

The influence of hormonal therapy on postmenopausal women with diabetes mellitus

Abstract

Aim. At many postmenopausal women the diabetes mellitus (DM) could appear. This study was designed to test whether hormonal therapy (HT) favorably affects changes in postmenopausal women with DM. **Methods.** The study was composed of 190 postmenopausal women from CI Parhon, National Institute of Endocrinology Bucharest who were randomly divided as follows: Group 1 (n=120) placebo, who refused the HT and Group 2 (n=70) those who received HT. The patients from Group 1 were divided in patients with DM (n=21) and patients with normal blood sugar (n=99). The women from the 2nd Group were divided into women with DM (n=12) and women with normal blood sugar (n=58). The age at menopause installation, body mass index (BMI), glutamic-oxaloacetic transaminase (GOT), glutamate-pyruvate transaminase (GPT), smoking and alcohol consumption were analysed.

Results. The age at menopausal installation in the 1st Group had a mean values of 47.52 years for those with DM and 46.88 years for those with normal blood sugar. In the 2nd Group, the mean age was 44.33 years for those with DM and 44.91 years for those with normal blood sugar. The BMI showed that in the 2nd Group, the values were lower and the patients with DM had a normal BMI comparing with the 1st Group. GOT values showed to be in normal range for both groups. Moreover, the values from the 2nd Group with HT and DM showed to be much lower than Group 1, without HT. The GPT values were in accordance with GOT values. Smoking was evaluated in terms of smokers and non-smokers as follows: in the 1st Group, 10 (47.6%) patients with DM and 13 (13.13%) with normal blood sugar were smokers. From the 2nd Group only 4 (33.3%) with DM and 34 (58.62%) with normal blood sugar were smokers. From the alcohol consumption point of view, from the 1st Group all the patients 21 (100%) with DM consumed alcohol and only 87 (87.8%) with normal blood sugar consumed. From the 2nd Group, 6 (50%) with DM consumed alcohol and only 19 (32.7%) with normal blood sugar consumed. **Conclusions.** HT intervention significantly reduced the analysed parameters, in terms of BMI, GOT and GPT in postmenopausal women with DM. Smoking and alcohol consumption showed to present no changes induced by HT. Therefore, more data is needed to test whether these parameters could be influenced by HT in postmenopausal women with or without DM.

Keywords: estrogen, therapy, menopause, diabetes mellitus, blood glucose

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Introduction

Nowadays, many women may experience different changes especially after menopause including the body fat mass and diabetes mellitus (DM)⁽¹⁾. The risk for such disorder like DM is mainly the loss of estrogen. In this regard, the use of estrogen at women in postmenopausal period is believed to have beneficial effects, especially on glucose status but also on other blood parameters⁽²⁾. Although the data are still scarce, these features suggest further a reduction in the incidence of DM. Until present some studies showed that a replacement therapy like the hormonal one could increase insulin resistance and glucose tolerance^(3,4). Other research studies have shown little benefit of hormonal therapy (HT) or even negative effects^(5,6). Many previously studies which investigated the HT on body weight and glucose level were limited by the number of patients⁽⁷⁾. Therefore, the present study proposes to test whether the HT intervention had beneficial effects on postmenopausal women, especially on those with DM.

Methods

Between 2012 and 2015, a total of 190 postmenopausal women from CI Parhon, National Institute of Endocrinology Bucharest, Romania were enrolled in the study. Postmenopause was defined as a minimum of 12 consecutive months

of amenorrhea. The women were randomly divided into Group 1 (placebo), who refused the HT (n=120) and Group 2, those who received HT (n=70). The patients from Group 1 were divided in patient with DM (n=21) and patients with normal blood sugar (n=99). The women from the 2nd Group were divided into women with DM (n=12) and women with normal blood sugar (n=58). The age at menopause installation, BMI, GOT, GPT, smoking and alcohol consumption were analysed.

Blood samples were collected in the morning after a 12-h overnight. Serum GOT and GPT levels were determined by colorimetric method described by Ritman and Frankel⁽⁸⁾. BMI was calculated as the weight in kilograms divided by the square of the height.

Exclusion criteria in both groups included hypertension (systolic blood pressure ≥ 140), anemia, renal insufficiency, evidence of significant liver disease and hysterectomy. The inclusion criteria were as follows: perimenopausal and menopausal status based on anamnesis following the installation age or after follicle stimulating hormone level (> 25 UI/L).

All postmenopausal women were randomly allocated HT (i.e. Climene (2 mg estradiol valerate micronized and 1 mg cyproterone acetate micronized), Estraderm and Dydrogesteron (estradiol patch, TTS 25,50,100 mg), Livial (2.5 mg tibolone), Premarin (0.625 mg conjugated estrogens),

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Kliogest (1 mg estradiol/norethisterone acetate), Femoston (1mg estradiol or a combination of 1mg estradiol and 10 mg hydrogesterone), one each day or the placebo.

Only the patients hosted in 2015 in the Institute gave written informed consent. The protocol was approved by the CI Parhon, National Institute of Endocrinology Bucharest from Romania.

Statistical analysis

The features were compared between two groups using CHI-square test. Simple regression analysis was performed to assess the linear relationship between study parameters and descriptive statistics were used for baseline data. Results were considered significant at $p < 0.05$. All p values were 2-tailed.

Results

The age at menopausal instalation in the 1st Group had a mean age of 47.52 ± 2.2015 years for those with DM and 46.88 ± 3.339 years for those with normal blood sugar. In the 2nd Group, the mean age was 44.33 ± 3.750 years for those with DM and 44.91 ± 4.766 years for those with normal blood sugar (Figures 1 and 2).

The women from the 1st Group, without HT had a mean BMI of 32.00 ± 4.231 kg/m² for those with DM ($p < 0.001$) and 28.83 ± 5.287 kg/m² for those with normal blood sugar. In the 2nd Group, with HT the mean BMI was 23.58 ± 4.395 kg/m² for those with DM and 29.04 ± 4.242 kg/m² for those with normal blood sugar. Therefore, it can be seen the fact that in therapy Group (Group 2), the BMI was lower and the

patients with DM were having a normal BMI comparing with the 1st Group in which the patients were having 1st degree of obesity (Figures 3 and 4).

The women from the 1st Group had GOT values of 36.143 ± 7.23 mg/dl for those with DM and 39.121 ± 14.81 mg/dl for those with normal blood sugar. In the 2nd Group, it was registries values of 33.250 ± 16.16 mg/dl for those with DM and 36.931 ± 16.63 mg/dl for those with normal blood sugar. Although GOT values of both groups showed to be in normal range, the values from the 2nd Group with HT and DM showed to be much lower than Group 1, those without HT (Figures 5 and 6).

In the case of GPT, the values were in accordance with the GOT values. Therefore, the 1st Group had values of 11.381 ± 1.244 mg/dl for those with DM and 34.589 ± 24.99 mg/dl for those with normal blood sugar. In the 2nd Group, it were registries values of was 37.583 ± 13.681 mg/dl for those with DM and 34.845 ± 13.177 /dl for those with normal blood sugar (Figures 7 and 8).

The postmenopausal women were further analysed by smoking and non-skoking status. It was seen that in the 1st Group, the patients who are smoking were 10 (47.6%) with DM and 13 (13.13%) with normal blood sugar. From the 2nd Group 4 (33.3%) with DM and 34 (58.62%) with normal blood sugar (Figures 9 and 10).

In the case of alcohol consumption, the patients who responded positive for the consumption were selected as follow: from the 1st Group, the group without HT, all the patients 21(100%) with DM consumed alcohol and only 87 (87.8%)

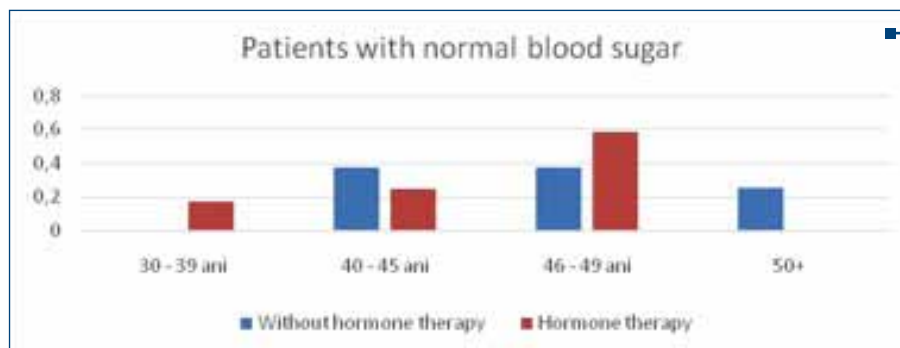


Figure 1. The distribution of the age at menopause instalation with or without HT and normal blood sugar

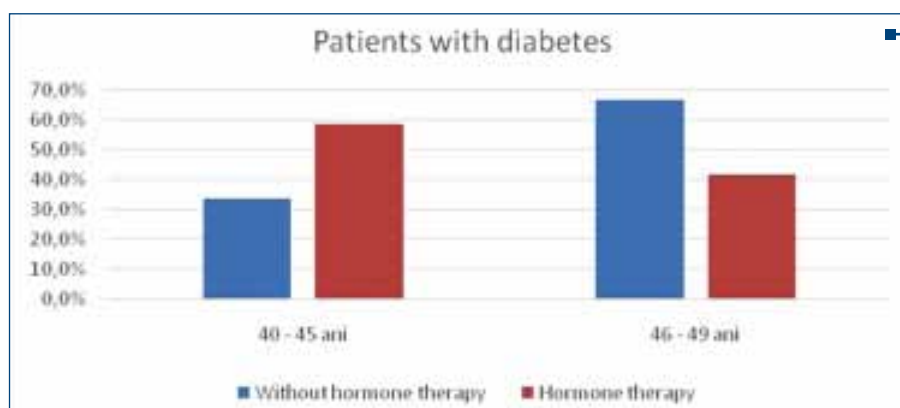


Figure 2. The distribution of the age at menopause instalation with or without HT and DM

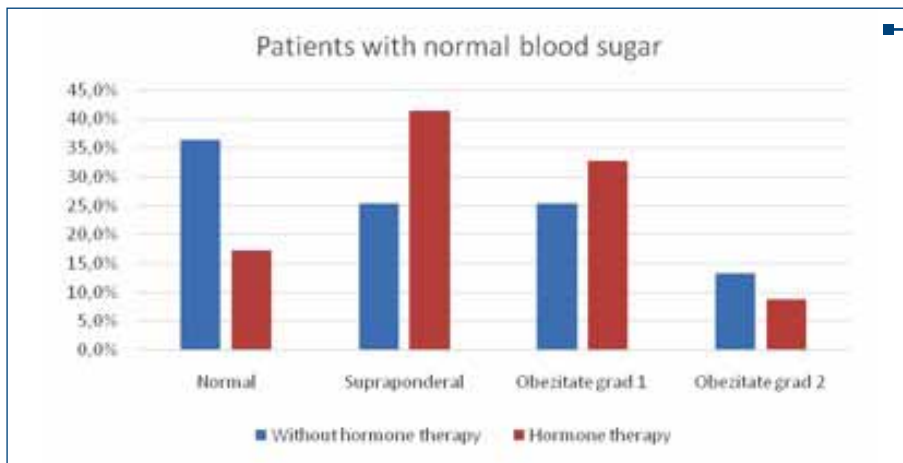


Figure 3. The distribution of BMI at the women with or without HT and normal blood sugar

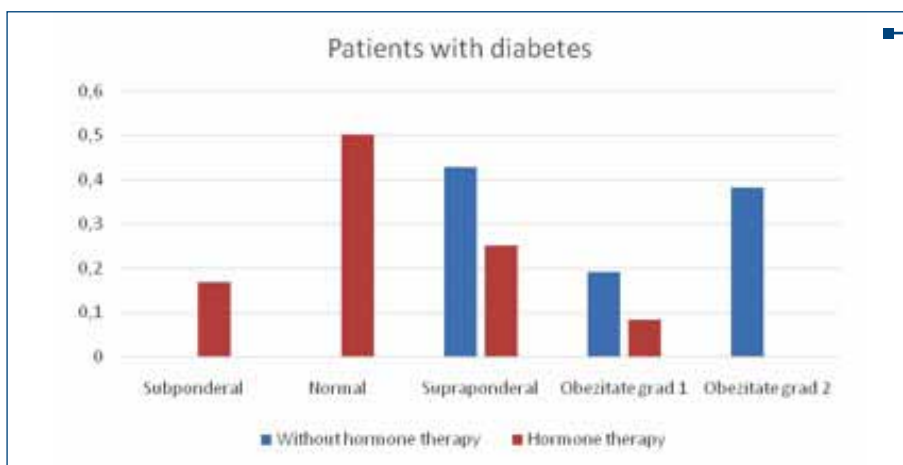


Figure 4. The distribution of BMI at the women with or without HT and DM

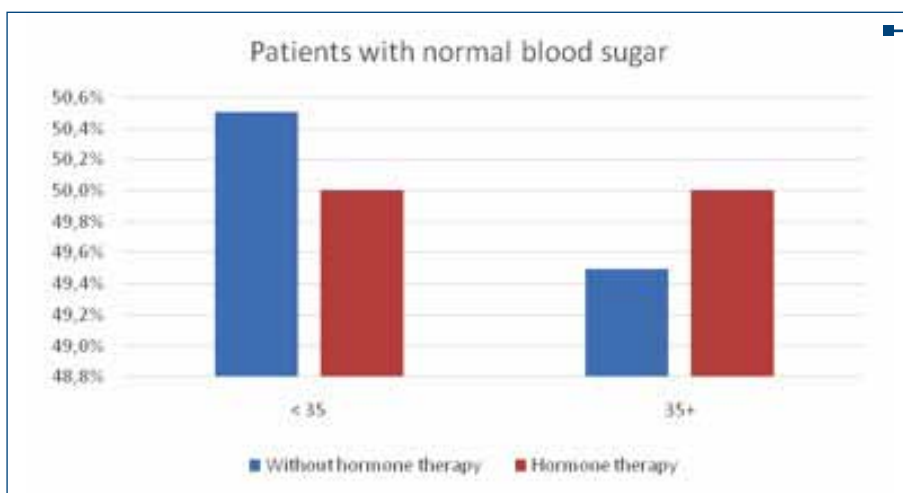


Figure 5. The distribution of GOT at the women with or without HT and normal blood sugar

with normal blood sugar consumed alcohol. From the 2nd Group with HT, 6 (50%) with diabetes consumed alcohol and only 19 (32.7%) with normal blood sugar consumed alcohol (Figures 11 and 12).

Discussion

Many previous studies which determined the effects of HT on postmenopausal women were limited by small number of patients. One study indicated that continuously HT ne-

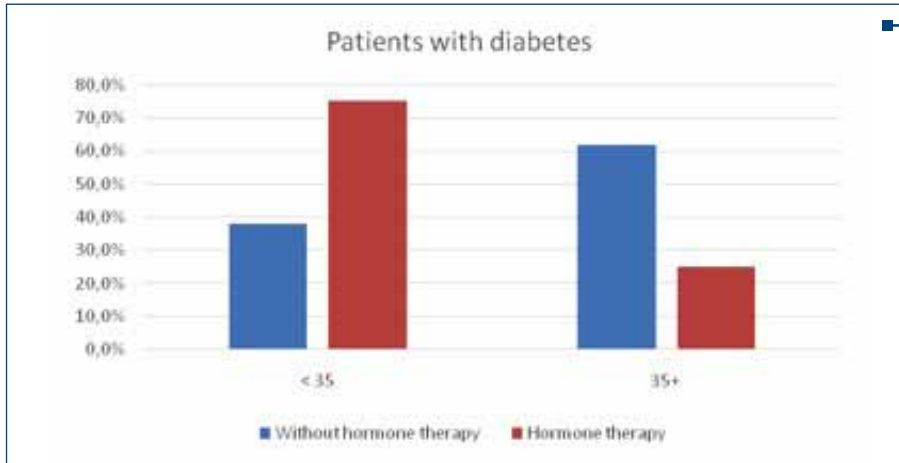


Figure 6. The distribution of GOT at the women with or without HT and DM

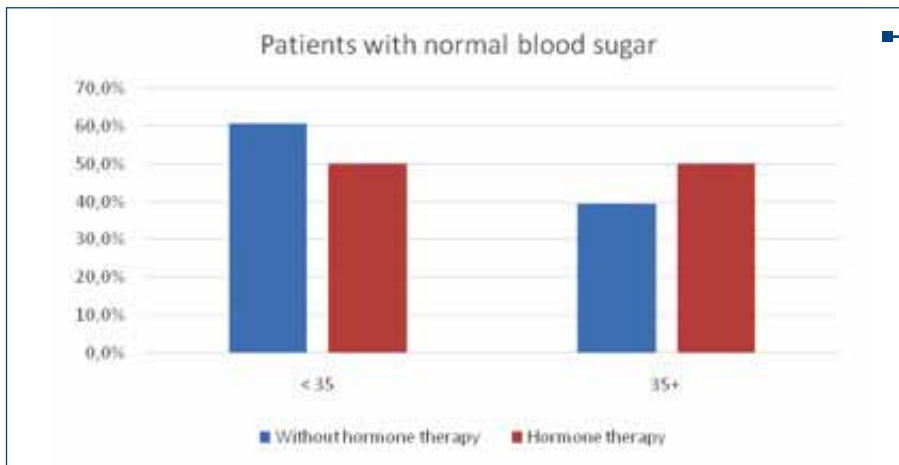


Figure 7. The distribution of GPT at the women with or without HT and normal blood sugar

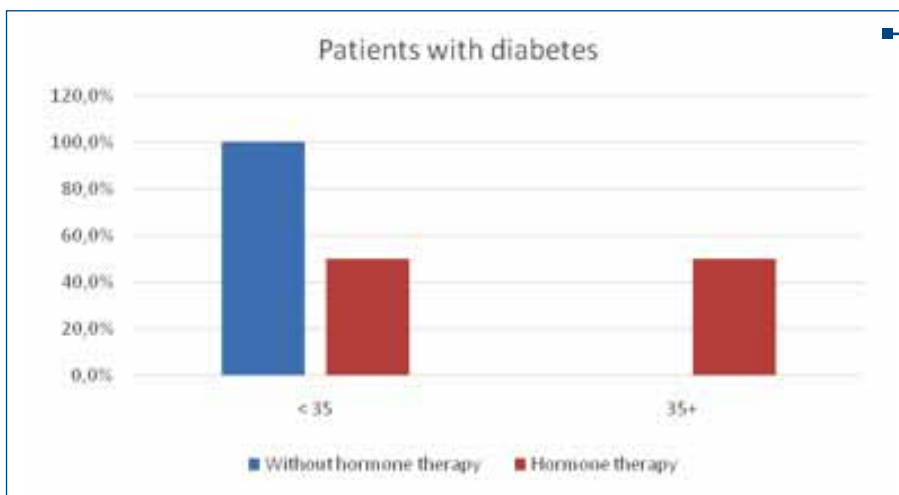


Figure 8. The distribution of GPT at the women with or without HT and DM

ither decreases nor increases early postmenopausal weight gain. Interestingly, the same study showed that HT could minimize the shift the hormonal balance between gynoid to android⁽⁹⁾. Another prospective study found that meno-

pausal HT significantly reduced fat mass accumulation in women⁽¹⁰⁾. Another study reported that waist circumferences were much smaller in long-term HT users than in without HT with similar age and BMI⁽¹¹⁾.

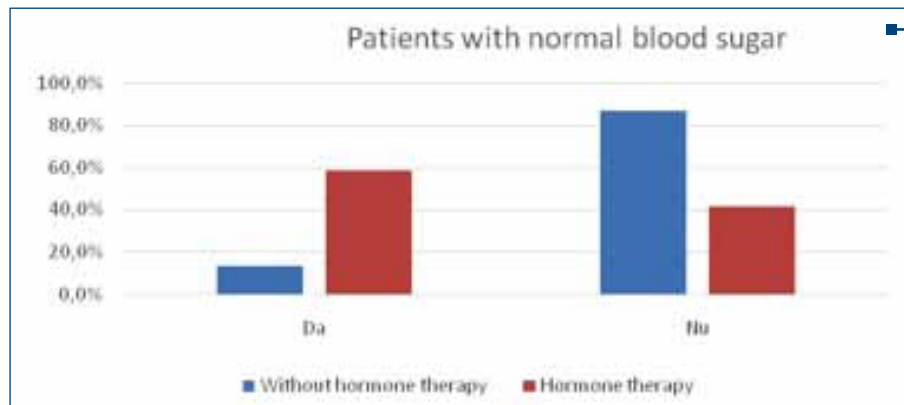


Figure 9. The distribution of smoking at the women with or without HT and normal blood sugar

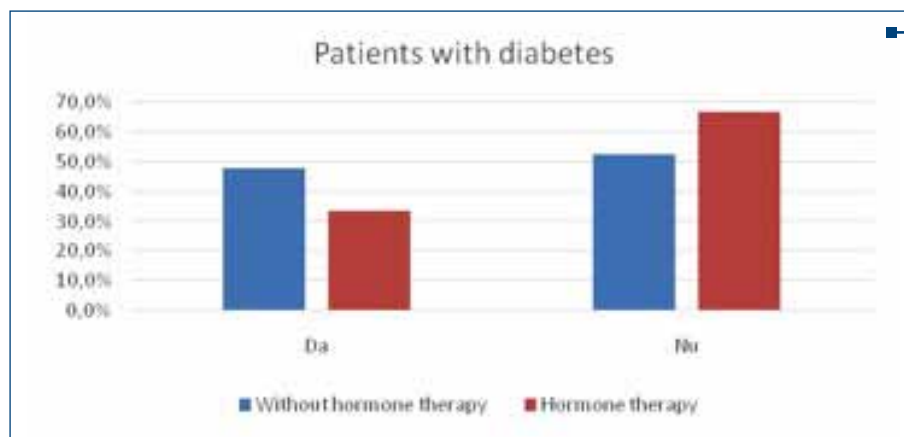


Figure 10. The distribution of smoking at the women with or without HT and DM

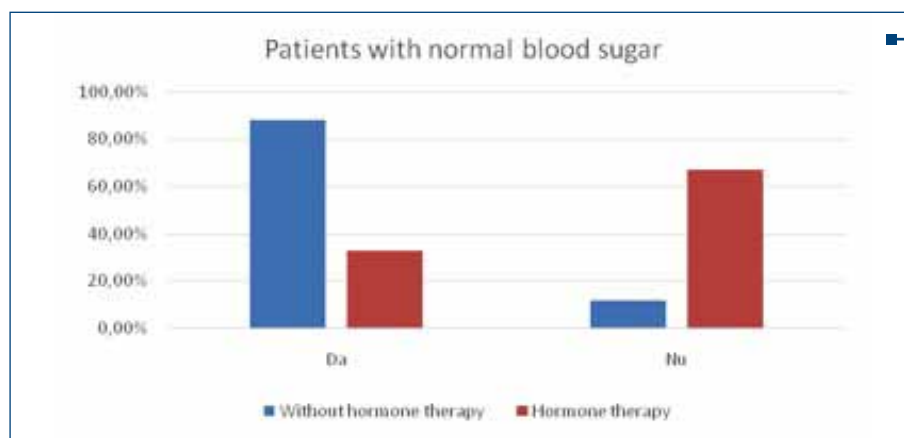


Figure 11. The distribution of alcohol consumption at the women with or without HT and normal blood sugar

A recent trial, which excluded women who reported a diagnosis of diabetes at baseline, found that estrogen and progesterone intervention reduced the incidence of DM⁽¹²⁾. This reduction could be explained from a decrease in insulin resistance based on the modified homeostasis⁽¹³⁾.

The major strengths of the present study were the relatively large sample size, the randomized and placebo-controlled design, the longer duration of follow-up and postmenopausal women. Our findings showed to be in accordance with the

previous studies. All the women from both groups presented normal values of ages at menopause installation being included in postmenopausal period. Our results suggested further that HT had a beneficial effect on BMI. In this respect, the women from the HT group had a lower BMI, especially those with diabetes in comparison with those from the group without HT. To gain more insight into the mechanisms of the HT effects of estrogen in diabetic postmenopausal women, we measured parameters like GOT and GPT which according

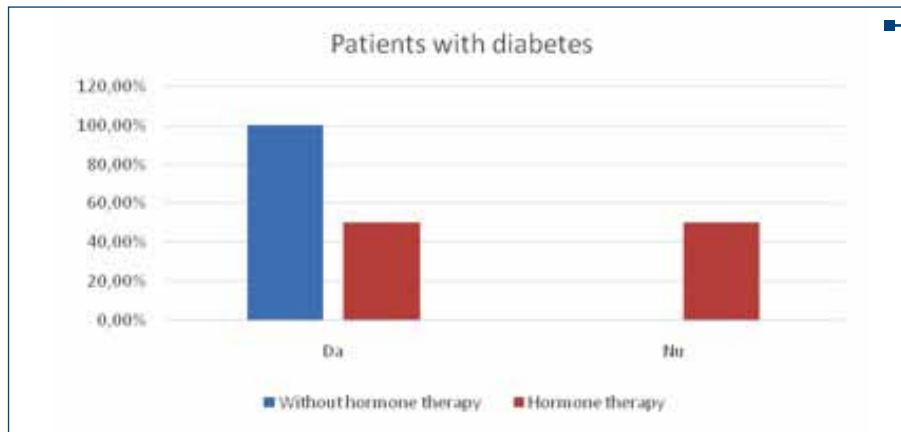


Figure 12. The distribution of alcohol consumption at the women with or without HT and DM

to other clinical studies, are potentially affected by estrogen in healthy postmenopausal women^(14,15). The blood analysis, included GOT and GPT transaminases sustained the beneficial effect of HT on postmenopausal women. Therefore, the values of GOT from the group with HT and diabetes showed to be much lower than those without HT and diabetes (i.e. 33.250 mg vs. 36.143 mg). In the case of GPT, the group with HT showed to have the lowest values in comparison with the group without HT and diabetes (i.e. 37.583 mg vs. 11.381 mg). The results concerning the smoking condition and alcohol consumption are not showing a support of the HT. Therefore, in the group with HT the percentage of the normal blood sugar was lower (i.e. 33.3%) at women with DM comparing with women from the group with normal blood sugar (i.e. 47.6%). The consumption of alcohol seems to have similar values with the smoking conditions (50% from the group with HT vs. 100% without HT and DM).

The counseling of the women at menopause with DM represents a clinical approach and the utilization of HT should be carefully individually evaluated. At the women taken into the study it was administered the lowest efficient dose of HT. The type of estrogen, the way and the time of administration had been close evaluated and discussed taking into consideration the associated risk factors, treatment objectives

and the wish of the patient. Having in the view the fact that other studies showed that dydrogesterone improves the resistance to insulin, and that medroxyprogesterone acetate it worse it^(6,12,14,16,17), we prefer the use of Duphaston which contain the dydrogesterone as progesterone. HT seems to confer a good protection against DM development at the women from the perimenopause period. Although, the HT role in primary or secondary prevention of a DM remains at the present still in debate, it should not be utilized for this indication in the first place. In this case, a healthy still life for example stopping the smoking, the reduction of stress and of alcohol consumption, regulate physical exercises, a healthy alimentation and the loss of weight seems to contribute at the decreasing DM risk at this age group. Therefore, vigilant monitoring is essential.

Conclusions

Our results suggested that HT had a beneficial effect on BMI, GOT and GPT in postmenopausal women with diabetes comparing with postmenopausal women without HT. In respect with smoking and alcohol consumption, the data were not sufficient further to sustain this effect. However, more direct evidence of whether these parameters link HT and blood sugar levels is needed. ■

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