THERAPY WITH CLIMARA IN SURGICAL MENOPAUSE

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THERAPY WITH CLIMARA IN SURGICAL MENOPAUSE (Abstract): Hormone replacement therapy in surgical menopause is a prophylactic measure that is used for preventing the short and long term effects of the lack of ovarian hormones. Material and methods: This is a retrospective study conducted between 2004 and 2006 at the Iasi “Elena-Doamna” Hospital of Obstetrics and Gynecology on two series of patients: 46 patients with surgical menopause who received treatment with transdermal estradiol (Climara), and 20 surgical menopause patients not receiving this treatment who served as controls. Results: A decreases in the average levels of total cholesterol, triglycerides and LDL cholesterol and an increase in the HDL cholesterol level were identified in the series receiving Climara compared to the controls. The climacteric symptoms improved in the patients receiving treatment. Conclusions: Transdermal therapy with estradiol (Climara) is an effective method of treatment in surgically induced menopause. Key words: SURGICAL MENOPAUSE, CLIMARA, CARDIO-VASCULAR DISEASE

Surgically induced menopause by bilateral oophorectomy is followed by short and long term effects: cardiovascular disease and osteoporosis. Cardiovascular diseases are one of the main causes of illness and death for women in industrialized countries (1,2).

Epidemiological studies (3) show that the incidence of cardiovascular diseases increases in postmenopausal women The risk for ischemic heart diseases is higher in women with ovariectomy, and hormone replacement therapy reduces this risk (4, 5). Studies show that a decrease in ovary function from bilateral ovariectomy increases the risk of myocardial infarction and the use of estrogens reduces this risk (6,7,8). The positive effect of estrogenic therapy with estradiol on cardiovascular diseases was proved ever since many years.

The favorable effect of estrogenic therapy in women with surgical menopause is due to the action on plasma lipoproteins and endothelial function (9, 10, 11).

MATERIAL AND METHODS

Our study is a retrospective study carried out at the Iasi “Elena-Doamna” Hospital of Obstetrics and Gynecology during 2004-2006. 46 patients with bilateral oophorectomy received transdermal therapy with 3.9 mg estradiol (Climara) (series I) and 20 patients with surgical menopause
not receiving this treatment served as control group (series II).

The following data were recorded: age, socio-economic status, personal history, type of intervention, symptoms, and biological blood levels during the research. A standard file was used to record all changes noticed during therapy.

The collected data were transferred to EXCEL and SPSS 17.0 databases and processed with the predefined statistical functions. For the statistical analysis (ANOVA) both descriptive and analytical methods were used. The statistical indicators used were:

- Mean value: simple arithmetic mean, median, module;
- Dispersion: standard deviation, variance.

Data were presented with 95% confidence intervals, and for testing the differences the $\chi^2$ and t-Student’s t-tests were used.

The correlation between parameters was analyzed by using the Pearson’s correlation coefficient ($r$), which ranges between $-1 < r < +1$, indirect correlation if the values are negative, and direct correlation if the values are positive, and its square form ($R^2$).

**RESULTS**

**Age-distribution.** After comparatively analyzing patients’ age in the two study series and applying the ANOVA test, the following were noticed:

- In the series of women with surgical menopause treated with Climara (series I), the age varied between 35 and 60 years, with a moderate variance in the range of values (11.41%); the mean age of this series was 49.22;
- In the series of women with surgical menopause without treatment (series II), the age ranged between 40 and 60, with a slightly reduced variance in the range of values compared to series I (10.50%); the mean age of this series was 50.40.

**Rural-urban distribution** was homogenous for both study series – the patients came mainly from urban areas: series I – 89.1%, series II – 70% ($\chi^2=2.42$; GL=1; $p=0.119$).

**Distribution of patients according to marital status** showed a higher percentage of married women: series I (95.7%) and series II (100%), no other significant differences between the two series being recorded ($\chi^2=0.03$; GL=1; $p=0.868$).

**Distribution of patient according to educational level** showed statistically significant differences between the two series ($\chi^2=3.95$; GL=1; $p=0.047$), in series I the percentage of women with high school education being significantly higher (89.1% vs. 65%).

**Case history**

The distribution of patients according to body mass index showed that there were more overweight women in the series receiving Climara (45.7% vs 35%), and no obese women in series II (19.5% vs 0%), this distribution being statistically significant ($\chi^2=7.18$; GL=2; $p=0.028$).

The average BMI values showed significant differences ($t=4.15$; GL=64; $p<0.001$) and according to that series I was classified as being made of overweight women while series II was generally made of normal weight women.

The average blood pressure was normal for both series I (13.1/7.98 mmHg) and series II (13/8 mmHg).

Case history data revealed:

- Series I: hemorrhagic uterine fibro-
ma (71.7%); obesity (15.2%); dysfunctional hemorrhage (10.9%);

- Series II: hemorrhagic uterine fibroma (50%); varices (45.0%); uterine fibroma (25%); AHT (25%); chronic cervicitis (20%).

Most women were menopausal for 1-4 years, 50% in both study series, followed by those menopausal for less than 1 year (32.6% in series I and 45% in series II), distribution of frequency which is not statistically significant ($\chi^2=2.16$; GL=2; p=0.340).

**Symptoms**

**Hot Flushes:** - in series I, when the study was initiated 73.9% of the patients were experiencing hot flushes, its frequency decreasing to 41.3% after 12 months, with alternating periods of hot flushes, and at the end of the study this symptom was present in only 8.7% of the cases ($\chi^2=40.53$; GL=3; p<0.001);

- at the beginning of the study hot flushes were experienced by 80% of the women in series II, its incidence significantly decreasing with every subsequent medical check up, being present in about 30% of the women when last monitored ($\chi^2=10.56$; GL=3; p=0.014).

**Migraine:** - in series I, at the beginning of the study, 28.3% of the patient complained of migraine, the same percentage being recorded after 6 months of therapy but with migraine-free intervals in 19.6% of the women; at the end of the study this symptom was reported by 4.3% of the patients ($\chi^2=11.33$; GL=3; p=0.010);

- in series II, at the beginning of the study in 50% of the women had migraines their incidence decreasing after 2 years below 10% ($\chi^2=13.37$; GL=3; p=0.004).

**Instability /agitation:** - in series I, instability/agitation was rarely found at the initial examination investigation, after one year it being still present in only one patient ($\chi^2=2.23$; GL=3; p=0.525);

- in series II, at the beginning of the study, instability/agitation was found in 10% of the women; after 6 months 50% of the patients in this series presented this symptom in 40% of them alternating with symptom-free interval; at the end of the study instability/agitation was found in 25% of the patients in this series ($\chi^2=7.99$; GL=3; p=0.046).

**Insomnia:** - in series I insomnia significantly decreased in frequency during the study interval, and varied in intensity from 43.5% to 6.5% ($\chi^2=19.20$; GL=3; p=0.0002);

- in series II, insomnia was present in about 30% of the cases throughout the study ($\chi^2=0.17$; GL=3; p=0.982).

**Libido:** - in series I, after 6 months monitoring, 35% of the patients had normal libido, and at the end of the study 37% of the patients ($\chi^2=20.05$; GL=3; p=0.0002);

- in series II, libido was a very rare symptom ($\chi^2=1.04$; GL=3; p=0.792).

**Pollakiuria:** - series I: pollakiuria was met in 8.7% of the cases at the beginning of the study, but its frequency diminished until it disappeared at the end of the study ($\chi^2=4.16$; GL=3; p=0.245);

- in series II, pollakiuria was present every now and then in about 20% of the cases throughout the study ($\chi^2=0.28$; GL=3; p=0.965).

**Exercise urinary incontinence:** - this symptom was met in 4.3% of series I patients at the beginning of the study and its frequency diminished until it disappeared at the end of the study ($\chi^2=2.26$; GL=3; p=0.520);

- in series II, IUE was a symptom reported intermittently by 1-2 patients
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$\chi^2 = 0.64; \text{GL} = 3; p = 0.887$.

**Biochemical parameters**

**Blood glucose level:** The average blood glucose levels were initially significantly higher in series I (p<0.05). During their monitoring, a significant decrease was recorded in series I, while in series II patients the levels kept increasing so that at the end of the study significantly higher blood glucose levels were recorded in series II (p<0.05).

**Triglycerides:** During the monitoring, the beneficial effect of the treatment with Climara was evident, the average triglyceride levels being significantly lower when compared with those in series II patients (p<0.001) in which triglyceride level significantly exceeding the reference range (figure 1).

![Fig. 1. The evolution of average triglycerides levels in the study series](image)

**Total cholesterol:** All along the monitoring, the average total cholesterol levels in series I women decreased significantly below the reference range, while in series II they kept increasing slightly exceeding the upper reference range. The average total cholesterol levels showed significant differences between the two series (p<0.05), emphasizing the beneficial effect of the treatment with Climara (figure 2).

![Fig. 2. The evolution of average total cholesterol levels in the study series](image)
**LDL cholesterol:** The average LDL cholesterol levels were significantly higher at the beginning of the study in series I when compared with those recorded in series II (p<0.05), but during the monitoring we noticed the beneficial effect of the treatment with Climara expressed in significant decreases in LDL-cholesterol levels, while in the series without treatment its average levels increased in time (p<0.001) (figure 3).

Fig. 3. The evolution of the average LDL cholesterol levels in the study series

![Graph showing LDL levels](image)

**HDL cholesterol:** The average HDL cholesterol levels have increased in both study series, but in the patients treated with Climara, all along the monitoring the average values were significantly higher (p<0.001).

**DISCUSSION**

One of the most important roles of hormone replacement therapy is that it eliminates the symptoms of menopause, especially of the vasomotor and urogenital symptoms that appear immediately after oophorectomy (12).

The long term benefit is that it lowers the risk of developing cardiovascular diseases. The protective cardiovascular effect of estrogen therapy manifests through favorable effects on lipid metabolism (13).

In our study comparing the menopause symptoms in the two patient series the following are evident:

- at baseline:
  - no significant differences in the investigated symptoms (p>0.05);
- at 24 months:
  - series I: libido was significantly more frequent (p=0.017) and hot flushes disappeared (p<0.001).
  - series II: significantly more hot flushes (p=0.065), associated with irritability/agitation (p=0.012), insomnia (p=0.030) and polakiuria (p=0.041).

As to biochemical parameters at 24 months: - triglycerides, total cholesterol and LDL cholesterol levels decreased significantly (p<0.001) in the patients on Climara treatment;

- HDL cholesterol levels have increased in both study series. In series I patients the levels were significantly higher (p<0.001), demonstrating the cardiovascular protective effect of Climara treatment.

No patient discontinued therapy at two years.

**CONCLUSIONS**

The clinical benefits of hormone replacement therapy in the elimination of
menopause symptoms are widely accepted, as proved by our study in which the patients receiving Climara became menopause-symptom free.

Long term prevention of cardiovascular diseases is an important benefit. In series I patients significant decreased in triglycerides, total cholesterol and LDL cholesterol levels, and increases in HDL cholesterol levels, with protective cardiovascular role, were found.

The treatment must be initiated as soon as possible.

Climara administrated in surgical menopause women resulted in a short and long term improvement in their quality of life. Climara is well tolerated by women in surgical menopause.

REFERENCES