

Hormone replacement therapy and arterial blood pressure in postmenopausal women with hypertension

Ioannis Karalis, Gareth D. Beevers, Michele Beevers & Gregory Y. H. Lip

To cite this article: Ioannis Karalis, Gareth D. Beevers, Michele Beevers & Gregory Y. H. Lip (2005) Hormone replacement therapy and arterial blood pressure in postmenopausal women with hypertension, *Blood Pressure*, 14:1, 38-44, DOI: [10.1080/08037050510008788](https://doi.org/10.1080/08037050510008788)

To link to this article: <https://doi.org/10.1080/08037050510008788>



Published online: 08 Jul 2009.



Submit your article to this journal [↗](#)



Article views: 132



View related articles [↗](#)



Citing articles: 2 View citing articles [↗](#)

ORIGINAL ARTICLE

Hormone replacement therapy and arterial blood pressure in postmenopausal women with hypertension

IOANNIS KARALIS, D. GARETH BEEVERS, MICHELE BEEVERS & GREGORY Y. H. LIP

From the University Department of Medicine, City Hospital, Birmingham B18 7QH, UK

Abstract

Background. Data on the effect of hormone replacement therapy (HRT) on blood pressure (BP) in hypertensive menopausal women are limited. **Objective.** To investigate the association between HRT and longitudinal changes in BP in hypertensive menopausal women. **Patients and methods.** We recruited a total of 161 hypertensive menopausal women (mean age = 52.2 ± 6.6 years) attending the hypertension clinic in our hospital that required HRT to attenuate the effect of menopause symptoms. These women were followed for up to 36 months, being evaluated every 6 months with measurements of their BP, weight and the number of drugs needed to control their BP. We also measured serum cholesterol levels before and after the initiation of HRT. **Results.** The systolic BP remained unaffected throughout the whole follow-up period, whereas the diastolic BP was slightly reduced at 6, 24 and 36 months. This decrease was accompanied by an increased need for antihypertensive medication throughout the entire follow-up period, while the body weight also increased at 18, 24 and 36 months. No particular differences were noted with respect to ethnicity, history of pre-eclampsia or surgical menopause, before and after the initiation of HRT. Serum cholesterol levels remained unchanged during the evaluation period. Oestrogen–progestogen combination therapy use was associated with a lower diastolic BP and a smaller number of antihypertensive drugs compared to other forms of HRT. **Conclusion.** HRT use does not have an adverse gross effect on BP in hypertensive menopausal women who need it, although there may be an increased need for antihypertensive therapy during the 36-month follow-up period of our study.

Key Words: *Hormone replacement therapy, hypertension, menopause*

Introduction

Hormone replacement therapy (HRT) is effective in relieving menopausal symptoms, such as hot flushes, sweating, vaginal atrophy, urinary symptoms and (some tend to believe) emotional instability (1). Furthermore, long-term therapy has a definite beneficial effect on osteoporosis (2). However, significant doubts have recently been raised over its value in prevention of cardiovascular morbidity and mortality (3). Certainly, oestrogens alone or in combination with a progestogen seem to exert a beneficial effect on serum lipid and plasma fibrinogen levels, while having neutral or slightly beneficial effects on blood pressure (BP), in studies largely confined to normotensive women (4–6). Nonetheless, studies supporting the beneficial effects

of HRT on cardiovascular risk factors have been criticized for the “healthy cohort effect” (7), whereby menopausal women on HRT are more likely to adopt healthy habits and characteristics, including stopping smoking, healthy dietary habits and regular exercise, as well as having regular visits to their physicians.

Over the last few years, a series of prospective randomized trials has published their results on the effect of HRT on cardiovascular disease (8–13). More than 20000 menopausal women were included, for an average follow-up period of over 4 years. Both oestrogen-alone and oestrogen–progestogen combined preparations failed to reveal a beneficial role for HRT as a secondary preventive measure mainly in older patients with ischaemic

heart disease or a stroke. Even worse, the Women's Health Initiative (WHI) trial was stopped prematurely after demonstrating a significantly increased risk for strokes in healthy women on combination oestrogen–progestogen therapy (13). Thus, the impact of HRT on the incidence of major, potentially fatal conditions seems to be overall unfavourable, since the slight beneficial effect on colorectal cancer and disabling femoral fractures is offset by the increased risk of venous thromboembolism and breast cancer, the latter being impressively demonstrated in the Million Women Study (14). As a result, previous observational studies suggesting that HRT substantially reduces the risk of coronary heart disease now tend to be considered unreliable and severely biased, so the expectations raised in the past have been disappointing and unconfirmed.

In hypertensive women, with their increased cardiovascular risk, there has been some scepticism regarding the use of HRT, as it was well known that oestrogen use (in the form of oral contraceptive pills) in premenopausal women was associated with an increase in systolic (SBP) and diastolic BP (DBP) (15). The available data on HRT use in hypertensive women have been in small cohorts or for short follow-up periods, although the reports, mainly from registry data or subgroups of large clinical trials, are generally reassuring (16–18).

In 1994, we reported a cohort of 75 hypertensive menopausal women, where the introduction of HRT did not adversely affect mean BP, despite a small increase in mean weight (16). This cohort has now been extended to 161 women, where the effect of HRT on BP, body weight and plasma total cholesterol can be further analysed in relation to age, ethnicity, past obstetric history and the type of HRT preparation (that is, oestrogen–progesterone vs natural or synthetic oestrogen alone).

Patients and methods

We conducted an open prospective longitudinal study, recruiting hypertensive menopausal women referred to the specialist BP clinic of our hospital, run by Professors Beevers and Lip. This clinic receives a wide range of hypertension referrals from local general practitioners and physicians, as this is the "hypertension service" for the hospital/district. All patients required HRT to ameliorate menopausal vasomotor symptoms. The diagnosis of hypertension was based either on the medical history and the regular use of antihypertensive medication or by documenting a BP of $>140/90$ mmHg in at least three different visits (at least 1 month apart each)

with a minimum of two measurements made each time. The postmenopausal status, on the other hand, was documented either by a definite medical history of surgical menopause [i.e. a total abdominal hysterectomy (TAH) and a bilateral salpingo-oophorectomy (BSO)] or by natural menopause as confirmed by laboratory investigation (that is, high FSH/LH levels with low oestradiol levels).

All women were asked about their medical history, including any vascular complications of hypertension, prior use of oral contraceptive pills and hypertensive response to them, parity and pre-eclampsia during any of their pregnancies, as well as smoking and alcohol consumption. The date of HRT initiation was recorded, together with the age of the patient at that point, the type of the regimen, BP levels and antihypertensive medication before HRT introduction. We recorded height and body weight, as well as serum cholesterol levels before HRT initiation.

The patients were regularly followed up on a 3–6-monthly basis for up to 3 years. During each visit, we recorded their BP, weight and whether there was a change in the number of drugs needed to control their BP. SBP and DBP (phase V) were measured by trained observers, with the patients seated and after a 5-min rest. The Omron HEM 705 CP was used for the BP measurement in the last 3 years, while the Hawksley Random Zero sphygmomanometer was used prior to that. All observers were specifically trained in BP measurement using the British Hypertension Society video, and the BP measurements were regularly serviced and calibrated according to current recommendations.

Data are presented as mean \pm SD (standard deviation) or median (interquartile range, IQR), as appropriate. A paired Student's *t*-test was used to identify any statistically significant individual variations in the patients' BP and weight, while the general linear model was used for analysis of covariance and two-way repeated measures analysis of variance (ANOVA) to assess changes in BP. A *p*-value <0.05 was considered statistically significant.

Results

We studied a cohort of 161 women (mean age 52.2 ± 6.6 years; 113 Whites, 31 Afro-Caribbeans and 17 South Asians) who were followed up for up to 36 months (mean follow-up time 23.1 ± 11.4 months). Seven patients stopped HRT during the follow-up period because of an excessive rise in BP, although in all cases, this was decided by their

own general practitioner, usually on the basis of a single raised BP reading.

Seventy-one women (44.1%) had had a surgical menopause (either TAH or BSO) while the rest had a history of natural menopause, as confirmed by hormonal measurements. The average parity was 2.7 ± 1.8 . Only 35 patients (21.7%) were active smokers during the initiation of HRT, while the mean alcohol consumption was 1.8 ± 2.7 units per week. The majority of our population (76.9%) was overweight, with a body mass index (BMI) greater than 25. An oral conjugated oestrogen HRT was used in 49 patients, while conjugated oestrogens combined with progestogen were used in 62, oestrogen patches in 27, and other types, including oestrogen injections and the synthetic oestrogen, tibolone, were used in 23 women (Fig. 1). Four women discontinued their therapy because of a lack of symptom improvement.

Past medical history

Fifty-six women (34.8%) had a history of pre-eclampsia, while four had a history of hypertension following the use of oral contraceptives. One woman

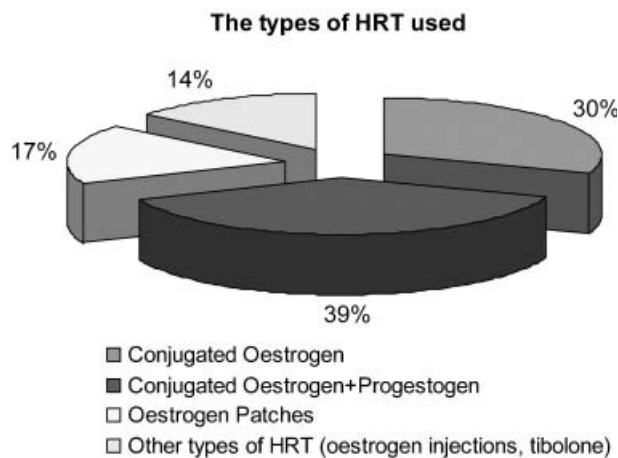


Figure 1. The different types of HRT used, shown schematically.

had previous angina, one had had a stroke and one had previously diagnosed left ventricular failure. The mean ECG–Sokolow–Lyon index was 27.1 ± 9.3 mm. No cardiovascular events occurred during the follow-up period.

Effects on BP, antihypertensive therapy and weight (Table I)

There were no significant changes in mean SBP throughout the follow-up period. There was a slight decrease in mean DBP which was statistically significant at 6, 24 and 36 months (p -values of 0.022, 0.014 and 0.018, respectively), although this was accompanied by an increase in the number of antihypertensive drugs taken compared to baseline ($p < 0.05$) at all time points. There was also an increase in mean body weight at 18, 24 and 30 months after the initiation of HRT ($p = 0.033$, 0.026 and 0.022, respectively).

Effects of ethnicity (Table II)

In white patients ($n = 113$, mean age 52.1 ± 6.6 years), there was a statistically significant reduction in the mean DBP only at 24 months ($p = 0.028$), with no statistically significant changes in the mean SBP or body weight. However, these patients did increase the number of antihypertensive drugs, when compared to baseline ($p < 0.05$ for 12, 18, 24 and 30 months, Table IIa). In Afro-Caribbean patients ($n = 31$, mean age 54.0 ± 6.8 years) there were no significant changes in SBP or DBP or the number of antihypertensive drugs prescribed, although there was a slight increase in body weight, recorded at 18 and 24 months ($p = 0.033$ and 0.026, Table IIb). In South Asian patients ($n = 17$, mean age 49.9 ± 5.4 years), the small number attending the whole follow-up period (just eight of them) makes statistical analysis difficult but there was an increased need for antihypertensive drugs ($p = 0.006$ at 30 months and $p = 0.003$ at 36 months) and a concomitant

Table I. Systolic (SBP) and diastolic blood pressure (DBP), body weight and number of antihypertensive drugs used during the follow-up period in 161 patients receiving HRT (all types).

Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (n)	161	149	131	98	84	80	77
SBP (mmHg)	156.5 ± 23.2	154.0 ± 22.1	156.3 ± 21.6	156.0 ± 20.2	155.7 ± 20.7	155.7 ± 22.3	155.3 ± 22.8
DBP (mmHg)	92.7 ± 12.5	$90.3 \pm 10.4^*$	91.4 ± 11.3	91.4 ± 12.0	$89.7 \pm 11.2^*$	91.2 ± 10.8	$89.5 \pm 11.3^*$
Weight (kg)	75.2 ± 15.0	76.1 ± 15.8	75.6 ± 16.6	$73.5 \pm 13.7^*$	$75.6 \pm 14.0^*$	$77.7 \pm 15.8^*$	77.3 ± 15.0
No of antihypertensive drugs used	1.4 ± 1.1	$1.6 \pm 1.1^*$	$1.5 \pm 1.1^*$	$1.6 \pm 1.1^*$	$1.8 \pm 1.2^*$	$1.8 \pm 1.1^*$	$1.7 \pm 1.2^*$

* $p < 0.05$. Attendance (n) signifies the number of paired observations to the initial time point, for each subsequent time point. Data are mean \pm SD (standard deviation) for each time point. However, comparisons were held only among paired observations through the different time points, since for most of the subjects data were not available for the whole evaluation period.

Table II. Systolic (SBP) and diastolic blood pressure (DBP), body weight and number of drugs used during the follow-up period of patients using HRT: effects of ethnicity.

(a) White patients							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	113	103	91	66	58	58	57
SBP (mmHg)	157.5 ± 23.5	155.2 ± 22.4	156.7 ± 22.2	158.7 ± 21.3	154.6 ± 20.2	157.6 ± 23.0	158.5 ± 23.1
DBP (mmHg)	92.4 ± 12.5	90.0 ± 10.7	91.2 ± 12.2	92.4 ± 11.4	88.6 ± 11.1*	91.5 ± 11.0	89.8 ± 12.0
Weight (kg)	74.3 ± 15.4	75.6 ± 16.3	75.4 ± 17.9	74.0 ± 14.9	76.2 ± 15.5	76.6 ± 16.9	77.7 ± 16.3
No of antihypertensive drugs used	1.4 ± 1.2	1.5 ± 1.1	1.4 ± 1.1*	1.7 ± 1.1*	1.7 ± 1.2*	1.8 ± 1.1*	1.7 ± 1.3
(b) Black patients							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	31	30	25	19	15	14	12
SBP (mmHg)	154.9 ± 25.4	154.5 ± 21.3	154.0 ± 22.4	156.3 ± 15.6	160.7 ± 19.0	154.0 ± 21.4	151.2 ± 14.5
DBP (mmHg)	93.5 ± 13.3	92.7 ± 9.1	91.2 ± 9.3	93.7 ± 10.4	92.1 ± 12.3	92.9 ± 11.5	89.5 ± 4.7
Weight (kg)	80.4 ± 14.3	83.0 ± 14.3	80.8 ± 13.6	77.9 ± 10.3*	77.6 ± 10.9*	83.2 ± 10.6	78.4 ± 9.1
No of antihypertensive drugs used	1.9 ± 1.1	2.1 ± 1.0	1.8 ± 1.0	1.7 ± 1.1	2.0 ± 1.1	1.8 ± 1.1	1.5 ± 1.1
(c) South Asian patients							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	17	16	15	13	11	8	8
SBP (mmHg)	152.5 ± 17.4	145.9 ± 21.9	158.0 ± 16.3	142.3 ± 15.5*	154.6 ± 26.2	145.0 ± 16.7	138.8 ± 24.6
DBP (mmHg)	92.5 ± 11.0	88.2 ± 11.1	93.1 ± 9.0	83.0 ± 14.5	92.6 ± 10.4	86.3 ± 7.0*	87.5 ± 14.1*
Weight (kg)	69.1 ± 10.7	68.1 ± 11.2	66.4 ± 9.6	65.6 ± 10.7	67.7 ± 8.0	73.3 ± 17.8	71.3 ± 12.7
No of antihypertensive drugs used	0.9 ± 0.7	0.9 ± 0.8	1.1 ± 0.7	1.3 ± 0.9	1.5 ± 0.8	1.6 ± 0.7*	1.8 ± 0.5*

* $p < 0.05$. Attendance (*n*) signifies the number of paired observations to the initial time point, for each subsequent time point. Data are mean ± SD (standard deviation).

decrease in mean SBP and DBP levels ($p < 0.05$). No significant weight changes were recorded in those patients (Table IIc). The three ethnic groups did not differ significantly in age ($p = 0.113$).

Effects of different types of HRT (Table III)

Conjugated oestrogens alone ($n = 49$) were not associated with any significant alterations in SBP or DBP or body weight, although there was an increase in the number of antihypertensive drugs used which was statistically significant at 12, 18, 24 and 30 months ($p = 0.033, 0.002, 0.011$ and 0.01 , respectively, Table IIIa). With the combination of conjugated oestrogens–progestogen ($n = 62$), SBP was unchanged throughout, whereas the mean DBP was slightly decreased (statistically significant only at 6 and 36 months). However, this was accompanied by an overall increase in the number of drugs used ($p < 0.05$ at 24 and 30 months). The average weight of this group remained unaffected (Table IIIb). With oestrogen patches, there was a mild decrease in DBP ($p < 0.05$ at 24 and 30 months) and an increase in drug intake (statistically significant only at 6 months). The average weight in these patients increased ($p = 0.012$ and 0.045 at 12 and 24 months, respectively, Table IIIc).

The number of women using the synthetic oestrogen, tibolone, which might be expected to have a different impact, was limited and therefore detailed analyses were not performed. Age, BMI,

parity and smoking habits did not differ significantly among the three HRT preparation groups.

Effects of past history of pre-eclampsia

Fifty-six women (mean age 51.8 ± 6.14 years) gave a past medical history of pre-eclampsia, but on comparing them with women with no such history, there was no difference in BP or the number of drugs being taken at baseline or at follow-up. However, the use of conjugated oestrogens alone (rather than the use of oestrogen–progestogens or oestrogen patches) was associated with higher mean SBP and DBP ($p < 0.0005$ in both cases). Body weight was the least affected by oestrogen–progestogen preparations and the most by oestrogen patches ($p = 0.004$). In women without a medical history of pre-eclampsia, the different types of HRT did not affect any of the observed variables. The type of menopause (surgical or natural menopause) did not influence BP changes with HRT.

Effects of age on response to HRT

We investigated the effects of HRT in different age groups, by comparing patients above and below the median age (52 years) of our cohort. Eighty-one women were aged ≤ 52 years (mean age 47.0 ± 4.0 years) while 80 were above this age (mean age 57.5 ± 4.2 years). As shown in Table IVa, the younger group presented an increased need for

Table III. Systolic (SBP) and diastolic blood pressure (DBP), body weight and number of drugs used during the follow-up period of patients on different types of HRT.

Conjugated oestrogens							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	49	45	42	33	28	27	28
SBP (mmHg)	156.5 ± 27.3	156.8 ± 24.5	157.6 ± 23.2	158.6 ± 20.0	163.0 ± 22.4	160.0 ± 21.3	157.9 ± 23.6
DBP (mmHg)	93.4 ± 14.9	92.6 ± 11.3	93.9 ± 13.9	93.8 ± 12.4	93.2 ± 10.3	94.1 ± 11.2	92.4 ± 12.6
Weight (kg)	76.7 ± 14.8	77.2 ± 15.2	74.1 ± 12.8	72.1 ± 13.2*	73.1 ± 13.3	77.5 ± 13.4	75.7 ± 12.9
No of antihypertensive drugs used	1.5 ± 1.2	1.5 ± 1.2	1.5 ± 1.2*	1.9 ± 1.2*	2.0 ± 1.3*	2.0 ± 1.2*	1.7 ± 1.3
Conjugated oestrogens+progestogen							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	62	58	48	37	33	29	30
SBP (mmHg)	156.4 ± 20.6	152.3 ± 21.8	155.3 ± 20.5	154.5 ± 20.7	150.5 ± 17.8	152.5 ± 25.4	154.2 ± 24.8
DBP (mmHg)	92.3 ± 11.4	88.1 ± 11.0*	89.9 ± 9.1	89.8 ± 13.0	87.2 ± 11.4	90.4 ± 10.2	87.6 ± 10.7*
Weight (kg)	75.4 ± 16.4	75.3 ± 17.5	73.9 ± 16.8	74.5 ± 17.1	80.3 ± 18.7	79.5 ± 19.5	80.4 ± 20.9
No of antihypertensive drugs used	1.3 ± 1.1	1.5 ± 1.1	1.3 ± 1.0	1.4 ± 1.1	1.5 ± 1.2*	1.6 ± 1.1*	1.6 ± 1.1
Oestrogen patches							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	27	25	24	20	16	18	14
SBP (mmHg)	160.7 ± 24.1	155.9 ± 22.1	158.9 ± 23.9	156.6 ± 19.7	153.5 ± 18.6	152.2 ± 19.6	152.2 ± 20.8
DBP (mmHg)	94.9 ± 11.9	92.3 ± 8.0	92.5 ± 9.1	94.0 ± 9.4	87.4 ± 7.2*	86.8 ± 8.9*	88.6 ± 9.1
Weight (kg)	74.6 ± 14.6	79.0 ± 15.8	83.8 ± 23.1*	74.3 ± 11.3	76.5 ± 12.5*	77.4 ± 15.6	76.8 ± 11.1
No of antihypertensive drugs used	1.5 ± 1.1	1.8 ± 1.1*	1.7 ± 1.0	1.7 ± 0.8	1.9 ± 0.9	1.9 ± 0.8	1.9 ± 1.2

* $p < 0.05$. Attendance (*n*) signifies the number of paired observations to the initial time point, for each subsequent time point. Data are mean ± SD (standard deviation).

antihypertensive medication throughout the follow-up period. One-way ANOVA suggests that this increased need was specifically associated with the use of oestrogen patches, rather than conjugated oestrogens or oestrogens–progestogen preparations ($p < 0.0005$). Quite unexpectedly, the older group of patients (Table IVb) was largely unaffected.

Serum cholesterol changes

Non-fasting serum total cholesterol levels were measured in 73 patients (52 White, 13 Afro-Caribbean and eight South Asian), before and after the initiation of HRT, with a time interval of 13.0 ± 8.9 months. Mean serum cholesterol levels prior to HRT were 6.18 ± 1.34 mmol/l and following HRT 6.20 ± 1.31 mmol/l (paired *t*-test, $p = 0.820$). The type of HRT did not influence changes in serum cholesterol levels (data not shown).

Discussion

After the menopause, cardiovascular risk factors and vascular events in women change dramatically. Data from studies that have been conducted over the last 30 years are largely inconsistent, with reports of HRT lowering (19,20), increasing (21,22) or not affecting (4,16,23,24) BP mostly in normotensive women.

Whereas most of the studies refer to normotensive menopausal women, some that have been conducted in hypertensive subjects. For example, Mercurio et al. (25) studied 30 postmenopausal women with mild hypertension, who were randomized to either patches of transdermal oestradiol 17β or a matched placebo. The 24-h ambulatory BP decreased significantly in those receiving HRT with a restoration of the night-time BP fall in the non-dippers group. These authors also reported a significant decrease in ambulatory BP in a smaller group of postmenopausal women with mild to moderate hypertension, while receiving transdermal oestradiol (26).

Nonetheless, a beneficial effect of HRT on BP is not supported by all authors. For example, Miya et al. (27) studied a group of 21 hypertensive postmenopausal women with known left ventricular hypertrophy, where 11 were treated with a combination of oral conjugated oestrogen plus progesterone for a 12-month period. The HRT group showed a significant reduction of left ventricular mass together with a reduction of serum angiotensin-converting enzyme activity and levels of plasma aldosterone, but no effect on the BP was recorded. Similarly, Hayward et al. (28) studied a population of 12 diabetic women (six of them were also hypertensive); the HRT was well tolerated but failed to affect both clinic and ambulatory BP measurements. In a randomized controlled trial by

Table IV. Systolic (SBP) and diastolic blood pressure (DBP), body weight and number of drugs used during the follow-up period of patients belonging to different age groups.

(a) Age ≤ 52 years							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	81	75	67	49	47	44	38
SBP (mmHg)	152.6 \pm 22.9	151.8 \pm 23.9	155.5 \pm 22.2	153.7 \pm 21.1	151.7 \pm 21.5	151.6 \pm 24.2	152.1 \pm 26.7
DBP (mmHg)	92.4 \pm 13.5	91.2 \pm 10.8	92.8 \pm 12.2	93.3 \pm 13.5	91.7 \pm 11.4	91.6 \pm 11.6	91.2 \pm 12.4
Weight (kg)	75.7 \pm 13.5	76.8 \pm 14.4	74.8 \pm 13.6	76.0 \pm 11.6	77.2 \pm 13.9*	78.6 \pm 15.9*	77.5 \pm 15.4
No of antihypertensive drugs used	1.2 \pm 1.2	1.3 \pm 1.1	1.3 \pm 1.1*	1.6 \pm 1.2*	1.7 \pm 1.2*	1.9 \pm 1.2*	1.7 \pm 1.3*
(b) Age > 52 years							
Time	0	6 months	12 months	18 months	24 months	30 months	36 months
Attendance (<i>n</i>)	80	74	64	49	37	36	39
SBP (mmHg)	160.5 \pm 23.1	156.3 \pm 20.1	157.2 \pm 21.0	158.3 \pm 19.3	160.7 \pm 18.8	160.8 \pm 18.9	158.4 \pm 18.1
DBP (mmHg)	92.9 \pm 11.4	89.4 \pm 10.0*	90.0 \pm 10.2	89.6 \pm 10.1	87.2 \pm 10.5*	90.8 \pm 9.8	87.9 \pm 10.0*
Weight (kg)	74.7 \pm 16.4	76.2 \pm 17.5	73.2 \pm 14.9	70.5 \pm 15.6	71.0 \pm 14.9	73.2 \pm 17.0	74.9 \pm 16.1
No of antihypertensive drugs used	1.7 \pm 1.0	1.8 \pm 1.0	1.7 \pm 1.0	1.7 \pm 0.9	1.8 \pm 1.0	1.7 \pm 0.9	1.7 \pm 1.1

* $p < 0.05$. Attendance (*n*) signifies the number of paired observations to the initial time point, for each subsequent time point. Data are mean \pm SD (standard deviation).

Kornhauser et al. (29), no rise in BP was found after 90 days in hypertensive women with two forms of HRT, but there was an unexpected fall in BP in those women allocated to placebo.

In the present study, there was no evidence of a significant BP effect of HRT. Overall the BP remained stable or even reduced through time, although this was accompanied by an increase in the use of antihypertensive agents. Had antihypertensive drug therapy not been increased, we might have observed a rise in BP. Thus, we cannot be sure whether HRT adversely affects hypertensive women. If it does, then this may explain the borderline trend for HRT to have adverse effects in the long-term placebo-controlled trials conducted largely in older high-risk women. Whether the increased need for antihypertensive drugs was a result of HRT treatment itself or of the recorded increase in body weight also remains a question. We recognize the lack of a matched placebo control group as a limitation in our study. Also, we have deliberately not given detail on antihypertensive therapies *per se*, as these changed over the course of the follow-up period, as did doses. While the ethnic subgroup data are relatively small, given the lack of ethnic data in the literature on this subject, we believe we present unique data on HRT and BP in ethnic groups.

Regarding the different types of HRT available, our study suggests that the oestrogen-progestogen combination is preferable (at least compared to conjugated oestrogens alone) since it appears to have a minimal effect on BP and is associated with the least increase in antihypertensive demands and body weight. The small number of patients on tibolone did not allow us to make any comparisons of oestrogen and non-oestrogen preparations.

Unexpectedly, the younger group of the patients seemed to be more affected by the initiation of HRT, increasing the number of the BP drugs used during the follow-up period, compared to the older one. Given the results of the Women's Health Initiative trial (13), demonstrating an increased risk for stroke in women aged 50–79 years old on conjugated oestrogens-progestogen, we would expect a different result. It is also interesting that serum cholesterol levels were not affected before and after the initiation of HRT or by any specific HRT regime. Certainly, a beneficial effect of HRT not only on BP but on metabolic indices also, such as total cholesterol levels, low-density lipoprotein and fibrinogen, has been reported (30). The short time lapse at which a second blood sample was obtained in many patients is a potential confounder.

It seems that HRT is relatively safe and should not be withheld from patients wherever appropriate. In our cohort, HRT was stopped in seven patients (out of 161) because of an increase in their BP; however, the decision was made by their general practitioners, usually on a single measurement basis, and not by us. The scepticism about the use of HRT in postmenopausal women, and in particular hypertensive ones, regarding their haemodynamic effects, originates from studies published in the 1970s or early 1980s when the form and the doses of HRT provided were different than those currently used (24,25).

In conclusion, HRT use does not have an adverse gross effect on BP in hypertensive menopausal women who need it, although there may be an increased need for antihypertensive therapy during the 36-month follow-up period of our study. The increased need for antihypertensive drugs implied in

our study, viewed under the perspective of the latest randomized controlled trials demonstrating a neutral or unfavourable effect of HRT on cardiovascular events, raises the question of whether the results would be any different given the BP was more aggressively controlled in those trials.

References

1. Belchetz PE. Hormonal treatment of postmenopausal women. *N Engl J Med*. 1994;330:1062.
2. The Writing Group for the PEPI Trial. Effects of hormone therapy on bone mineral density: results from the postmenopausal estrogen/progestin interventions (PEPI) trial. *JAMA*. 1996;276:1389–96.
3. Grodstein F, Stampfer MJ, Colditz GA, et al. Postmenopausal hormone therapy and mortality. *N Engl J Med*. 1997;336:1769–75.
4. The Writing Group for the PEPI Trial. Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The postmenopausal estrogen/progestin interventions (PEPI) trial. *JAMA*. 1995;273:199–208.
5. Butkevich A, Abraham C, Phillips RA. Hormone replacement therapy and 24-hour blood pressure profile of postmenopausal women. *Am J Hypertens*. 2000;13:1039–41.
6. Cacciatore B, Paakkari I, Hasselblatt R, et al. Randomized comparison between orally and transdermally administered hormone replacement therapy regimens of long-term effects on 24-hour ambulatory blood pressure in postmenopausal women. *Am J Obstet Gynecol*. 2001;184:904–9.
7. Posthuma WF, Westendorp RG, Vandenbroucke JP. Cardioprotective effect of hormone replacement therapy in postmenopausal women: is the evidence biased? *BMJ*. 1994;308:1268–9.
8. Hulley S, Grady D, Bush T, et al. The Heart and Estrogen/progestin Replacement Study (HERS) Research Group. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA*. 1998;280:605–13.
9. Grady D, Herrington D, Bittner V, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy. Heart and Estrogen/Progestin Replacement Study follow up (HERS II). *JAMA*. 2002;288:49–57.
10. Hulley S, Furberg C, Barrett-Connor E, et al. Noncardiovascular disease outcomes during 6.8 years of hormone therapy. Heart and Estrogen/Progestin Replacement Study follow up (HERS II). *JAMA*. 2002;288:58–66.
11. Viscoli CM, Brass LM, Kernan WN, et al. A clinical trial of Estrogen-Replacement therapy after ischemic stroke. *N Engl J Med*. 2001;345:1243–9.
12. Cherry N, Gilmour K, Hanaford P, et al., (the ESPRIT team). Oestrogen therapy for prevention of reinfarction in postmenopausal women: a randomised placebo controlled trial. *Lancet*. 2002;360:2001–8.
13. Wassertheil-Smoller S, Hendrix SL, Limacher M, et al. Effect of Estrogen plus Progestin on stroke in postmenopausal women. The Women's Health Initiative: a randomized trial. *JAMA*. 2003;289:2673–84.
14. The Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in Million Women Study. *Lancet*. 2003;362:419–27.
15. Chasan-Taber L, Willett WC, Manson JE, et al. Prospective study of oral contraceptives and hypertension among women in the United States. *Circulation*. 1996;94:483–9.
16. Lip GYH, Beevers M, Churchill D, Beevers DG. Hormone replacement therapy and blood pressure in hypertensive women. *J Hum Hypertens*. 1994;8:491–4.
17. Kawecka-Jaszcz K, Czarnecka D, Olszanecka A, et al. The effect of hormone replacement therapy on arterial blood pressure and vascular compliance in postmenopausal women with arterial hypertension. *J Hum Hypertens*. 2002;16:509–16.
18. Umeda M, Ichikawa S, Kanda T, et al. Hormone replacement therapy increases plasma level of angiotensin II in postmenopausal hypertensive women. *Am J Hypertens*. 2001;14:206–11.
19. Butkevich A, Abraham C, Phillips RA. Hormone replacement therapy and 24-hour blood pressure profile of postmenopausal women. *Am J Hypertens*. 2000;13:1039–41.
20. Cacciatore B, Paakkari I, Hasselblatt R, et al. Randomized comparison between orally and transdermally administered replacement therapy regimens of long-term effects on 24-hour ambulatory blood pressure in postmenopausal women. *Am J Obstet Gynecol*. 2001;184:904–9.
21. Utian WH. Effect of postmenopausal estrogen therapy on diastolic blood pressure and body weight. *Maturitas*. 1978;1:3.
22. Wren BG, Routledge DA. Blood pressure changes. Oestrogens in climacteric women. *Med J Aust*. 1981;2:528–31.
23. Pripp U, Hall G, Csemiczky G, et al. A randomized trial on effects of hormone replacement therapy on ambulatory blood pressure and lipoprotein levels in women with coronary artery disease. *J Hypertens*. 1999;17:1379–86.
24. Schunkert H, Danser AHJ, Hense HW, et al. Effects of estrogen replacement therapy on the rennin-angiotensin system in postmenopausal women. *Circulation*. 1997;95:39–45.
25. Mercuro G, Zoncu S, Piano D, et al. Estradiol-17beta reduces blood pressure and restores the normal amplitude of the circadian blood pressure rhythm in postmenopausal hypertension. *Am J Hypertens*. 1998;11:909–13.
26. Mercuro G, Zoncu S, Pilia I, et al. Effects of acute administration of transdermal estrogen on postmenopausal women with systemic hypertension. *Am J Cardiol*. 1997;80:652–5.
27. Miya Y, Sumino H, Ichikawa S, et al. Effects of hormone replacement therapy on left ventricular hypertrophy and growth-promoting factors in hypertensive postmenopausal women. *Hypertens Res*. 2002;25:153–9.
28. Hayward CS, Samaras K, Campbell L, Kelly RP. Effect of combination hormone replacement therapy on ambulatory blood pressure and arterial stiffness in diabetic postmenopausal women. *Am J Hypertens*. 2001;14:699–703.
29. Kornhauser C, Malacara JM, Garay ME, Perez-Luque EL. The effect of hormone replacement therapy on blood pressure and cardiovascular risk factors in menopausal women with moderate hypertension. *J Hum Hypertens*. 1997;11:405–11.
30. Affinito P, Palomba S, Bonifacio M, et al. effects of hormonal replacement therapy in postmenopausal hypertensive patients. *Maturitas*. 2001;40:75–83.