



ORIGINAL RESEARCH

THE IMPACT OF THE WOMEN'S HEALTH INITIATIVE STUDY ON THE INITIATION AND CONTINUATION OF HORMONE THERAPY IN A TERTIARY MENOPAUSE UNIT IN TURKEY

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ABSTRACT

Objective: To determine the initiation and continuation rate of hormone therapy (HT) following publication of the Women's Health Initiative (WHI) study.

Methods: A survey was performed on 816 postmenopausal women between July 2002 and July 2005. Questions included sociodemographic characteristics, determinants of HT, use of knowledge and source of information regarding the WHI study.

Results: The average age was $49,3 \pm 3,6$ years. Among the participants 22,1% were using HT whereas 77,9% were not. Of the women; 131, 99, 60, 157 were graduated from university, high school, middle and primary school respectively. HT usage was 25% among primary school and 20% among university graduates, which appeared not to be affected by educational level. The rate of starting HT was 18,6% in the second half of 2002. Initiation of HT was 30,5% in 2003, than decreased to 21,5% in 2004 and 20,9% in 2005. Among women for whom HT was initiated after WHI, the continuation rate was 41%.

Conclusion: Our survey showed the negative impact of WHI findings on both about the initiation and continuation of HT in our menopause unit in Turkey. Information was mainly obtained through the media or physician, may well have an important impact on the continuation or discontinuation of HT.

Keywords: Hormone treatment, WHI, Menopause

TÜRKİYEDE TERSİYER BİR MENOPOZ MERKEZİNDE WOMEN'S HEALTH İNİTİATİVE ÇALIŞMASININ HORMON TEDAVİSİ DEVAMI VEYA KESİLMESİNE OLAN ETKİSİ

ÖZET

Amaç: Women's Health Initiative (WHI) çalışmasının yayınlanmasının takiben hormon tedavisinin (HT) sürdürülmesi veya kesilmesine olan etkisini incelemek.

Materyal ve Metod: Çalışma Temmuz 2002 ile Temmuz 2005 tarihleri arasında 816 postmenopozal kadın ile gerçekleştirildi. Hastalara sosyo-demografik özellikleri, HT kullanım bilgileri, WHI çalışması hakkında bilgiler soruldu.

Bulgular: Kadınların ortalama yaşları $49,3 \pm 3,6$ ve cevap oranları %54,7 idi. Katılımcıların %22,1'i HT almakta iken, %77,9'i HT kullanmamaktaydı. Kadınların üniversite mezunu, lise, ortaokul ve ilkokul mezunu olanları sırasıyla 131, 99, 60, 157 şeklinde idi. İlkokul mezunlarında HT kullanım oranı %25, üniversite mezunlarında %20 olması tedavinin eğitim durumundan etkilenmediğini göstermekte idi. 2002 yılının ikinci yarısında HT başlama oranı 18,6%, 2003'te % 30,5 şeklinde olup 2004 yılında %21,5'e, 2005 yılında %20,9 oranına geriledi. WHI çalışmasından sonra HT başlanan kadınlarda tedaviye devam oranı %41'di.

Sonuç: Çalışmamız WHI sonuçlarının menopoza HT devamı ve kesilmesi üzerine etkide bulunduğunu göstermektedir. WHI hakkında bilginin en çok medyadan veya doktorlardan elde edildiği ve HT devamı veya kesilmesi üzerine belirgin etkisi olduğu saptandı.

Anahtar Kelimeler: Hormon tedavisi, WHI, Menopoz

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INTRODUCTION

Menopause is a time of great psychological and physiological change and many women report symptoms such as hot flushes that negatively affect their quality of life. Hormone therapy was offered to almost all postmenopausal women to relieve the symptoms in the short term and as a preventive medicine in the long term. In 1995, approximately 38% of postmenopausal women in the USA were taking hormone therapy (HT)¹. Several observational studies had suggested that HT offered women some protection against coronary heart disease and osteoporosis²⁻⁵. More recently, 2 large randomized clinical trials, The Heart and Estrogen / Progestin Replacement Study (HERS)⁶ and the Women's Health Initiative (WHI) have been published⁷. These clinical trials demonstrate that the risks associated with HT outweigh the benefits for women. The studies found an association between prolonged use of HT and increased risk of breast cancer, thromboembolism and infarctions. Widespread coverage of the study results by media and professional journals raised concerns among the public health care providers and particularly among women using postmenopausal HT. Many women stopped treatment abruptly because of the global panic which was related to health concerns⁸⁻⁹. Thus in the post WHI era, compliance seems to be largely influenced by fears expressed by both medical personnel and the public. The lay press also provided wide coverage on this issue. Time Magazine in its July 2002 issue published a cover article entitled as "Truth about Hormones" and claimed that women were confused with the new information¹⁰.

In Turkey the scientific and public debate about the results of WHI is still ongoing and influencing the initiation and continuation of HT in postmenopausal women.

We conducted a survey to evaluate the perception of the WHI results among women who present to our tertiary menopause unit. The objective was to determine the initiation

and continuation of HT following the publication of the WHI study.

PATIENTS AND METHODS

We performed a survey on 816 postmenopausal women who presented to Marmara University Menopause Unit in Istanbul between July 2002 and July 2005. Menopause is defined as the cessation of menstruation for at least 12 months or serum FSH levels > 40 mIU/ml. Women who had undergone hysterectomy with bilateral oophorectomy were defined as surgically menopausal. Surveys were performed by two physicians (PY, MU) who worked at the menopause unit by either direct interview or phone calls. Our questionnaire addressed sociodemographic characteristics including present age, age at menopause, body mass index (BMI), educational status, as well as determinants of HT use, knowledge and source of information regarding the WHI study.

We aimed to obtain information about women's attitudes regarding HT use and reasons to continue or discontinue use of HT. Women were also asked if they had been provided with information about the risks and benefits of HT and about the source of their information. The study has been approved by the ethical committee.

The variables were compared with chi-square test and student's t test where appropriate and $p < 0.05$ was regarded as statistically significant. The results were interpreted by using the SPSS 12.0 (SPSS, Inc, Chicago, IL, U.S.A) program.

RESULTS

In total, 816 women were asked to participate in this study. The response rate was 54.7%. Thus 447 women were included in the analysis.

The sociodemographic characteristics of the women are shown in table I. The mean age at presentation was 49.3 ± 3.6 years with a range of 44-62 years. A total of 396 (88.6%) women were natural and 51 (11.4%) women were surgical menopausal women. Among the



participants of the survey, 22.1% (99/447) were using HT whereas 77.9% (348/447) were not using HT. Body mass index (BMI) was similar between HT user and nonuser with a mean value as 26.7 ± 3.8 . Continuous combined HT regimen was used by 73.7% (73/99) of women and sequential HT was used by 26.3% (26/99) of HT users. HT usage was significantly higher among surgically menopausal women (66% (34/51)) than among natural menopausal women (20% (81/396)) ($p < 0.05$). HT users were younger than non-users (48.6 ± 2.4 vs 49.4 ± 2.3 respectively) and this difference was statistically significant ($p < 0.01$).

The educational level was categorized as primary, middle, high school and university graduates. Primary-middle school graduates were defined as having low educational status (LES) and high school-university graduates were defined as having high educational status (HES). Of the participating women 131, 99, 60, 157, women were university, high school, middle school and primary school graduates

respectively. The educational status of women were defined as high in 49% (230/447) and low in 51% (217/447) accordingly. HT usage was not significantly affected by educational level ($p > 0.05$). The rate of HT use among primary school and university graduates was 25% and 20% respectively.

Women were categorized according to the reasons for attendance to our clinic between July 2002 – July 2005. The most common reason was routine control with a rate of 66,99% (295/447), followed by 27,06% (121/447) with vasomotor symptoms. Osteoporotic and urogenital complaints were mentioned by 6,04% (27/447) and 0,89% (4/447) of the women respectively.

Among the postmenopausal women who attended our clinic, the rate of starting HT was 18,6% in the second half of 2002 immediately after the publication of the study. In 2003 initiation of hormone use was 30,5%, than decreased to 21,1% in 2004 and 20,9% in 2005.

Table 1: Demographic characteristics of the study.

	Total		HT users		non-HT users		p value
	mean	± SD	mean	± SD	mean	± SD	
Age	49.3	± 2.3	48.6	± 2.4	49.4	± 2.3	$p < 0,001$
BMI	26.7	± 3.8	26.7	± 4.2	26.7	± 3.6	$p > 0,05$
	n	(%)	n	(%)	n	(%)	p value
Menopause							
Natural	396	88.6	82	21	314	79	
Surgical	51	11.4	17	33	34	67	
Educational Status							
Primary school	157	35.1	41	41.4	116	33.3	$p > 0,05$
Middle school	60	13.4	9	9.1	51	14.7	$p > 0,05$
High school	99	22.2	22	22.2	77	22.1	$p > 0,05$
University degree	131	29.3	27	27.3	104	29.9	$p > 0,05$
Total	447	100	99	100	348	100	

HT: hormone treatment, BMI : body mass index

**Table II:** Main reasons given for discontinuation of hormone treatment.

<i>Reason</i>	<i>Number of subjects</i>
Fear of cancer	46 (46,4%)
Decreasing vasomotor symptoms	36 (36,3%)
Weight gain	10 (10,1%)
Bleeding complaints	5 (5,0%)
Other	3 (3,0%)
Total	99 (100%)

Women for whom HT was initiated after the WHI study publication, the continuation rate of treatment was 41%. The continuation rate of HT was 54% (54/99) in 2002, 31% (31/99) in 2003, 21% (21/99) in 2004 and 16% (16/99) in 2005. The reasons for discontinuation of HT were categorized in five groups, shown in table II. Women discontinued therapy mostly because of fear of cancer 46,4% (46/99), decreasing vasomotor symptoms 36,3% (36/99), weight gain 10,1% (10/99), bleeding complaints 5,0% (5/99) and other reasons 3,0% (3/99).

Women were questioned to assess their knowledge about the WHI study. Of the participants, 51,7% (231/447) obtained knowledge through the media, 23% (103/447) received information from a physician, 21,3% (95/447) from friends and 4% (18/447) could not remember the study and its conclusions. Furthermore, when the current opinion of the participants about HT was questioned, 47,4% (212/447) of the women had concerns of cancer, 21,7% (97/447) of women found HT useful for vasomotor symptoms, 10,3% (46/447) of women believed that HT was effective for the prevention of osteoporosis and 16,6% (74/447) of the women stated that HT was beneficial for the cardiovascular system whereas 4% (18/447) of the women did not have an opinion.

DISCUSSION

The last decade has witnessed a dramatic shift in the evidence on the use of hormone treatment by postmenopausal women. The

past observational studies were consistent in indicating a positive impact for cardiovascular disease, lipid and carbohydrate metabolism, and bone health²⁻⁵. Furthermore, encouraging information was noted in studies of Alzheimer disease although evidence was inconclusive¹¹.

However, the evidence from randomized trials challenged our prior beliefs and management. The HERS study found a 50% increase in cardiac events in the first year of hormone therapy use among women with established coronary heart disease⁶. This trend was supported in the WHI with increased risk for coronary heart disease⁷. Furthermore, the WHI results indicated an increased risk for breast cancer, stroke and pulmonary embolism. Although there were protective effects against hip and vertebral fractures and colorectal cancer, the overall risks were considered to outweigh the benefits.

Widespread media attention to the WHI trial results may have resulted in comparable dissemination of this information across diverse socioeconomic groups. A variety of studies from different countries showed HT discontinuation rates and the changing approach to HT after the WHI study results. Travers et al and Clanget et al claimed that there was a significant decrease in HT usage years after the WHI study in Australia and Germany¹²⁻¹³. Buist et al stated a rapid decline in HT use including 100.000 women¹⁴. Leung et al reported a 43,5% decline in prescribing conjugated equine estrogens and its related products after the second half of 2002 in



Hong Kong¹⁵. Blümel et al found a 8,6% drop in all hormone prescriptions for menopause in Chile¹⁶. Both of these studies pointed out changes in the attitudes of gynecologists as well as in patients' attitudes. Heitmann et al reported that the most common reason for stopping HT was the higher risk benefit ratio (54%)¹⁷.

A couple of years prior to the WHI study publication, we reported 71,2% continuation rate in our tertiary menopause unit¹⁸. The educational status of the patients was related to starting HT but was not related to the discontinuation of HT. Bleeding episodes and fear of cancer were the 2 most common reasons for discontinuation of treatment. In the present study, similar to our previous data, the discontinuation of HT was not affected by educational status and fear of cancer was a common reason to stop treatment. On the contrary, in the present survey after the WHI study, we did not find any relation between education level and starting HT.

In the present study, the initiation of hormone treatment was 18,6% which is lower than our previous 60% rate (unpublished data). Our data indicated an increased HT initiation rate among our patients in 2003. This increase was most probably due to group counseling, meetings performed by senior counselors in order to inform patients about WHI study results at the end of the year 2002. In the following years the rate of initiation of HT declined to 21%. In our survey the continuation of HT was found to be 41% after the WHI publication. This rate was lower than in our previous 2 studies before the WHI^{18,19}. We first reported 71,2% continuation rate in 1998 and 71,7% continuation rate after 2 years in 2001.

After the WHI study publication, in the light of the North American Menopause Society (NAMS) guidelines, we preferred to individualize HT in postmenopausal women²⁰. We mostly started HT for women who had vasomotor symptoms. Our previous data indicated that the reason for taking HT was vasomotor symptoms in 42% of the patients¹⁸. In the present study, we found 41%

continuation rate after the WHI study publication, which overlaps with the rate of women who started HT because of their vasomotor symptoms in our previous study¹⁸.

Indeed our results showed that 51,7% of the participants obtained knowledge about the WHI from the media whereas only 23% received information from physicians. The physician as source of information may well be associated with the total HT use rate of the participants of our survey (22,1%). Hoffman et al found that the most frequent source of information on HT was newspapers or magazines (43,8%) and television or radio (31,7%)²¹. The declined rate of starting HT, after the WHI study in our menopause unit, was most probably due to media influence which appears to be independent of educational status.

Populations were influenced at different times after publication of the clinical trials. Haas et al reported that before publication of the randomized trial results, HT usage was increasing at 1% per quarter and after publication of the HERS study, HT usage decreased by 1% per quarter²². After publication of the WHI study, usage declined by 18% per quarter²². Kim et al found the decreasing time as 3 months and pointed out that trial results can have a rapid effect on practice²³. In a study by Ettinger et al, discontinuation of HT was 56% 6-8 months after the WHI findings, despite not being well informed²⁴. In the present study, the decrease in HT use was most significant in the 6 months following the WHI (18.6%), although relatively increased in the consecutive years.

The current consensus is that HT should be reserved for the treatment of menopausal symptoms at the lowest effective dose for the shortest duration.

Deciding about starting or stopping HT requires a comprehensive discussion between the physician and the patient regarding benefits and risks. The source of information about HT, either media influence or physician's advice, may have an important impact on continuation or stopping HT. Ultimately the decision to start and continue



HT is up to individual women and is made on the basis of the information she receives from her physician and from the media.

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