
... SELECTED ABSTRACTS ...

The following abstracts, from peer-reviewed journals containing literature on hepatitis and its medical management, were selected for their relevance to this supplement.

Trial Results

Sodium reduction and weight loss are effective in the treatment of middle-aged patients with hypertension. These interventions are also recommended for older hypertensive patients, but the experimental basis for this recommendation is limited. The Trial of Nonpharmacologic Interventions in the Elderly (TONE) was conducted to determine the feasibility, efficacy, and safety of sodium reduction and weight loss in older patients with hypertension. The TONE trial was a randomized controlled trial that enrolled 975 men and women aged 60 to 80 years with systolic blood pressure lower than 145 mm Hg and diastolic blood pressure lower than 85 mm Hg while receiving treatment with a single antihypertensive agent. The 585 obese participants were randomized to reduced sodium intake, weight loss, both, or usual care, and the 390 nonobese patients were randomized to reduced sodium intake or usual care. Withdrawal of antihypertensive medication was attempted after 3 months of intervention. The primary outcome was occurrence of high blood pressure at one or more follow-up visits after attempted withdrawal, treatment with antihypertensive medication, or occurrence of a clinical cardiovascular complication during follow-up (median, 29 months). Over the entire period of follow-up the incidence rate for endpoints was only 0.69 (95% CI, 0.59-0.81) as large for those assigned to sodium reduction as those not assigned to sodium reduction ($P < 0.001$). Among the obese patients, the hazard ratios were 0.60 (95% CI, 0.45-0.81; $P < 0.001$), 0.64 (95% CI, 0.49-0.85; $P = 0.002$), and 0.47 (95% CI, 0.35-0.64; $P = 0.001$) for sodium reduction alone, weight loss alone, and combined treatments, respectively. The frequency of cardiovascular events was similar in all groups. The average sodium intake was reduced by 40 mmol per day and average weight loss achieved was 3.5 kg. The trial provided convincing evidence of the feasibility of dietary lifestyle modifications to control high blood pressure and reduce the need for antihypertensive medications in older patients with hypertension. The TONE results have important implications for both public health professionals and clinical practitioners.

Whelton PK, Appel LJ, Espeland MA, et al Sodium retention and weight loss in the treatment of hypertension in older persons. A randomized controlled trial of nonpharmacologic interventions in the elderly (TONE) JAMA 1998;279:839-846

Syst-Eur Trial

The prevalence of isolated systolic hypertension increases with age, occurring in more than 25% of those aged 80 years and older. The Systolic Hypertension in Europe (Syst-Eur) trial was a placebo-controlled, double-blind trial conducted by the European Working Party on High Blood Pressure in the Elderly to evaluate the benefits of antihypertensive treatment in the elderly. The patients were at least 60 years of age and had sitting systolic blood pressure of 160 to 219 mm Hg and sitting diastolic pressure lower than 95 mm Hg. Patients ($n = 4695$) were randomized to active treatment with the calcium channel blocker nitrendipine (10-40 mg daily), with the possible addition of enalapril (5-20 mg daily) and hydrochlorothiazide (12.5-5 mg daily), or placebo. The primary endpoint was fatal or nonfatal stroke. The trial was stopped after the second interim analysis because a significant decrease in the endpoint of stroke was found. At 2 years, the sitting systolic and diastolic blood pressures had fallen by 13 mm Hg and 2 mm Hg in the placebo group compared with 23 mm Hg and 7 mm Hg in the active treatment group. Active treatment reduced the occurrence of all strokes by 42% ($P = 0.003$) and that of nonfatal strokes by 44% ($P = 0.007$). Nonfatal cardiac endpoints, including sudden death, were reduced by 26% ($P = 0.03$). The results provided evidence that calcium channel blockers and converting enzyme inhibitors improve the long-term morbidity and mortality in older patients with isolated systolic hypertension. The benefit of active treatment occurred soon after randomization, when most patients were still on nitrendipine monotherapy. Treatment with nitrendipine, which is of the dihydropyridine class of calcium channel blockers, did not increase the rate of noncardiovascular death, cancer, or bleeding compared with placebo.

Saessen JA, Fagard R, Thijs L, et al Randomised double-blind comparison of placebo and active treatment for older patients with isolated hypertension Lancet 1997;350:757-764.

Blood Pressure and Cardiovascular Disease in the Elderly

Although elevated blood pressure has been consistently viewed as a hazard for development of cardiovascular disease in the age range 65 to 74 years, there appears to be a perception that hypertension may actually be protective beyond 75 years of age. The authors examined the relationship of systolic and diastolic blood pressure to the average annual incidence of initial or recurrent cardiovascular events or overall and cardiovascular mortality in 845 men and 1145 women from the Framingham study. The subjects were 75 to 94 years of age and were either free of cardiovascular disease or had interim cardiovascular disease. Over a 38-year period, cardiovascular morbidity and mortality increased with increasing blood pressure levels in patients free of cardiovascular disease. However, among those who already had a cardiovascular event, there was a distinct U-shaped curve of cardiovascular mortality rate in relation to systolic blood pressure in men, and the mortality rate increased substantially below a systolic pressure of 120 mm Hg in both men and women. The authors suggest that the excess mortality rate at low blood pressure levels could be the result of low ejection fractions rather than the impact of low blood pressure. Thus inclusion of the substantial proportion of this age group who have cardiovascular disease accounts for the increased mortality reported at lower blood pressure.

Kannel WB, D'Agostino RB, Silbershatz H. Blood pressure and cardiovascular morbidity and mortality rates in the elderly. *Am Heart J* 1997;134:758-763.

Clinical Practice Guidelines and Patient Outcomes

The bulk of medical care is delivered by primary care practitioners who are interested in whether clinical practice guidelines (CPGs) have a beneficial effect on patient outcomes. This study was conducted to evaluate the impact of CPGs on patient outcomes in a primary care setting. A search of the medical literature identified studies that assessed the effectiveness of CPGs in primary medical care. Relevant trials were selected if they involved a randomized method, concerned primary care, were related to clinical care, and examined patient outcomes. Thirteen trials were selected for the appraisal. Extracted data included number of physicians, number of patients, proportion followed to completion, length of follow-up, study method, method of guideline implementation, medical conditions studied, effect on patient outcomes, and method of measuring the effect. The most common conditions studied were hypertension (6 studies), asthma (2 studies), and cigarette smoking (2 studies). Overall, 5 of the 13 studies showed a significant improvement in outcomes as a result of the CPGs, and these improvements were only for some of the patients in the study. The change in outcomes was usually modest and none of the studies was conducted long enough to evaluate an impact on mortality. Only 2 of the 13 trials used appropriate methods and enrolled enough subjects to produce sound results. The authors concluded that there was little evidence that use of CPGs significantly improves clinical outcomes in primary care. Lack of effectiveness in these studies could be due to use of poor methodology, guidelines that were based on out-of-date consensus statements, and use of inappropriate outcome measures. Family physicians are the best suited to conduct further research on the effectiveness of the newer evidence-based CPGs.

Worrall G, Chaulk P, Freaque D. The effects of clinical practice guidelines on patient outcomes in primary care: A systematic review. *Can Med Assoc J* 1997;156:1705-1712

Lack of Daily Blood Pressure Control in the Hypertensive Population

Epidemiologic studies in the United States and Europe show that only a small fraction of patients with hypertension have blood pressure controlled to 140/90 mm Hg or lower. Although these findings are believed to be largely related to poor adherence to antihypertensive therapy, a white-coat effect, which could lead to a distorted view of blood pressure control, cannot be discounted. Data were obtained from randomly selected individuals from Monza, Italy, who agreed to participate (n = 1651). The authors measured clinic, home (morning and evening), and ambulatory blood pressure. Each individual was then classified as normotensive, untreated hypertensive (clinic blood pressure >140 mm Hg systolic or >90 mm Hg diastolic), or treated hypertensive. The clinic blood pressure of the treated hypertensive subjects (147/90 mm Hg) was only slightly higher than that of the untreated hypertensive subjects (148/93 mm Hg) and the blood pressure of both groups was considerably higher than that of the normotensive population (120/78 mm Hg). The averaged home and ambulatory blood pressures were lower than clinic measurements in both treated and untreated hypertensive subjects, but higher than similar measurements in normotensive individuals. Both day and night pressures were similarly elevated. Blood pressure control was considered to be satisfactory in 28% and 36% of treated hypertensive patients by clinic and ambulatory measurements, respectively. The results indicate that the number of patients with inadequate blood pressure control was high, because the blood pressure was elevated to a similar extent in treated and untreated subjects regardless of the method of monitoring. The authors concluded that high blood pressure values could not be ascribed to a white-coat effect, but rather were a true reflection of a lack of daily-life blood pressure control.

Mancia G, Sega R, Milesi C, Cesana G, Zanchetti A. Blood pressure control in the hypertensive population. *Lancet* 1997;349:454-457

Efficacy of β -Blockers in the Elderly

In contrast to the diuretics, clear-cut data on the safety and efficacy of β -blockers in elderly patients are lacking. Also the Joint National Committee no longer recommends β -blockers for elderly patients, although they continue to remain an important treatment after myocardial infarction and for other clinical settings. In order to clarify indications for use of β -blockers, the authors performed a meta-analysis to compare the efficacy of β -blockers in relation to the diuretics, particularly with respect to blood pressure reduction, cardiovascular morbidity and mortality, and all-cause mortality. Included in the meta-analysis were 10 trials that involved 16,164 patients and used β -blockers or diuretics as first-line agents and reported morbidity and mortality outcomes in elderly patients with hypertension. With regard to blood pressure control, the response rate to β -blockers ranged from 22% to 48% compared with a response rate of 46% to 88% with the diuretics. Diuretic therapy was superior to β -blocker therapy for all endpoints and reduced the incidence of cerebrovascular events (odds ratio [OR], 0.61 vs 0.74), stroke mortality (OR, 0.67 vs 0.76), coronary heart disease (OR, 0.74 vs 1.01), cardiovascular mortality (OR, 0.75 vs 0.98), and all-cause mortality (OR, 0.86 vs 1.01). The effect of different diuretic regimens was uniform. This analysis demonstrates that β -blockers have a poorer antihypertensive effect compared with diuretics and in addition do not reduce coronary heart disease morbidity and cardiovascular and all-cause mortality. The hemodynamic mismatch caused by β -blocker therapy in the elderly very likely accounts for the poor efficacy of this antihypertensive class in this subset of patients.

Messerli FH, Grossman E, Goldbouri U. Are β -blockers efficacious as first-line therapy for hypertension in the elderly? A systematic review. *JAMA* 1998;279:1903-1907.

CME QUESTIONS: TEST #049812S

The Johns Hopkins University School of Medicine designates this continuing medical education activity for 2 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association. Each physician should claim only those hours of credit that he or she actually spends on the educational activity. Credits are available until the expiration date of December 31, 2000.

Instructions

After reading this Special Report, select the best answer to each of the following questions. At least seven of the 10 answers must be correct to receive CME credit. Estimated time for this activity is 2 hours.

1. **The percentage of patients with hypertension who have blood pressure controlled to 140/90 mm Hg is:**
 - a) less than 30%
 - b) 45%
 - c) 65%
 - d) more than 75%
2. **The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) recommends all of the following except:**
 - a) calcium channel blockers as first-line treatment for isolated systolic hypertension
 - b) ACE inhibitors for heart failure due to systolic dysfunction
 - c) lifestyle modifications for patients in risk group A only
 - d) once-daily medication
3. **Which of the following statements regarding β -blockers is true?**
 - a) β -blockers are superior to diuretics in reducing cardiovascular morbidity and mortality in the elderly
 - b) β -blockers are superior to diuretics in reducing stroke events in the elderly
 - c) β -blockers are recommended for the treatment of hypertension in patients with a previous myocardial infarction
 - d) β -blockers are recommended for first-line treatment of hypertension in the elderly
4. **β -blockers have all of the following effects in the elderly except:**
 - a) they lower the cardiac output during exercise
 - b) they may benefit older patients with essential tremor
 - c) they may exacerbate comorbidities common in older patients such as sexual dysfunction
 - d) they have a direct effect on high peripheral vascular resistance
5. **In the HOT trial, the optimal diastolic blood pressure for lowest risk of cardiovascular events was:**
 - a) 80 mm Hg
 - b) 83 mm Hg
 - c) 87 mm Hg
 - d) 90 mm Hg
6. **The results of the HOT trial showed all of the following except:**
 - a) long-acting calcium channel blockers were effective first-line therapy
 - b) an aggressive antihypertensive regimen reduced blood pressure by 20 mm Hg to 30 mm Hg
 - c) coadministration of low-dose aspirin with antihypertensive therapy provided no added cardiovascular protection
 - d) the findings of the HOT trial showed no J-shape curve in the treatment of hypertensive patients

(CME QUESTIONS CONTINUED ON FOLLOWING PAGE)

CME TEST FORM		<small>(PLEASE PRINT CLEARLY)</small>	
AJMC Test #049812S		Name _____	
Please circle your answers:		Address _____	
1. a b c d	2. a b c d	City _____	
3. a b c d	4. a b c d	State/ZIP _____	
5. a b c d	6. a b c d	Phone # _____	
7. a b c	8. a b c d	Please enclose a check for \$10, payable to American Medical Publishing, and mail with this form to: The AJMC CME Test American Medical Publishing 1816 Englishtown Road, Suite 101 Old Bridge, NJ 08857	
9. a b c d	10. a b c d		
New Developments in the Treatment of Hypertension: What the HOT Study Means to the JNC-VI			
(Test valid through December 31, 2000. No credit will be given after this date.)			

PROGRAM EVALUATION

Long Island Jewish Medical Center and Johns Hopkins University School of Medicine would like to have your opinion. Please fill out the questionnaire below, tear off along the dotted line, and mail along with your CME test form. We thank you for your evaluation, which is most helpful.

On the whole, how do you rate the information presented in the article?

excellent good fair poor

Is the information presented useful in your practice?

yes no

Comments:

Do you have recommendations to improve this program?

yes no

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Were any portions of this program unsatisfactory or inappropriate?

yes no

If so, which?

Do you find the information presented in these articles to be fair, objective, and balanced?

yes no

Is there subject matter you would like included in the future?

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In your opinion, were the authors biased in their discussion of any commercial product or service?

yes no

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Program Evaluation

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(CME QUESTIONS CONTINUED FROM PREVIOUS PAGE)

7. Which of the following statements is *not* true of the cost-effectiveness of antihypertensive therapy in relation to the HOT study results:

- a) treatment to lower the diastolic blood pressure from 90 mm Hg to 85 mm Hg or less is highly cost effective
- b) treatment to lower the diastolic blood pressure to a target of 90 mm Hg or less is highly cost effective
- c) adding aspirin to antihypertensive therapy is cost effective

8. All of the following are true for the treatment of hypertension in a managed care setting *except*:

- a) the high prevalence provides opportunities to assess different management strategies
- b) the risk strata allow investment in interventions that are likely to have the greatest impact
- c) the cost increase for antihypertensives is less than for other medications
- d) complications are delayed and costly and can be prevented by early intervention

9. All of the following statements regarding physician adherence to guidelines are true *except*:

- a) the explosion of medical knowledge has led to decreased awareness of guidelines
- b) physicians usually agree with guidelines created by a panel of experts
- c) physicians may have low outcome expectancy as to the success of lifestyle modifications
- d) physicians may lack self-efficacy because of lack of reimbursement for services by third-party payers

10. The following shifts in emphasis characterize the evolution of managed care from a fee-for-service system *except*:

- a) shift from treatment of disease to promotion of wellness
- b) shift from inpatient to outpatient care
- c) shift from being population-centered to being patient-centered
- d) shift from autonomy to accountability