Hormone Replacement Therapy and 24-Hour Blood Pressure Profile of Postmenopausal Women

Alexander Butkevich, Carmella Abraham, and Robert A. Phillips

Menopause is associated with an increase in blood pressure (BP) and a decrease in physiologic nocturnal BP fall. These factors may play a role in the increased risk of cardiovascular events after menopause. Some studies indicate that transdermal estrogen replacement therapy may help restore the 24-h BP profile, but data on the effect of oral conjugated estrogens are lacking. We compared 24-h ambulatory BP profiles of 42 postmenopausal women not receiving hormone replacement therapy (HRT) and 20 women receiving HRT. HRT was associated with a significant increase in the proportion of dippers (50% in women not receiving HRT and 80% in women receiving HRT, \( P = .048 \)).


KEY WORDS: Menopause, hormone replacement therapy, blood pressure profile.

Menopause is associated with several cardiovascular changes. These include elevated systolic BP, increased left ventricular wall thickness, decreased systolic performance, and decreased nocturnal BP fall (dipping).\(^1,2\) All these factors are implicated in the increased risk of cardiovascular events that occurs after menopause.

A growing body of evidence indicates that hormone replacement therapy (HRT) is beneficial in postmenopausal women. It is associated with symptomatic improvement, regulation of dysfunctional uterine bleeding, prevention of atrophic changes in the urogenital tract, and a lower risk of osteoporosis and Alzheimer’s disease.\(^3,4\) The cardiovascular benefits of HRT include reduction of arterial stiffness,\(^5\) improvement in endothelium-dependent vasodilatation,\(^6\) reduction of BP,\(^7\) and a normalization of lipid profile.\(^8\) These effects may result in a reduced risk of cardiovascular events (coronary heart disease and stroke) and their associated morbidity and mortality.\(^4,9\)

Some data suggest that postmenopausal women who receive transdermal estradiol 17\(\beta\) are more likely to be dippers than those who do not.\(^7\) However, oral estrogen preparations are more commonly used by postmenopausal women. In addition to having different estrogen composition, oral preparations undergo a significant first-pass liver metabolism, which results in a reduced bioavailability and a hormonal profile different from that of transdermal estrogens.\(^10\) The aim of our study was to determine whether the increase in nocturnal BP dipping is a general finding associated with the use of estrogens rather than a specific effect of transdermal estradiol 17\(\beta\). This could have important implications because among people with hyperten-
sion, dippers have a lower cardiovascular risk than nondippers.11,12

MATERIALS AND METHODS

We analyzed ambulatory blood pressure monitoring (ABPM) recordings of 62 postmenopausal women who had BP readings >140/90 in the physician’s office, were referred to the Hypertension Section of the Mount Sinai Medical Center in New York City for 24-h ABPM, and who were not treated with antihypertensive medications. Monitoring was performed with SpaceLabs 90207 or 90217 monitor (SpaceLabs Medical Inc., Redmond, WA). Menopausal and HRT status were assessed by a questionnaire on the day of ABPM.

The data were downloaded from the monitor to the 90121 ABP Report Management System (SpaceLabs Medical Inc., Redmond, WA) and then to the MS Access 97 database (Microsoft Corp., Redmond, WA). Twenty-four-hour ABPM recordings were edited according to previously described criteria.13 Daytime and nighttime were defined according to previously published recommendations14 between 7:00 AM and 10:00 PM for daytime and between 10:00 PM and 7:00 AM for nighttime. Dipping was defined as a nocturnal decrease of 10 mm Hg in systolic BP relative to daytime values.

The data were analyzed with the use of MS Access 97 and MS Excel 97 (Microsoft Corp., Redmond, WA) commercial programs. Statistical analyses were performed with the use of SigmaStat 2.0 (SPSS Inc., Chicago, IL). A t test was used for pairwise comparison of the numeric variables. The proportions of dippers were compared with use of the z test.

RESULTS

The study population consisted of 42 postmenopausal women not receiving HRT and 20 postmenopausal women receiving HRT. The subjects’ characteristics and dipping status are summarized in Table 1.

The difference in age and BP between the two groups was not significant. The mean body mass index (BMI) of women receiving HRT was significantly lower than that of the group not receiving HRT ($P = .004$). However, the proportion of obese subjects, defined as BMI $>27$ kg/m$^2$, was not significantly different between the groups (10% in the group receiving HRT, 31% in the group not receiving HRT, $P = .137$). Fifty percent of the postmenopausal women not receiving HRT were dippers, as compared with 80% of those receiving HRT. This difference was statistically significant ($P = .048$).

DISCUSSION

This cross-sectional study examined the hypothesis that postmenopausal HRT is associated with an increase in nocturnal BP dipping. We compared the mean daytime and nighttime BP and proportions of dippers among postmenopausal women receiving HRT and not receiving HRT. In keeping with the findings of previous studies, we found no increase in daytime BP associated with HRT. There were significantly more dippers among women in the group receiving HRT than in the group not receiving HRT. Although subjects not receiving HRT did exhibit a nocturnal decrease in diastolic BP, Verdercchia et al15 demonstrated that it is the decrease in systolic BP that confers a reduced cardiovascular risk. Therefore, we limited our definition of dipping to nocturnal decrease in SBP. Furthermore, when we applied the original definition of dippers used by O’Brien et al16 (nocturnal decrease of 10/5 mm Hg) the results were very similar: 80% dippers in the group receiving HRT and 48% in the group not receiving HRT, $P = .035$.

In a double-blind crossover study in postmenopausal women with mild hypertension, Mercuro and colleagues7 demonstrated that transdermal estradiol 17b can partially normalize a blunted nocturnal BP decline. To date, no study has demonstrated a similar effect of other estrogens. Our data provide indirect evidence that orally administered conjugated estrogens may increase nocturnal BP dipping as well.

One possible confounding factor in our study is that women receiving HRT had a lower BMI than women not receiving HRT. Although the relationship between BMI and dipping status is not established, some data17,18 suggest that for BMI $<27$ kg/m$^2$ there is no relationship between BMI and dipping and that obese persons (defined as body mass index $>27$ kg/m$^2$ for women) may be less likely to be dippers than lean subjects. The difference in BMI, however, is unlikely to account for the difference in dipping status, as the proportion of obese subjects did not vary significantly between the two groups in our study.

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<tr>
<th>TABLE 1. PATIENT CHARACTERISTICS</th>
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<tr>
<td><strong>No HRT</strong></td>
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<td>No. of patients</td>
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<td>Age, years</td>
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<td>BMI, kg/m$^2$</td>
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<tr>
<td>Diastolic BP, mm Hg</td>
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HRT = hormone replacement therapy; BMI = body mass index; BP = blood pressure; ABPM = ambulatory blood pressure monitoring.

Values are as mean ± SD.

* $P < .05$ v no HRT.
A significant body of evidence indicates that hypertensive dippers have a lower risk of cardiovascular and renal complications of hypertension than nondippers with a similar level of daytime BP.\textsuperscript{11,12} Thus, it is appealing to hypothesize that some of the protective cardiovascular effects of estrogens may be explained by increase in nocturnal drop in BP. A larger prospective study is needed to confirm this effect of oral HRT on 24-h BP profile.

ACKNOWLEDGMENTS

This work was supported in part by a grant 5MO1 RR00071 for the Mount Sinai General Research Center from the National Center for Research Resources, National Institutes of Health, and by a private grant from Mr. Howard L. Printz.

REFERENCES