Critically Appraised Topic

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Does treatment of new-onset hypertension reduce risk of stroke in the elderly?

An 83-year-old woman with a known history of osteoporosis presents to your clinic for a yearly evaluation and renewal of her prescription for alendronate (Fosamax). She had been fairly healthy and lives independently, remaining active in the community with various volunteer activities. At a recent health fair, a nurse measured her BP and said it was 180/94 mm Hg. This alarmed the patient because she had never been treated for hypertension in the past. She had no known history of cardiovascular problems; she denied headaches, dizziness, or visual disturbances. Examination findings were height, 5 ft 3 in with a slightly kyphotic posture; weight, 120 lb; BP, 170/90 mm Hg; pulse, 76 beats per minute; respirations, 14 breaths per minute. Cardiac auscultation revealed a regular rate and rhythm with no murmurs. Funduscopic examination revealed no vascular abnormalities. The well-known standard of care for new-onset hypertension in adults is antihypertensive therapy; however, you question whether adding a new medication would impact the risk of stroke or cardiovascular mortality in this 83-year-old woman.

CLINICAL QUESTION

Does the initiation of antihypertensive therapy decrease incidence of stroke or cardiovascular mortality in the elderly (80 years or older)?

SEARCH CRITERIA AND RESULTS

Initially, the Cochrane Database of Systematic Reviews was searched; the last update of this topic was in 1998. The authors concluded that evidence was lacking for treatment of hypertension in the very elderly.[1] A search was then conducted in MEDLINE using the major subject heading *hypertension* with a subheading of *drug therapy*. The search was then limited to articles in English published in the past 10 years and to the group *aged, 80 and over*. A similar search was conducted in CINAHL and PubMed:. Abstracts were evaluated for inclusion of elderly patients and the search was expanded to include the terms *elderly*, *longitudinal study*, *drug utilization*, *age factors*. A more precise search was performed on popular journal archives such as *JAMA*, *British Medical Journal*, *Journal of Human Hypertension*, *The Lancet*, *Archives of Internal Medicine*, and *The New England Journal of Medicine* using similar terms to include older but relevant studies.

A total of eight randomized controlled trials (RCTs) along with two meta-analyses were identified and evaluated for inclusion of patients older than 80 years and strength of evidence. Four of the RCTs and one meta-analysis focused on isolated systolic hypertension. Of the remaining five studies, one RCT was excluded because it did not include patients older than 74 years. Another was excluded because the average patient age was 72 years and the trial was conducted in the 1970s.

One study that combined systolic and diastolic hypertension was the pilot study of the Hypertension in the Very Elderly Trial (HYVET-Pilot).[2] This study was unique in that all the participants were at least 80 years old. The completed trial results were not published until after this search was conducted.[3] Ultimately, this trial, the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension),[4] and the INDANA (Individual Data Analysis of Antihypertensive Drug Intervention) Group meta-analysis[5] were used to answer our clinical question.

EVALUATING THE EVIDENCE

The **STOP-H Trial** was conducted in Sweden in 1991.[4] This double-blind randomized placebo trial included 1,627 males and females aged 70 to 84 years. The qualifications for this study were systolic BP 180 to 230 mm Hg and diastolic BP 90 mm Hg or higher, and also included isolated elevated diastolic BP (higher than 105 mm Hg but lower than 120 mm Hg). The participants were not being actively treated when baseline values were obtained and had not experienced an MI or stroke in the past 12 months. Outcome measures were cardiovascular disease, fatal and nonfatal MI, and stroke. Various individual beta-blockers as well as a combination of a beta-blocker and diuretic were chosen as treatments.[4]

In addition to finding that treating patients up to age 84 years significantly lowered BP, an overall decrease was seen in the primary end points of stroke, MI, and cardiovascular-related death. A decrease in all-cause mortality was also observed. The number needed to treat (NNT) was 23 for primary end points and 30 for all-cause mortality. Overall, this trial concluded that treat-

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ing hypertension into the early ninth decade of life is beneficial.[4] However, we were concerned about the applicability to our patient because she is at the high end of the age range of this study. How many of the 1,627 participants were in their eighth decade and if they benefitted as much as the participants in their 70s is not known.

In 1999 the **INDANA Group** pooled data from a group of published trials regarding the treatment of combined hypertension in the elderly.[5] The meta-analysis reviewed five trials with participants older than 80 years: the European Working Party on High Blood Pressure in the Elderly, Systolic Hypertension in the Elderly Program (SHEP) Pilot, SHEP, and STOP-Hypertension. The primary outcome examined was the effect of antihypertensive therapy on stroke. Among the participants in active treatment groups, 57 of 874 had stroke events compared with 77 of 796 participants in placebo groups (NNT = 32). A trend toward decreased incidence of cardiovascular events and heart failure was observed; however, this was not statistically significant. This meta-analysis indicated that treating hypertension in the very elderly can reduce the incidence of stroke.[5]

The randomized, double-blind, placebo-controlled **HYVET Trial** examined the effects of treating hypertension in 3,845 persons 80 years or older.[3] The average age of the participants was 83.6 years. Various exclusion criteria were utilized in order to obtain a "fit" elderly population in the study, including hemorrhagic stroke in the past 6 months, heart failure requiring pharmacotherapy, and secondary hypertension. All participants had a minimum systolic pressure of 160 mm Hg at the start of the trial. Fatal and nonfatal stroke were the primary end points. Secondary end points were all-cause mortality, cardiovascular mortality, and stroke mortality. Approximately 11.8% of the participants had a history of cardiovascular disease. The first-line antihypertensive treatment was 1.5 mg of indapamide sustained-release, a thiazidelike diuretic. (Indapamide is not available in the United States in the sustained-release form.) If further treatment was needed, perindopril, 2 to 4 mg, was given in order to reach a target BP of 150/80 mm Hg. The median follow-up was 1.8 years.[3]

After 2 years, systolic BP decreased an additional 15 mm Hg and diastolic BP decreased an additional 6.1 mm Hg in the active treatment group compared with the BP measurements in the control group.[3] A 30% reduction in stroke occurrence was statistically significant in the treatment group; a 39% reduction in stroke mortality and 21% reduction in all-cause mortality were also seen, as well as statistically significant reductions in cardiovascular-related mortality and heart failure. The NNT to prevent stroke was 103 and to prevent stroke mortality was 104 over the 2-year period. The treatment group also reported fewer significant adverse events.[3] This study provided clear evidence that treating systolic BP of 160 mm Hg or higher in the very elderly is beneficial.

The design of the newly released HYVET is excellent; however, the available data still have limitations. A study with an average participant age older than 83.6 years could further guide treatment decisions for our very oldest patients. In addition, the evaluated studies excluded patients with significant comorbidities; therefore, extrapolation of the results of the HYVET and STOP-Hypertension trials to a more frail elderly population may not be possible. Furthermore, both STOP-Hypertension and HYVET used diuretics with or without a beta-blocker or an ACE inhibitor, so whether other commonly used antihypertensive therapies, such as angiotensin receptor antagonists, calcium channel blockers, or combination therapies, would have the same protective effect is not known.

CLINICAL BOTTOM LINE

Based on this evidence, we will treat our patient with indapamide, 1.25 mg daily, with follow-up in 2 weeks. The target BP is 150/80 mm Hg. The indapamide dosage may need to be increased or an ACE inhibitor added to our patient's regimen in order to reach the target BP. Electrolytes and renal function should be measured at the initiation of any diuretic treatment and periodically thereafter to monitor for any significant changes throughout therapy.

The geriatric population is growing; an estimated 1 of every 5 Americans will be older than 65 years by the end of 2030. Hypertension is present in 67.1% of men and 82% of women older than 75 years.[6] The question of whether to treat hypertension in our very oldest patients is one that we will increasingly face in the coming years. The publication of the HYVET results provides the best evidence to date that stroke incidence in this age-group can be reduced. JAAPA

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Note: The number needed to treat (NNT) was not reported for any of these studies. The author calculated NNT using the following formula: 1 / (number of events in the control group / number of subjects in the control group) – (number of events in the treatment group / number of subjects in the treatment group). For example, the STOP-Hypertension trial reported that 94 primary end-point events occurred among 815 participants in the control group and 58 primary end-point events occurred among 812 participants in the treatment group: NNT = 1 / (94 / 815) – (58 / 812) = 23. Therefore, 23 patients would need to be treated to prevent one of the primary end-point events: MI, stroke, or other cardiovascular death.

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