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This complimentary e-newsletter from The North American Menopause Society (NAMS) presents clinical questions and cases commonly seen in a menopause specialist's practice. Recognized experts in the field provide their opinions and practical advice. Robert A. Wild, MD, PhD, MPH, NCMP, the Editor of *Menopause e-Consult*, encourages your suggestions for topics to be addressed in future issues. Note that the opinions expressed in the commentaries are those of the authors and are not necessarily endorsed by NAMS or Dr. Wild. Previously published issues may be viewed on the NAMS Web site (www.menopause.org/econsult.html).

Question

How should a perimenopausal woman with prehypertension be managed and how can menopause affect the progression and management of hypertension?

Commentary by:



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“Prehypertension” as defined by the Seventh Report of the Joint National Committee on Prevention (JNC7)¹ is blood pressure between 120/80 mmHg and 140/89 mmHg. Based on the 1999-2000 National Health and Nutrition Examination Survey,² the prevalence of prehypertension was estimated to be 23% in US adult women. The JNC7 authors felt it was important to identify this group of patients as prehypertensive due to their increased risk of developing hypertension and their potential for increased risk of cardiovascular events.^{3,4} Thus, identifying the prehypertensive perimenopausal woman is an important undertaking in order to

manage her risk of cardiovascular disease (CVD), in particular, stroke.

How does menopause impact blood pressure in women? It has been well documented that hypertension increases with age in both women and men. Observational data have shown an increase in hypertension after menopause.⁵ Even in patients who are free from hypertension at age 65, a significant proportion will develop hypertension by age 85.^{3,6,7} Risk for CVD increases in postmenopausal women. Hsia et al reported data from the Women's Health Initiative (WHI) on the prevalence of prehypertension and its association with cardiovascular morbidity and mortality.⁸ They showed that prehypertension was prevalent at baseline in up to 40% of women, with mild variations based on ethnicity. They demonstrated that, compared with normotensive women, prehypertension was associated with an increased risk of myocardial infarction, stroke, congestive heart failure, and cardiovascular death. They also reported an increased prevalence of diabetes and dyslipidemia in prehypertensive women. Greenlund et al showed that the frequency of prehypertension declines with advancing age in men, while for women it is greatest between ages 40 and 59, declining thereafter⁹ and corresponding to the age range for perimenopause.

Diabetes and overweight have been shown to increase the risk of CVD in patients with prehypertension.¹⁰

Other effects specific to hypertensive postmenopausal women are increased salt sensitivity¹¹ and greater plasma renin activity than perimenopausal women (but lower activity than men of the same age).¹² Although the role that sex hormones play in the regulation of hypertension is complex and beyond the scope of this *Menopause e-Consult*, two excellent reviews, one by Dubey et al¹³ and the second by Reckelhoff,¹⁴ are well worth reading.

Treatment. There is minimal data available about intervening in the prehypertensive patient. JNC7 recommends lifestyle interventions including diet, weight loss, and exercise. The 2007 American Heart Association (AHA) guidelines on CVD prevention in women encourage an optimal blood pressure of 120/80 mm Hg through similar lifestyle approaches such as weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fresh fruits, vegetables, and low-fat dairy products.¹⁵ They go on to say that:

“Pharmacotherapy is indicated when blood pressure is 140/90 mm Hg or at an even lower blood pressure in the setting of chronic kidney disease or diabetes (130/80 mm Hg). Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated or if there are compelling indications for other agents in specific vascular diseases. Initial treatment of high-risk women should be with beta blockers and/or ACE [angiotensin-converting enzyme] inhibitors/ARBs [angiotensin receptor blocker], with addition of other drugs such as thiazides as needed to achieve goal blood pressure.”

One study¹⁶ gives us some insight into treatment of the prehypertensive patient: Approximately 800 patients with prehypertension were randomized to two groups, placebo and an active treatment arm with candesartan (an ARB). The patients were followed for 2 years on treatment and for another 2 years off treatment (unless they developed hypertension). Patients treated with candesartan developed hypertension at a lower rate than those in the placebo group. At the end of 4 years, the treated

group still had a lower rate of hypertension; however, the curves did start to come closer together. This seems to indicate that treatment of prehypertensive patients with an ARB can delay the onset of hypertension. Recently, a group from Germany took this data and applied it to the German healthcare system. They estimated a significant cost savings if all prehypertensive patients were treated with either an ARB or an ACE inhibitor.

A review of the WHI hypertensive data by Oparil cautions that while estrogen may lower blood pressure, hormone therapy should not be used to treat blood pressure, and recommends that aggressive management of blood pressure with available drugs makes the most sense in postmenopausal patients.¹⁷

Conclusions. Based on the available information, it seems clear that it is important to identify perimenopausal women with prehypertension. Aggressive dietary and lifestyle interventions may delay onset of hypertension. As hypertension prevalence does increase after menopause, any interventions that reduce this rate are important. The role of pharmacotherapy is less clear, however. Prehypertension is associated with other cardiovascular comorbidities, such as dysglycemia and dyslipidemia. Aggressive cardiovascular risk evaluation and drug therapy for diabetes or lipid management are benefits of identifying these patients. We await future clinical trials to see if drug intervention in the prehypertensive patient decreases cardiovascular morbidity and mortality.

As far as the management of the postmenopausal hypertensive woman is concerned, reiteration of the current JNC7 and AHA guidelines is appropriate. Inclusion of diuretic therapy may be preferred, perhaps with drugs that block the renin-aldosterone-angiotensin system. In patients with abnormal lipid and lipoprotein metabolism, however, diuretics can adversely impact lipoproteins, so careful cardiovascular risk evaluation with a choice of antihypertensive therapy should always be on a case-by-case basis.

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Case:

In my office, I recently saw a 48-year-old perimenopausal woman who was experiencing severe vasomotor symptoms during the day and night, along with other typical menopause-related symptoms. Of more concern, however, was that she was feeling “dizzy” on a regular basis. How would I go about the workup for dizziness in a peri- or postmenopausal woman?

Management Issues by:



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Dizziness is an increasingly common complaint among women as they age. By age 75, dizziness is their most common complaint. Dizziness can include many different complaints such as vertigo, weakness, syncope, and motion sickness, so it is difficult to extrapolate what “dizziness” means to a particular patient. Evaluation can be time-consuming, with a very broad differential diagnosis, and can be overwhelming even for specialists. Many

women are sent directly to specialists such as cardiologists, neurologists, or otolaryngologists, but primary care clinicians have the opportunity to diagnose, treat, refer, and recognize serious illness needing emergent care.¹

What is dizziness in this woman? Dizziness can be divided into two different terms: vertigo and disequilibrium (non-vertigo).

“Vertigo” is classically the sensation of movement or spinning, often described by patients as objects moving around them or feeling that they are spinning relative to their surroundings. An episode can be quite severe and last from seconds to hours, with or without nausea and vomiting. Aural symptoms often accompany the dizziness. Lightheadedness or a sense of weakness should be investigated to rule out syncope. Vertigo can be subdivided into:

- Ménière’s disease—a quartet of hearing loss, tinnitus (a roaring sound in the ears), fullness, and vertigo
- Vestibular neuritis—labyrinthitis, caused by a single severe event followed by disequilibrium
- Benign paroxysmal positional vertigo (BPPV). BPPV is positional, experienced when lying down or changing position, lasts only seconds, and is not related to ear symptoms.

“Disequilibrium” is usually experienced as unsteadiness or motion sickness; it is constant, lasts longer than a few hours, and is accompanied by mild nausea. Many systems should be considered in a differential diagnosis, including strokes arrhythmia, myocardial infarction, and orthostatic changes. Medications are often the cause of these symptoms, especially when first initiated. Acoustic neuromas and other brain tumors should be considered if unilateral hearing loss is also present. Migraines with or without headaches are very common, especially in women with fluctuating hormones. We now know that hormone changes affect different receptors in the brain, specifically gamma-aminobutyric acid (GABA) receptors and neurotransmitters, which are linked to vestibular system sensitivity.²

Diagnosis. Is this patient suffering from a stroke, brain tumor, or could this be a menopausal symptom? A good history will help differentiate between mild, severe, or chronic problems. Other than the typical gynecologic review of systems, important questions include:

1. Are the symptoms positional?
2. What is the duration of the dizziness?
3. Are there aural symptoms such as ear pain or hearing loss?
4. What medications are being used and if so, have they just been started or stopped, or has the dose recently changed?
5. Are there any cardiac symptoms such as shortness of breath or orthopnea?
6. Does the woman have central nervous system symptoms such as weakness, sensation changes, headaches, visual changes, or emotional changes?
7. Has there been any trauma?
8. Is the dizziness chronic, acute, severe, mild, or recurrent?

If the symptoms are acute, consider vestibular neuritis. With this diagnosis, she should have had no aural symptoms, but there would be nausea and vomiting. The duration is usually days and is not recurrent, and the etiology is viral and not positional. The examination will usually reveal some nystagmus, disequilibrium, and normal hearing. If the diagnosis is acute with neurologic symptoms, proceed with an evaluation for a stroke (although only 1% of patients with isolated dizziness have stroke as an etiology), which includes an MRI and workup in the emergency room or by a specialist such as a neurologist, cardiologist or otolaryngologist depending on the medical concern. Neuritis is usually treated with steroids and normal activities can be continued.

If the symptoms are recurrent and positional, consider a diagnosis of BPPV, the most common cause of vertigo. These symptoms are frightening more than debilitating. The attacks are brief (lasting seconds) and patients feel normal between the attacks. A total of 50% of patients describe disequilibrium during the

attack, nystagmus is seen, and hearing is normal. BPPV occurs because calcium carbonate debris dislodge and enter into the semicircular canal of the ears. BPPV is treated by positional testing and particle repositioning by a physical therapist, otorhinolaryngologist, or trained family practice physician. If BPPV is not consistent, then the diagnosis might be a central structural lesion such as a tumor, multiple sclerosis, an Arnold-Chiari malformation, or an ataxia disorder. A neurologist referral is required.

Recurrent attacks of dizziness have variable durations and the most common diagnosis is Ménière's disease. If this is a new onset with attacks lasting minutes, it could possibly be a transient ischemic attack and a neurologist should be consulted. Other causes could include headaches or migraines with or without aural symptoms. Patients may or may not experience disequilibrium, but hearing is usually normal. Treat with migraine medications but remember that triptan will not help the dizziness. Panic disorders, cervical herniations, and cardiac disorders are other possible causes. A panic disorder can be ruled out by a psychological assessment, and a physical examination of the heart and spinal cord will rule out a herniation or cardiac problem.³

A much less known and less understood etiology of dizziness is perimenopause and hormone therapy (HT). In a recent survey in China, 31% of women with menopausal symptoms identified dizziness as their third most common complaint.⁴ Since hormones do affect the vestibular system, they increase a woman's susceptibility to dizziness. For instance, shifting hormone levels during pregnancy activate a susceptibility to morning sickness.⁵

Estrogen increases serotonin levels in the brain, making it sensitive to visual, auditory, and taste input, while progesterone and its metabolites bind GABA receptors to lessen excitation and decrease sensitivity of the brain. Studies using progesterone show decreased seizure activity. Some clinicians prescribe progesterone (not

progestins) for stress, insomnia, and to decrease premenstrual syndrome symptoms.⁶ In theory, as estrogen levels become erratic and fluctuate higher relative to progesterone during perimenopause, the vestibular system is more sensitive to motion and disequilibrium can result. A recent study found that women with osteoporosis have higher rates of idiopathic BPPV, suggesting that the increased bone breakdown during peri- and postmenopause increases calcium deposition in the ears' semicircular canals.⁷

Treatment: Diagnosis is the key to treatment. After ruling out a serious problem, clinicians can treat dizzy patients with physical therapy and antinauseants, which are available in two different types: vestibular suppressants such as antihistamines, benzodiazepines, or anticholinergics decrease dizziness but are not effective for prevention; and antiemetics control vomiting but do not control dizziness. Together, these medications work well except for an adverse effect of sedation.⁸ HT may help prevent dizziness, but this use has not been well studied.⁹ Perimenopausal patients may find progesterone supplementation helpful, especially prior to menses, to correct disequilibrium. Peri- and postmenopausal women with vertigo may find relief with combined HT (estrogen plus progesterone). When prescribing HT, remember that the more estrogen given, the more excitation to the vestibular system, so use a low dose. More research is coming.

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