CME CATEGORY IIIA - SELF STUDY

A SELECTION OF TEN CURRENT READINGS ON HYPERTENSION AVAILABLE AS FREE FULL-TEXT

Contributed by: A/P Prof Goh Lee Gan

The URLs of the articles are given below the reference.

ANTIHYPERTENSIVE THERAPY

Reading 1

Appel LJ. The verdict from ALLHAT— thiazide diuretics are the preferred initial therapy for hypertension. JAMA 2002 Dec 18; 288(23):3039-42.

http://jama.ama-assn.org/issues/v288n23/ffull/jed20075.html

Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, Md. (e-mail: lappel@jhmi.edu).

SUMMARY

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) is one of the most important trials of antihypertensive therapy. For decades, experts have passionately debated which class of drugs should be the initial therapy for hypertension. ALLHAT compared 3 distinct medications: amlodipine (representing dihydropyridine CCBs [DHP-CCBs]), lisinopril (representing ACE inhibitors), and doxazosin (representing alpha-blockers) with chlorthalidone (representing conventional thiazide therapy). In contrast to hundreds of trials with surrogate outcomes, the major outcomes in ALLHAT were clinically relevant cardiovascular events. The primary outcome was fatal coronary heart disease or nonfatal myocardial infarction. Secondary outcomes were all-cause mortality, fatal and nonfatal stroke, combined coronary heart disease, and combined cardiovascular disease. The planned follow-up was long (4-8 years). A previous report from ALLHAT documented that chlorthalidone was superior to doxazosin in preventing cardiovascular events, especially heart failure. The ALLHAT results provide compelling evidence that thiazide diuretics should be the initial drug of choice for patients with hypertension, especially compared with those agents that were directly tested in this trial.

An appropriate next question is what type of medication should be second-line therapy? In ALLHAT, the average number of medications used to control BP progressively increased from approximately 1.5 in first year of follow-up to 2.0 in the fifth year. While physicians may be tempted to use an on-patent CCB or ACE inhibitor, there is an impressive armamentarium of low-cost, off-patent drugs that can be used as add-on therapy after diuretics. These medications include a CCB (verapamil), 3 ACE inhibitors (captopril, enalapril, and lisinopril), several beta-blockers, low-dose reserpine, and a direct vasodilator (hydralazine). A logical strategy that incorporates these low-cost agents may differ from those that are more popular, but contemporary strategies may be somewhat artificial because of the heavy influence of marketing that preferentially leads to use of expensive medications. In short, physicians have the means to effectively control BP with inexpensive medications, even among patients who require multiple drugs. The results of ALLHAT, if disseminated and implemented, will likely have their greatest impact on patients with newly diagnosed hypertension. Hence, a large immediate shift in aggregate prescription patterns is unlikely. Finally, it is important to emphasize that treatment of hypertension is just one component of an overall strategy to prevent BP-related cardiovascular disease. Results from ALLHAT provide definitive data on one important aspect of hypertension management – selecting the best initial therapy. Attention must now return to other critical issues, specifically, controlling BP among patients with hypertension and preventing hypertension in the first place.

Reading 2

Bicket DP. Using ACE inhibitors appropriately. Am Fam Physician 2002 Aug 1; 66(3):461-8.

Family Practice Residency Program, University of Pittsburgh Medical Center-McKeesport, Pennsylvania 15132, USA. bicketdp@msx.upmc.edu

ABSTRACT

When first introduced in 1981, angiotensin-converting enzyme (ACE) inhibitors were indicated only for treatment of refractory hypertension. Since then, they have been shown to reduce morbidity or mortality in congestive heart failure, myocardial infarction, diabetes mellitus, chronic renal insufficiency, and atherosclerotic cardiovascular disease. Pathologies underlying these conditions are, in part, attributable to the renin-angiotensin-aldosterone system. Angiotensin II contributes to endothelial dysfunction, altered renal hemodynamics, and vascular and cardiac hypertrophy. ACE inhibitors attenuate these effects. Clinical outcomes of ACE inhibition include decreases in myocardial infarction (fatal and nonfatal), reinfarction, angina, stroke, end-stage renal disease, and morbidity and mortality associated with heart failure. ACE inhibitors are generally well-tolerated and have few contraindications. (Am Fam Physician 2002; 66:473.)

ANTIHYPERTENSIVE THERAPY

Reading 3

Kaplan NM. Management of hypertension in patients with type 2 diabetes mellitus: guidelines based on current evidence. Ann Intern Med 2001 Dec 18; 135(12):1079-83.

http://www.annals.org/issues/v135n12/full/200112180-00012.html

University of Texas South western Medical Centre, Dallas, Texas, USA.

ABSTRACT

Hypertension and diabetes are becoming increasingly common. Most patients with both disorders have a markedly worsened risk for premature microvascular and macrovascular complications. The appropriate management of hypertension seen in almost 70% of patients with type 2 diabetes mellitus remains controversial. However, over the past few years, many randomized, controlled trials have provided guidance for more effective therapy. These trials have established the need for a lower goal blood pressure (<130/80 mmHg) than has previously been recommended. In addition, they have proven the efficacy of drugs from three major classes of antihypertensive agents; however, comparative trials have failed to show definite superiority of any particular class in either lowering blood pressure or reducing cardiovascular morbidity and mortality. To achieve therapy goals, multiple antihypertensive drugs are usually needed. On the basis of their apparent superiority in slowing diabetic nephropathy, angiotensin-converting enzyme inhibitors should probably be the first choice. Second and third choices should be a long-acting diuretic and a calcium-channel blocker or a beta-blocker, respectively. Attention should also be directed toward non-pharmacologic and pharmacologic control of hyperglycemia and dyslipidemia.

Reading 4

Alderman MH. Hypertension control and kidney disease: some questions answered, many remain. JAMA 2002 Nov 20;288(19):2466-7.

http://jama.ama-assn.org/issues/v288n19/ffull/jed20064.html

Department of Epidemiology and Social Medicine, Albert Einstein College of Medicine, Bronx, NY. (e-mail: alderman@aecom.yu.edu).

SUMMARY

The African American Study of Kidney Disease and Hypertension (AASK) compared renal outcomes at different blood pressure goals with alternate antihypertensive drugs in patients with hypertensive nephrosclerosis. The primary end point was change in the glomerular filtration rate (GFR) with a secondary clinical composite end point composed of end-stage renal disease (ESRD), a threshold decline in GFR, and all-cause mortality. The AASK serves as an important reminder of the need to make therapeutic decisions on the basis of clinical outcomes. Precise design and elegant implementation help to explain both the strengths and limitations of AASK. The results reported provide important information about renal function and blood pressure control during antihypertensive care in patients with hypertensive nephrosclerosis but insufficient data on both clinical renal effects and cardiovascular outcomes. Even though knowledge of physiological functions is useful for patients with hypertensive nephrosclerosis, it is not the whole story. Patients and physicians are best served when clinical decisions can be based on evidence of benefit measured by the duration and quality of life.

Reading 5

Sturm JW, Davis SM, O'Sullivan JG, Vedadhaghi ME, Donnan GA. The Avoid Stroke as Soon as Possible (ASAP) general practice stroke audit. Med J Aust 2002 Apr 1;176(7):312-6.

http://www.mja.com.au/public/issues/176_07_010402/stu10389_fm.html

National Stroke Research Institute and Department of Neurology, Austin and Repatriation Medical Centre, West Heidelberg, VIC.

ABSTRACT

OBJECTIVES: To determine the prevalence of stroke risk factors in a general practice population and to identify pharmacotherapies currently used in management of stroke risk factors.

DESIGN: Multicentre, observational study by 321 randomly selected general practitioners who each collected data on 50 consecutive patients attending their surgery.

PATIENTS AND SETTING: 16 148 patients aged 30 years or older attending general practices across Australia during 2000.

OUTCOME MEASURES: Prevalence of hypertension, current smoking, diabetes, hypercholesterolaemia, atrial fibrillation, recent history of stroke or TIA; extent of pharmacotherapy use in risk-factor management.

RESULTS: 70% of patients had one or more risk factors and 34% had two or more. Hypertension was the risk factor with greatest prevalence (44%), followed by hypercholesterolaemia (43%) and current smoking (17%). The prevalence of risk factors generally increased with age, except for current smoking, where a decrease with age was seen. The most common pharmacotherapies were cardiovascular agents, followed by antiplatelet agents. Two-thirds of patients with hypertension were taking cardiovascular drugs, most commonly angiotensin-converting enzyme inhibitors.

CONCLUSIONS: Stroke risk factors are highly prevalent in general practice patients and GPs are ideally placed for opportunistic case-finding. There is considerable scope for improving management of stroke risk factors. The Avoid Stroke as Soon as Possible (ASAP) general practice stroke audit provides a baseline against which progress in risk-factor management can be measured.

Reading 6

Murchie P, Campbell NC, Ritchie LD, Simpson JA, Thain J. Secondary prevention clinics for coronary heart disease: four-year follow-up of a randomised controlled trial in primary care. BMJ 2003 Jan 11; 326(7380):84.

Department of General Practice and Primary Care, University of Aberdeen, Foresterhill Health Centre, Aberdeen AB25 2AY, UK. p.murchie@abdn.ac.uk

<u>ABSTRACT</u>

OBJECTIVES: To evaluate the effects of nurse-led clinics in primary care on secondary prevention, total mortality, and coronary event rates after four years.

DESIGN: Follow-up of a randomised controlled trial by postal questionnaires and review of case notes and national datasets.

SETTING: Stratified, random sample of 19 general practices in northeast Scotland.

PARTICIPANTS: 1343 patients (673 intervention and 670 control) under 80 years of age with a working diagnosis of coronary heart disease but without terminal illness or dementia and not housebound. Intervention: Nurse-led secondary prevention clinics promoted medical and lifestyle components of secondary prevention and offered regular follow-ups for one year.

MAIN OUTCOME MEASURES: Components of secondary prevention (aspirin, blood pressure management, lipid management, healthy diet, exercise, non-smoking), total mortality, and coronary events (non-fatal myocardial infarctions and coronary deaths).

RESULTS: Mean follow-up was at 4.7 years. Significant improvements were shown in the intervention group in all components of secondary prevention except smoking at one year, and these were sustained after four years except for exercise. The control group, most of whom attended clinics after the initial year, caught up before the final follow-up, and differences between groups were no longer significant. At 4.7 years, 100 patients in the intervention group and 128 in the control group have died: cumulative death rates were 14.5% and 18.9% respectively (P=0.038). 100 coronary events occurred in the intervention group and 125 in the control group: cumulative event rates were 14.2% and 18.2% respectively (P=0.052). Adjusting for age, sex, general practice and baseline secondary prevention, proportional hazard ratios were 0.75 for all deaths (95% confidence intervals 0.58 to 0.98; P=0.036) and 0.76 for coronary events (0.58 to 1.00; P=0.049).

CONCLUSIONS: Nurse-led secondary prevention improved medical and lifestyle components of secondary prevention and this seemed to lead to significantly fewer total deaths and probably fewer coronary events. Secondary prevention clinics should be started sooner rather than later.

SIGNIFICANCE OF SYSTOLIC HYPERTENSION

Reading 7

Basile JN. Systolic blood pressure. BMJ 2002 Oct 26; 325(7370):917-8.

http://bmj.com/cgi/content/full/325/7370/917

Primary Care, Ralph H Johnson VA Medical Centre, Division of General Internal Medicine/Geriatrics Medical University of South Carolina, Charleston, SC 29401 USA (Jan.Basile@med.va.gov)

SUMMARY

Elevation of systolic blood pressure predicts the risk of cardiovascular disease better than increases in diastolic blood pressure. It is the elevation in systolic blood pressure that still limits our ability to control blood pressure to the recommended goal of less than 140/90 mmHg. In a recent analysis of the Framingham heart study, knowing only the systolic blood pressure correctly classified the stage of blood pressure in 99% of adults over age 60 whereas knowing the diastolic blood pressure allowed only 66% to be classified correctly. Isolated systolic hypertension is defined as a systolic blood pressure more than or equal to 140 mmHg and a diastolic blood pressure less than 90 mmHg. Isolated systolic hypertension is the most common form of hypertension. Its prevalence increases with age occurring in two thirds of people 65 years of age and three quarters of those over 75 years of age. The elevation in systolic blood pressure may compromise coronary blood flow. This widening of the pulse pressure at specified levels of systolic blood pressure, as assessed in the Framingham heart study, is associated with an increased risk of developing coronary heart disease. Isolated systolic hypertension remains the most common form of hypertension and the most difficult to treat. Substantial evidence supports the value of treating isolated systolic hypertension and we must better inform doctors and the public about its consequences. It seems appropriate that we continually focus our efforts on more effective control of systolic blood pressure.

DIETARY SALT

Reading 8

Hooper L, Bartlett C, Davey Smith G, Ebrahim S. Systematic review of long term effects of advice to reduce dietary salt in adults. BMJ 2002 Sep 21; 325(7365):628.

MANDEC, University Dental Hospital of Manchester, Manchester M15 6FH. lee.hooper@man.ac.uk

ABSTRACT

OBJECTIVE: To assess the long-term effects of advice to restrict dietary sodium in adults with and without hypertension.

DESIGN: Systematic review and meta-analysis of randomised controlled trials.

DATA SOURCES: Cochrane library, Medline, Embase, and bibliographies.

STUDY SELECTION: Unconfounded randomised trials that aimed to reduce sodium intake in healthy adults over at least 6 months. Inclusion decisions, validity and data extraction were duplicated. Random effects like meta-analysis, sub-grouping, sensitivity analysis and meta-regression were performed.

OUTCOMES: Mortality, cardiovascular events, blood pressure, urinary sodium excretion, quality of life, and the use of antihypertensive drugs.

RESULTS: Three trials in normotensive people (n=2326), five trials in those with untreated hypertension (n=387) and three trials in people being treated for hypertension (n=801) were included, with follow-up from six months to seven years. The large high quality (and therefore most informative) studies used intensive behavioural interventions. Deaths and cardiovascular events were inconsistently defined and reported. There were 17 deaths, equally distributed between intervention and control groups. Systolic and diastolic blood pressures were reduced (systolic by 1.1 mmHg, 95% confidence interval 1.8 to 0.4 mmHg; diastolic by 0.6 mmHg, 1.5 to -0.3 mmHg) at 13 to 60 months, as was urinary 24-hour sodium excretion (by 35.5 mmol/24 hours, 47.2 to 23.9). Degree of reduction in sodium intake and change in blood pressure were not related.

CONCLUSIONS: Intensive interventions-unsuited to primary care or population prevention programmesprovide only small reductions in blood pressure and sodium excretion, and effects on deaths and cardiovascular events are unclear. Advice to reduce sodium intake may help people on antihypertensive drugs to stop their medication while maintaining good blood pressure control.

PATIENT BEHAVIOUR

Reading 9

Benson J, Britten N. Patients' decisions about whether or not to take antihypertensive drugs: qualitative study. BMJ 2002 Oct 19; 325(7369):873.

http://bmj.com/cgi/content/full/325/7369/873

General Practice and Primary Care Research Unit, Institute of Public Health, Cambridge CB2 2SR. jab62@medschl.cam.ac.uk

ABSTRACT

OBJECTIVE: To describe the ways in which patients taking antihypertensive drugs balance reservations against reasons for taking them.

DESIGN: Qualitative study using detailed interviews.

SETTING: Two urban general practices in the United Kingdom.

PARTICIPANTS: Maximum variety sample of 38 interviewees receiving repeat prescriptions for antihypertensives.

MAIN OUTCOME MEASURES: Interviewees' reservations about drugs and reasons for taking antihypertensives.

RESULTS: Patients have reservations about drugs generally and reservations about antihypertensives specifically. Reasons for taking antihypertensive drugs comprised positive experiences with doctors, perceived benefits of medication and pragmatic considerations. Patients weighed their reservations against reasons for taking antihypertensives in a way that made sense for them personally. Some individual patients weighed different reservations against different reasons for taking antihypertensives.

CONCLUSIONS: Patients' ideas may derive from considerations unrelated to the drugs' pharmacology. Doctors who want their patients to make well-informed choices about antihypertensives and to reach concordant decisions about prescribing should explore how individuals strike this balance to personalise discussion of drug use.

QUALITATIVE APPRAISAL OF CRITICISM OF HYPERTENSION

Reading 10

Horton R. Post-publication criticism and the shaping of clinical knowledge. JAMA 2002 Jun 5; 287(21):2843-7.

http://jama.ama-assn.org/issues/v287n21/ffull/joc11847.html

The Lancet, 32 Jamestown Rd, London NW1 7BY, England. richard.horton@lancet.com

<u>ABSTRACT</u>

CONTEXT: Letters to the editor are an important means for ensuring accountability of authors and editors. They form a part of the post-publication peer review process. I studied the critical footprint made in the medical literature by 3 randomized trials (Hypertension Optimal Treatment [HOT], Captopril Prevention Project [CAPPP], and Swedish Trial in Old Patients with Hypertension 2 [STOP-2]) published in The Lancet and investigated the extent to which that footprint was preserved in shaping clinical knowledge.

METHODS: Qualitative appraisal of the criticism of each trial were taken from published letters. Agreed weaknesses and unanswered criticisms were identified from the authors' reply. I searched MEDLINE for practice guidelines published after the trial report and sought evidence for incorporation of criticism into these guidelines.

RESULTS: From the time of publication to October 2000, HOT was cited in 9 of 36 practice guidelines; CAPPP, in 6 of 36; and STOP-2, not at all. HOT received 14 published criticisms, 5 comments and 3 questions, of which 15 were responded to. Only 1 criticism, lack of power, was referred to in 1 guideline. CAPPP received 14 criticisms, 9 comments and 3 questions, of which 8 were responded to. Only 1 criticism, imbalances between groups, was referred to in 1 guideline. STOP-2 received 12 criticisms, 9 comments, and 3 questions, of which only 6 were responded to.

CONCLUSIONS: More than half of all criticism made in correspondence went unanswered by authors. Important weaknesses in trials were ignored in subsequently published practice guidelines. Failure to recognize the critical footprint of primary research weakens the validity of guidelines and distorts clinical knowledge.