

Clinical and laboratory work-up prior to hormone replacement therapy in postmenopausal women

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Summary. In a retrospective study on 100 female patients (mean age 52 years), with a menopause lasting for 3.5 years, referred to the Menopausal Clinic of Beilinson Medical Center, we studied the pretreatment, clinical and laboratory work-up before administration of hormone replacement therapy (HRT). The work-up consisted of clinical and medical examination and history. Mammography is a necessary test for malignancy exclusion, and also the assessment of lipid metabolism. Pap smear is not so important since cervical cancer is a rare event in Jewish women and pelvic sonography cannot be a decisive diagnostic tool for ruling out malignancy. We conclude that HRT for prevention of osteoporosis and cardiovascular disease should be administered in a menopausal clinic by a gynecologist, after performing a few tests: confirmation of menopause by follicle-stimulation hormone (FSH) and E_2 , excluding malignancy by mammography, and confirmation of normal lipid metabolism.

Key words: Postmenopause; Hormone replacement therapy.

INTRODUCTION

Hormone replacement therapy (HRT) is nowadays unanimously accepted for relief of menopausal symptoms, and for prevention of osteoporosis and cardiovascular disease. In other words, HRT can make life not only longer but better too.

In spite of the increasing knowledge of the menopausal pathophysiology and

the various treatment modalities, some issues are not yet established. For example, who should treat the postmenopausal women: the family physician, the endocrinologist or the gynecologist, and what clinical and laboratory work-up must be carried out before HRT initiation.

The aim of the present report has been to improve the oral admission protocol and thus to reduce unnecessary tests.

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MATERIAL AND METHODS

For this retrospective report, we studied the files of 100 patients, mean age 52 years, with menopause lasting for a mean of 3.5 years, who were admitted to our ambulatory menopausal clinic during 1988. Sixty-three of these patients were referred because of menopausal complaints, 24% after surgical menopause, 12% because of their concern about osteoporosis, and the others because of a low bone mineral density (BMD).

The pretreatment study was carried out partly by the referring physician, and partly at the menopausal clinic.

Menopause was confirmed by follicle-stimulating hormone (FSH) >40 mIU/ml, and by estradiol (E₂) >20 pg/ml assessment. Serum were also analysed.

Since malignancy is common in the 5th decade of life, all patients underwent mammo-graphy, Pap smear, pelvic ultrasonography and blood stool analyses.

The decision of whether to initiate HRT was based on the pretreatment evaluation, and mainly upon the medical history and physical examination, and was taken usually on the second visit.

RESULTS

There was a perfect correlation between FSH and E₂ levels and menopause in 95 and 96 patients, respectively (Tables 1 and 2). One patient was found to suffer from mild diabetes mellitus. She was re-

Table 1. — FSH LH levels in 95 women of the study group.

| Cause of referral | Menopausal | Non-menopausal |
|--------------------------|------------|----------------|
| Self-awareness | 12 | 2 |
| Menopausal complaints | 61 | 5 |
| Low bone mineral density | 1 | 1 |
| Postoperation menopause | 22 | 0 |

Normal values:

FSH > 40 mIU/ml FSH < 40 mIU/ml
LH > 20 mIU/ml LH < 10 mIU/ml

Table 2. — E₂ levels in 96 women of the study group.

| Cause of referral | Menopausal | Non-menopausal |
|--------------------------|------------|----------------|
| Self-awareness | 21 | 2 |
| Menopausal complaints | 61 | 5 |
| Low bone mineral density | 1 | 1 |
| Postoperation menopause | 23 | 0 |

Normal values: > 20 pg/ml < 20 pg/ml

Table 3. — Screening for malignancy in the study group.

| | Mammo-graphy | PAP smear | Pelvic ultrasono-graphy | Occult stool test |
|---------------------------|--------------|-----------|-------------------------|-------------------|
| Number | 87 | 78 | 85 | 93 |
| Normal | 62 | 73 | 81 | 93 |
| Further evaluation needed | 25* | 5** | 4*** | 0 |

(*) In 9 breast biopsies were performed, 1 case of cancer of the breast found.

(**) Colposcopic evaluation revealed 2 normal, 3 suspicious, of which cervical biopsy revealed 2 cases with HPV infection and 1 normal.

(***) 3 exploratory laparotomies performed, 2 simple ovarian cysts, 1 para-ovarian cyst. One case of fibroid uterus still on follow-up.

ferred for further evaluation to the Endocrinological Department.

Serum cholesterol levels were above 200 mg% in 29% of our patients and in 57% over 250 mg% (normal range for our laboratory is 150-200 mg%).

The triglyceride levels (normal range 150-200 mg%) were above 200 mg% in 3% of our study group, and HDL-cholesterol below 35 mg% in 3% of the patients. Of significant clinical importance is the fact that 19% of the study cohort had cholesterol: HDL ratio above 5.

By mammography a case of breast cancer was diagnosed. Pap smear revealed 2 cases of HPV infections, ultrasonography was suspicious in 4 cases, but further evaluation did not confirm the diagnosis. Stool analyses for occult blood were all negative (Table 3).

Of the group of 100 women only 84% were admitted for HRT, 16% were excluded for the following reasons: 8 were still premenopausal, 2 because a past history of thrombophlebitis, one because of melanoma, one because of breast cancer, and 4 patients refused the HRT.

DISCUSSION

The major aim of HRT administration is prevention of osteoporosis and cardiovascular disease, and that can be achieved by natural or conjugated estrogen, opposed by progestogen in order to avoid endometrial hyperplasia. Prince *et al.* ⁽¹⁾ studied the effect of 3 approaches to the prevention of osteoporosis: a) exercise regimen; b) calcium supplementation and exercise; and c) exercise with continuous replacement of estrogen and progesterone. In their opinion, HRT with exercise is the most effective in prevention of bone loss.

Postmenopausal women on HRT have lower rates of cardiovascular disease than women of similar age who do not receive HRT. This may be due to the fact that estrogen reduces the levels of LDH and raises that of HDL. Recently the doses of estrogen have been decreased to levels that prevent osteoporosis, relieve menopausal symptoms and minimize adverse effects such as hypertriglyceridemia, thromboembolic complications and endometrial hyperplasia.

In their study, Walker *et al.* ⁽²⁾, using 0.625 mg and 1.25 mg of conjugated estrogen daily, reduced significantly LDH cholesterol, in dose-dependent manner. Estrogen reduced LDH levels by increasing LDL catabolism. Transdermal estrogen had no effect because both doses of conjugated estrogen seem equally effective in altering the HDL:LDL ratios favourably, but increase triglycerides in a dose-related fashion. The authors point out that increase in triglycerides by 0.625 mg should not induce clinical hypertriglyceridemia in women with normal triglyceride levels. Hence the importance of serum lipid analysis prior to starting HRT.

There are other possibilities of HRT, like the regimen described by Blum *et al.* ⁽³⁾, a combination of conjugated estrogen 0.625 mg, followed by clomiphene citrate, which prevent endometrial hyperplasia

but also monthly uterine bleeding, a reason for concern in many women.

Another regimen described by Jensen *et al.* ⁽⁴⁾ is a sequential combined estradiol valerate with the antiandrogenic progestogen cyproterone acetate which reduces serum cholesterol and LDL-cholesterol.

As to the question of who should treat the postmenopausal women, Barlow *et al.* ⁽⁵⁾ concluded that there is low overall use of HRT in general practitioners' menopause practice, despite the recent media coverage of its benefits in the prevention of osteoporosis and subsequent fractures.

Our conclusion is that HRT should be administered in a menopausal clinic, after a pretreatment work-up in order to exclude malignancy by mammography and after confirmed a normal lipid metabolism.

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