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ORIGINAL ARTICLE

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Changes in the use of hormone replacement therapy and alternative medications before and after the reports from the women's health initiative study and million women study: An overview

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OBJECTIVE(S) : To examine the prescribing patterns for estrogen plus progestin therapy (hormone therapy (HT) and estrogen alone therapy (ET) in the matured women clinic in our hospital before and after the published results of women's health initiative's (WHI) HT trial and Million Women Study.

METHOD(S) : We conducted a retrospective observational study on 929 women aged 30 to 80 years who were enrolled in matured women clinic in our hospital from January 1999 to December 2005 to estimate the prevalence of HT and ET. We used the record files of all patients for data analysis.

RESUTS : Before the published results of WHI trial there was a rise in ET use from 26% in 1999 to 45% in 2000 and a rise in HT from 39% in 1999 to 73% in 2001. Following the publication of Women's Health Initiative trial results in July 2002, ET prescriptions declined successively from 24% in year 2002 to nil in 2004. HT prescriptions also declined from 10% in 2002 to nil in 2004. The ET use rose to 6.4% in the year 2005 but HT use still remained nil. Use of isoflavon rose from 25% in the year 2003 to 60% in the year 2005. Reasons for stopping HT were side effects in 23% and decreased compliance in 20% while reasons were not clear in 27%. No increased risk of breast cancer, stroke or thromboembolism was noted in the study.

CONCLUSION(S) : The diffusion of the WHI HT trial results had an immediate impact on the discontinuation of HT and ET. However ET use later on picked up but HT did not. Administrative claims data can be a useful tool for monitoring an immediate impact of national guidelines or a national level outcome trial.

Keywords : HT, hormone therapy, ET, estrogen therapy, HRT, hormone replacement therapy, WHI, women's health initiative, MWC, matured women clinic, MWS, million women study.

Introduction

Until now, hormone replacement therapy (HRT) was quite straight forward but more recently the paper from the Women's Health Initiative Study (WHI)[1] and the Million Women Study (MWS)[2] have caused enormous alarm by reporting that heart attacks, strokes, venous thromboembolism, and breast cancer are more common in women receiving the treatment.

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After the report, government regulatory authorities issued advice to health professionals and women, and guidelines relating to the postmenopausal use of hormone replacement therapy were updated[3].

We examined the changes in HRT use before and after the publication of these reports and found the immediate impact of WHI trial and MWS on the discontinuation of HT & ET but no increased risk of breast cancer, stroke or thromboembolism in our study.

Methods

We conducted a retrospective observational study on 929 women aged 30 to 80 years, who were enrolled in our matured women clinic from January 1999 to December 2005 and did year wise analysis with respect to the number and

type of treatment (Hormonal/Alternative Medicines) given to women and observed the changing trends in the treatment used.

Women in age group 30-80 years included perimenopausal, postmenopausal, hysterectomized, and women with premature ovarian failure who sought HRT. The HRT was categorized as follows: conjugated equine estrogen (CEE) 0.625mg plus medroxyprogesterone acetate (MPA) 10mg in HT group and CEE 0.625 mg only in ET group.

All women received oral therapy. HT group received cyclical regimen and ET group received continuous therapy. Alternative medications (isoflavon, raloxifene) and calcium supplements were also prescribed to women attending the clinic from year 1999 to 2005 and overall analysis of their use was done. Data analysis was done from record files of individual women by direct questionnaire method. Year wise analysis in the trend of ET and HT use was done and P value was calculated by linear analysis of the trend.

Results

Vasomotor symptoms (28%) and musculoskeletal symptoms (24%) were the main indications of HRT (Figure 1). During the study period ET was used by 19% women, HT by 36.7% and isoflavon was used by 46% (Figure 2). We gave calcium supplement to all the women.

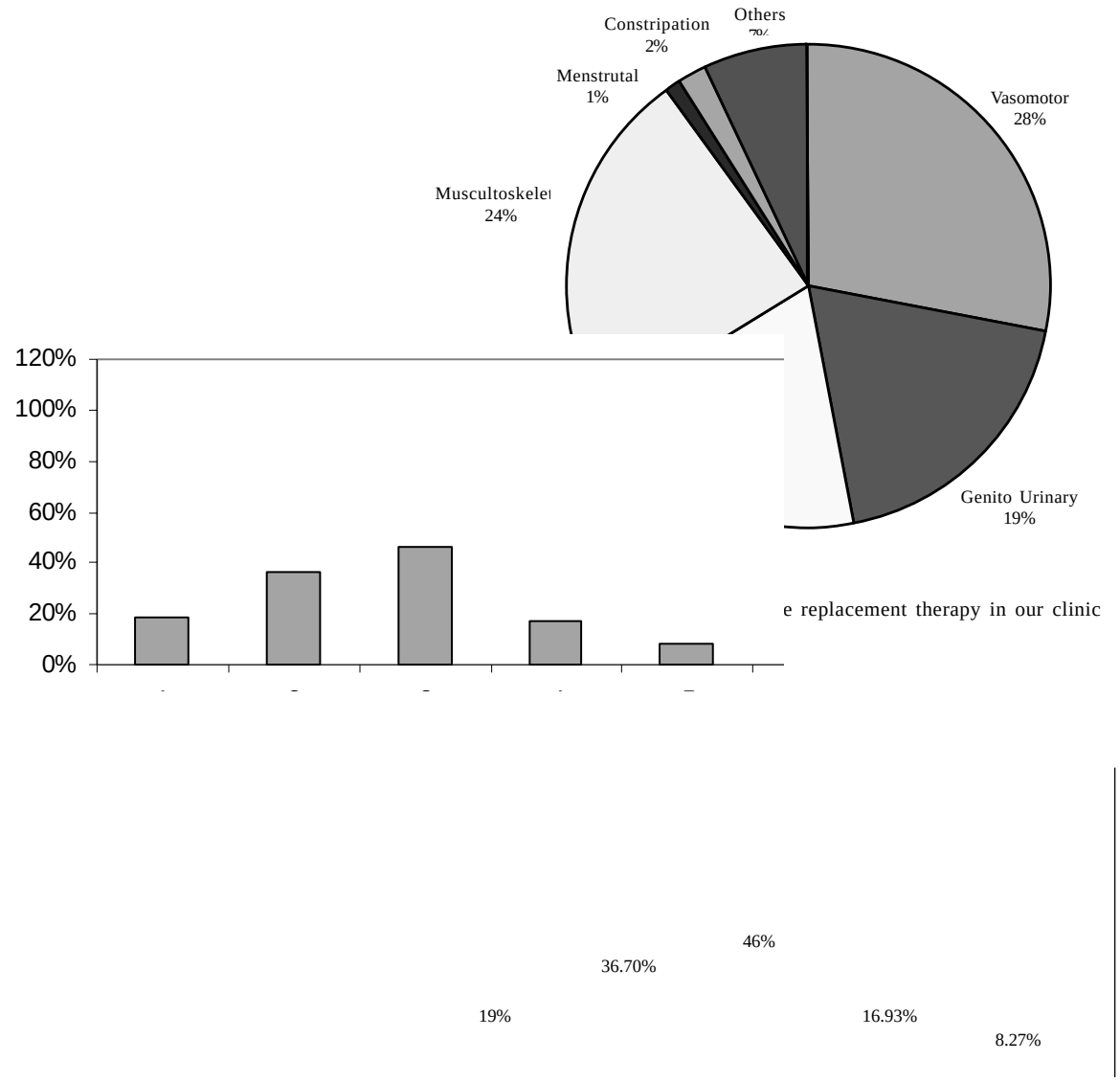

Figure 2. Hormon theraphy and alternative medications use

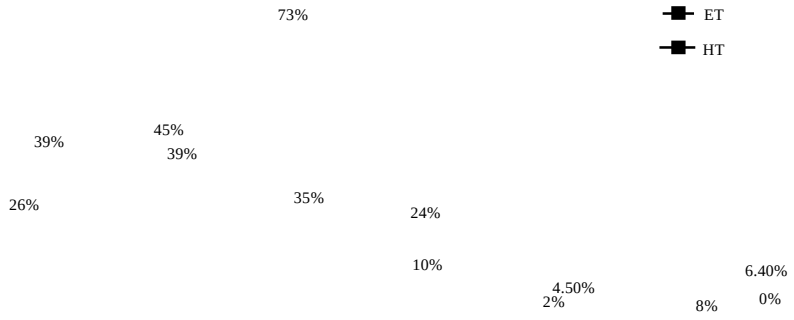

Figure 3. Year wise trend of HT and ET use in our clinic

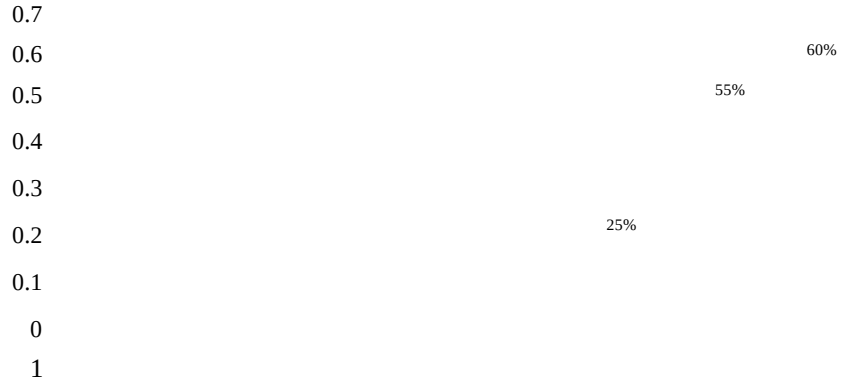

Figure 4. Year wise trend of Isoflavon use

Maximum use of ET was by 45% women in the year 2000 and HT by 73% in the year 2001. Thereafter there was a declining trend and none used HT or ET in the year 2004 (Figure 3). Use of isoflavon, started after 2002 and was 25% in 2003 rising to 60% in 2005 (Figure 4).

The reasons for stopping HT and ET in the study were development of side effects (bloating, fluid retention, nausea, headache, mastalgia, leg cramps and erratic vaginal bleeding) accounted in 23%, decreased compliance in 20% and cost consideration in 21%. The reasons in 27% of women and 9% were lost to follow-up.

Year	No. of women
1	93
2	120
3	135
4	167
5	171
6	113
7	130

One hundred and seventy five women used ET and 341 used HT. None of them developed stroke or breast cancer or venous thromboembolism.

Table 1 gives the statistical analysis for linear trend in ET use from year 1999 to 2005 showing significant P value of 0.01518.

Table 2 gives the statistical analysis for liner trend in HT use from year 1999 to 2005 showing significant P value of <0.0001.

Table 1. Statistical Analysis for linear trend in ET use

Year	Exposure score	Odds ratio relative to baseline
1999	130	1.00
2000	113	2.32
2001	171	0.95
2002	167	0.89
2003	135	0.15
2004	120	0.00
2005	93	0.19
	929	

(Chi square for linear trend: 5.895 p value: 0.01518)

Table 2. Statistical analysis for linear trend in HT use

Year	Exposure score	Odds ratio relative to baseline
1999	130	1.00
2000	113	1.03
2001	171	4.21
2002	167	0.18
2003	135	0.04
2004	120	0.00
2005	93	0.00
Chi Square for linear trend 79.292		P<0.0001

Discussion

Our results show an immediate reduction in HT and ET use after the termination of WHI HT trial. Self reported data from national pharmacy sales[4] and other cohorts[5,6] show similar reduction.

There was no risk of stroke, breast cancer and thromboembolism after HT/ET use from year 1999 to 2005, though the evidence from WHI HT trial has made it increasingly clear that the risk of using HT outweighs the benefits in women without menopausal symptoms[4]. We observed a sudden decline in HT & ET use after the termination of WHI trial from 2002 onwards falling from 24% to 0% (ET) and 1.2% to 0% (HT) in year 2004. The reasons for discontinuing HT and ET were development of side effects, decreased compliance, and cost factor. In 27% women reasons were not clear and probably the fear of developing cancer played a role.

PostWHI study results, there was not a decline in the use of alternative medications and a rise in use of isoflavon was noted as HT & ET use declined. Isoflavon use started after 2002 and was seen in 25% women in 2003 and 60% in 2005. More detailed articles have been published since the initial WHI HT trial findings showing an additional impact on isoflavon use [7,8,9]. Whether the subsequent WHI reports contributed to decline in HT and ET use requires additional analyses beyond the scope of our data collection.

The diffusion of the WHI HT trial results had an immediate impact on the discontinuation of HT and ET and is possibly responsible for the decline in initiation of these therapies. As the reasons for stopping HT and ET were not clear in 27% women, probably the results of WHI and MWS may be responsible. Moreover there was a rise in ET use after the publication of results of the two studies. The confusions need to be cleared from the patients' and doctors' mind by more studies, and women and their physicians need help in understanding the needs, risks and benefits of HT in individual patients.

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