	56,60	52	49,06	46	43,40	42	39,62

Also in the case of psychological symptoms, their disappearance, that their improvement at the 3 assessments, there was recorded a higher percentage at group 1 compared to group 2, but with no significant

differences (at 3 months: 8.06 versus 5.66%, p = 0.299, 6 months: 30.65 vs. 26.42%, p = 0.337; 12 months: 45.16% vs. 37.74%, p = 0.126).

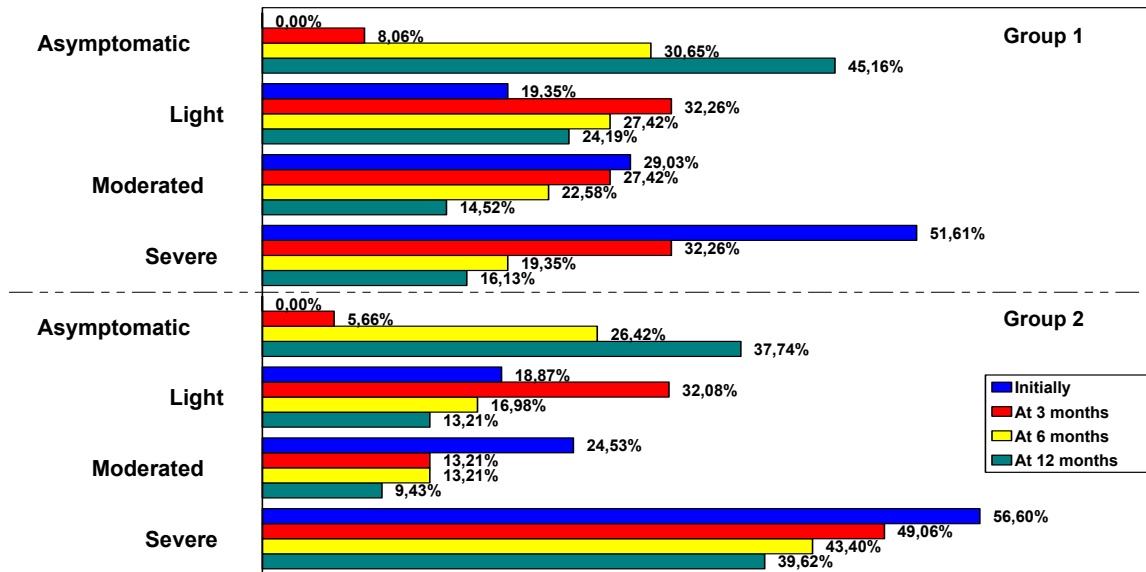


Fig. 3. Psychological symptoms evolution

The evolution of the urogenital symptoms (sexual problems, urination complaints, vaginal dryness), at the 2 groups during the study, is presented in Table 4.

Table 4. Urogenital evolution

	Initially		At 3 months		At 6 months		At 12 months	
	No.	%	No.	%	No.	%	No.	%
Group 1								
Asymptomatic			14	11,29	38	30,65	46	37,10
Light	24	19,35	32	25,81	26	20,97	32	25,81
Moderated	46	37,10	32	25,81	24	19,35	22	17,74
Severe	54	43,55	46	37,10	36	29,03	24	19,35
Group 2								
Asymptomatic			6	5,66	22	20,75	39	36,79
Light	20	18,87	24	22,64	24	22,64	13	12,26
Moderated	42	39,62	32	30,19	16	15,09	12	11,32
Severe	44	41,51	44	41,51	44	41,51	42	39,62

The disappearance of the urogenital symptoms was recorded at a significantly higher percentage in the first 6 months at group 1 (11.29% versus 5.66%, $p = 0.014$,

respectively 30.65% versus 20.75%, $p = 0.015$), but slightly higher at 12 months (37.10% versus 36.79%, $p = 0.948$).

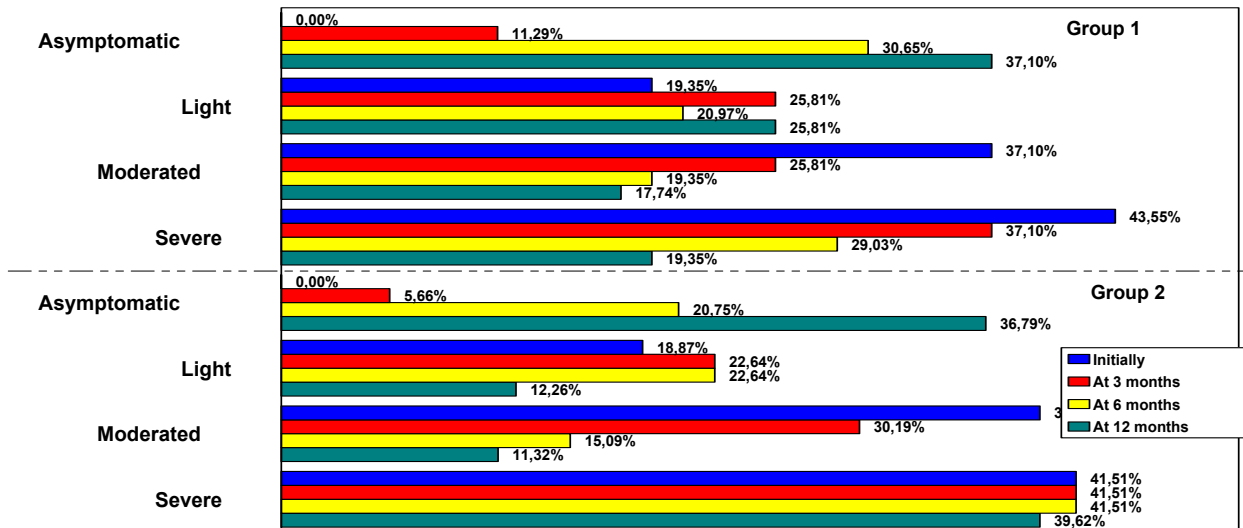


Fig.4. Urogenital symptoms evolution

CONCLUSIONS

Specific menopausal symptoms, contained in MRS assessment instruments used in this study, have responded to the treatment with phytoestrogens.

From the comparative analysis of the two groups, it can be concluded that phytoestrogens facilitate the disappearance, respectively the relief of symptoms, but these effects persist after treatment interruption.

Significant effects of phytoestrogens are recorded on somatic-vegetative and urogenital and less on the psychological symptoms.

Some symptoms such as irritability, hot flashes, vaginal dryness and sexual problems suffered significant changes in patients from group I.

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