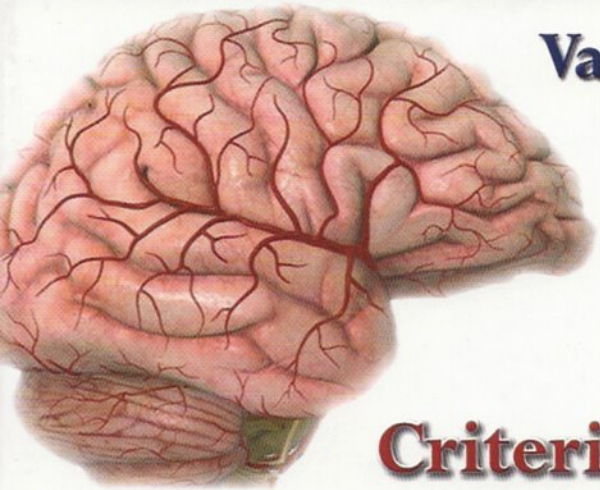
MEDICAL UPDATES

EGYPHAR

Issue No.:7 October 2011

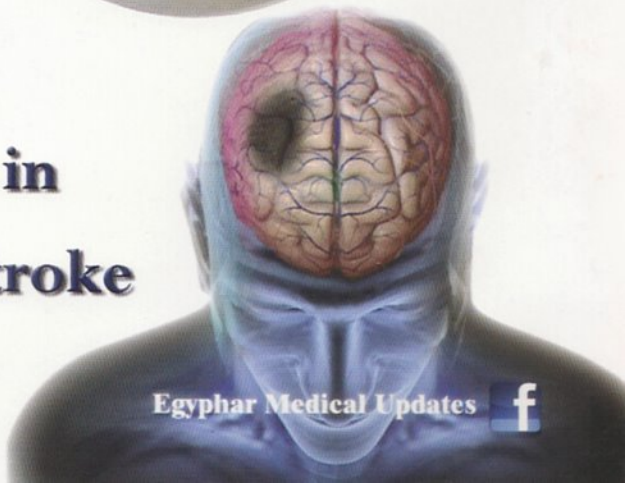


Vascular contributions to cognitive impairment and dementia

Criteria of choosing antihypertensive agents

Statins .....

An important role in lowering risk of 2nd stroke in young adults



Egyphar Medical Updates

Statins .....

An important role in lowering risk of 2nd stroke in young adults

Aug. 1, 2011

Cholesterol lowering drugs reduce risk of 2nd stroke even if cholesterol levels are normal

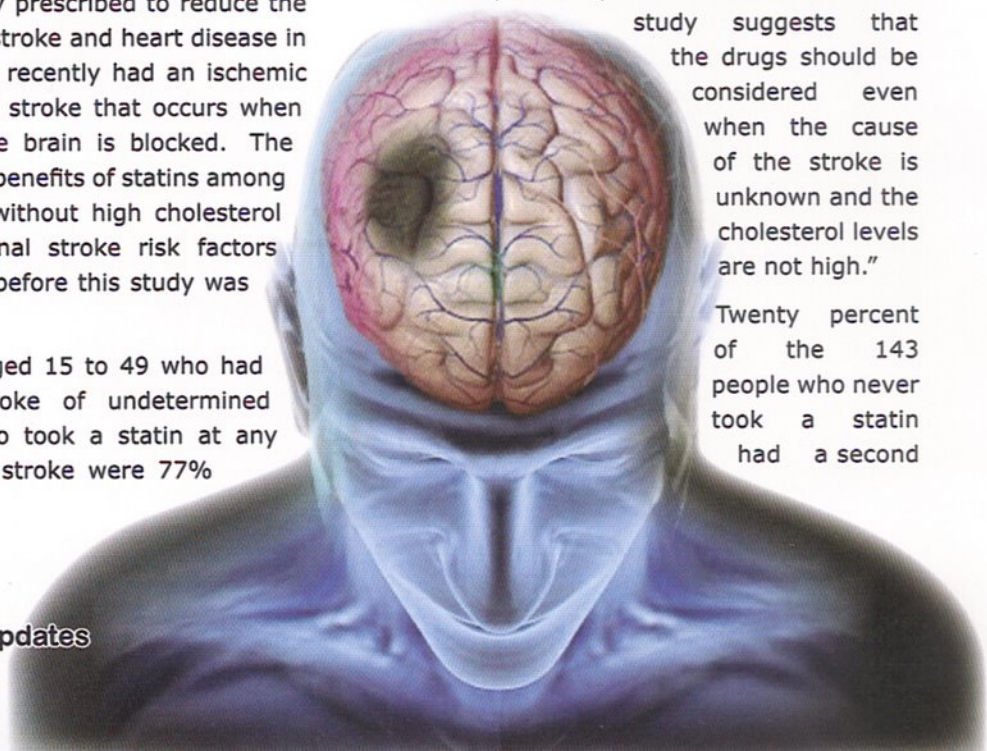
statins may help reduce the risk of recurrent strokes in young people even if they don't have high cholesterol levels, according to new research in the journal of Neurology.

Statins are widely prescribed to reduce the risk of recurrent stroke and heart disease in people who have recently had an ischemic stroke, a type of stroke that occurs when blood flow to the brain is blocked. The stroke-reduction benefits of statins among younger people without high cholesterol or other traditional stroke risk factors were not known before this study was conducted.

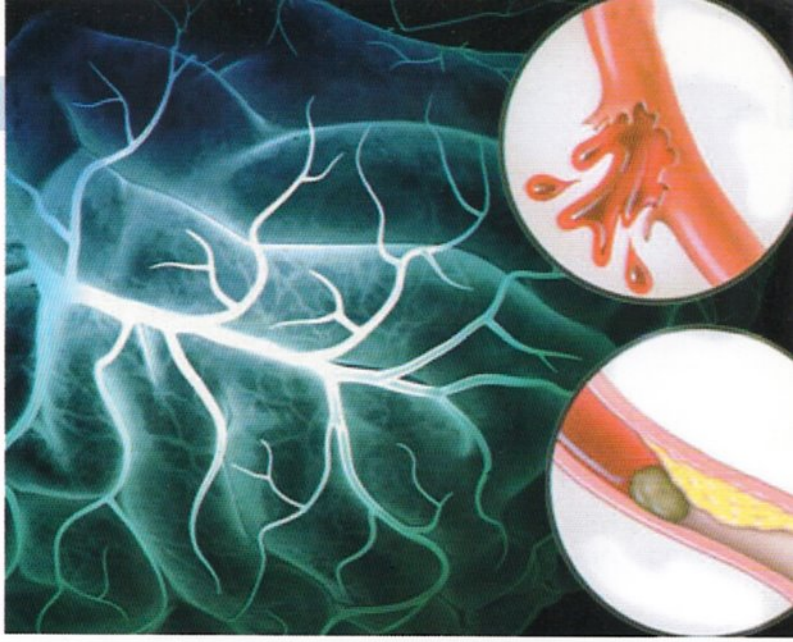
Of 215 people aged 15 to 49 who had an ischemic stroke of undetermined cause, those who took a statin at any point after their stroke were 77% less likely to have another stroke or develop blocked arteries elsewhere in the body when compared to their counterparts who were never treated with a statin.

"Because the cause of stroke in young people can be hard to identify, cholesterol-lowering drugs are often not used to prevent further strokes or vascular problems," says study author JukkaPutaala, MD, PhD, a neurologist at Helsinki University Central Hospital in Helsinki, Finland, in a news release. "This study suggests that the drugs should be considered even when the cause of the stroke is unknown and the cholesterol levels are not high."

Twenty percent of the 143 people who never took a statin had a second



Even those people who are younger and may not have the entire classic stroke risk factors are still at high risk for recurrence and could benefit from statin



stroke or vascular problem, compared with none of the 36 people who continuously took a statin after their stroke and four of 36 people who took a statin at some point after their stroke.

People who had taken a statin at some point were more likely to be older and have higher cholesterol levels and/or high blood pressure, compared to people who had never taken statin, the new study shows.

Study Expands Use for Statins

This study "shows us that even those people who are younger and may not have the entire classic stroke risk factors are still at high risk for recurrence and could benefit from a statin," says ShyamPrabhakaran, MD, a neurologist at Rush University Medical Center in Chicago. "We don't usually think of cholesterol-lowering drugs in this population because they usually have mild, if any, elevations in cholesterol."

The statins may reduce stroke risk by cooling inflammation, he says. "This expands the indications for statins to younger stroke patients who don't have atherosclerosis," or hardening of the arteries, he says.

Statins have beneficial effects on stroke risk above and beyond their cholesterol-lowering effect.

Statins have beneficial effects on stroke risk above and beyond their cholesterol-lowering effect, agrees Roger Bonomo, MD, director of stroke care at Lenox Hill Hospital in New York

SOURCES:

Roger Bonomo, MD, director, stroke care, Lenox Hill Hospital, New York.

Putaala, J, Neurology, 2011; vol 77: pp 426-430.

Shyam Prabhakaran, MD, neurologist, Rush University Medical Center, Chicago.

News release, American Academy of Neurology.

American Stroke Association
A Division of American Heart Association

Stroke. 2011 Jul 21

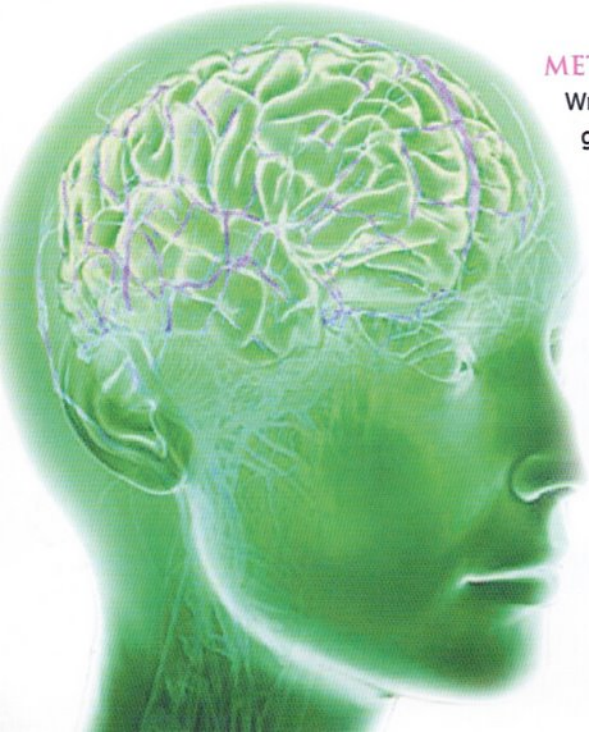
Vascular Contributions to Cognitive Impairment and Dementia

Gorelick PB, Scuteri A, Black SE, Decarli C, Greenberg SM, Iadecola C, Launer LJ, Laurent S, Lopez OL, Nyenhuis D, Petersen RC, Schneider JA, Tzourio C, Arnett DK, Bennett DA, Chui HC, Higashida RT, Lindquist R, Nilsson PM, Roman GC, Sellke FW, Seshadri S; on behalf of the American Heart Association Stroke Council, Council on Epidemiology and Prevention, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia.

ABSTRACT

BACKGROUND AND PURPOSE:

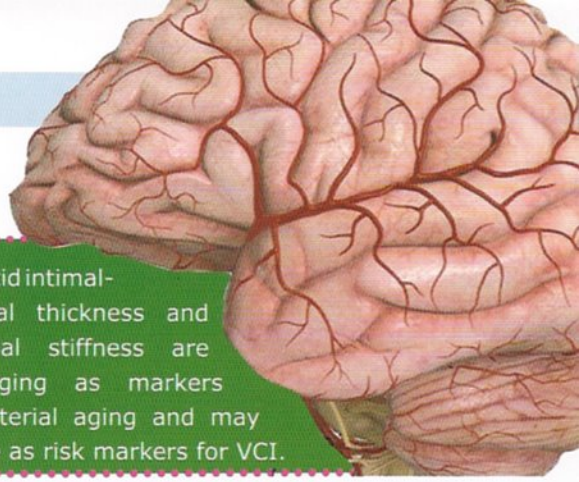
This scientific statement provides an overview of the evidence on vascular contributions to cognitive impairment and dementia. Vascular contributions to cognitive impairment and dementia of later life are common. Definitions of vascular cognitive impairment (VCI), neuropathology, basic science and pathophysiological aspects, role of neuroimaging and vascular and other associated risk factors, and potential opportunities for prevention and treatment are reviewed. This statement serves as an overall guide for practitioners to gain a better understanding of VCI and dementia, prevention, and treatment.



METHODS:

Writing group members were nominated by the writing group co-chairs on the basis of their previous work in relevant topic areas and were approved by the American Heart Association Stroke Council Scientific Statement Oversight Committee, the Council on Epidemiology and Prevention, and the Manuscript Oversight Committee. The writing group used systematic literature reviews (primarily covering publications from 1990 to May 1, 2010), previously published guidelines, personal files, and expert opinion to summarize existing evidence, indicate gaps in current knowledge, and, when appropriate, formulate recommendations using standard American Heart Association criteria. All members of the writing group had the opportunity to comment on the

recommendations and approved the final version of this document. After peer review by the American Heart Association, as well as review by the Stroke Council leadership, Council on Epidemiology and Prevention Council, and Scientific Statements Oversight Committee, the statement was approved by the American Heart Association Science Advisory and Coordinating Committee.



Carotid intimal-medial thickness and arterial stiffness are emerging as markers of arterial aging and may serve as risk markers for VCI.

RESULTS:

The construct of VCI has been introduced to capture the entire spectrum of cognitive disorders associated with all forms of cerebral vascular brain injury-not solely stroke-ranging from mild cognitive impairment through fully developed dementia.

Dysfunction of the neurovascular unit and mechanisms regulating cerebral blood flow are likely to be important components of the pathophysiological processes underlying VCI. Cerebral amyloid angiopathy is emerging as an important marker of risk for Alzheimer disease, microinfarction, microhemorrhage and macrohemorrhage of the brain, and VCI.

The neuropathology of cognitive impairment in later life is often a mixture of Alzheimer disease and microvascular brain damage, which may overlap and synergize to heighten the risk of cognitive impairment. In this regard, magnetic resonance imaging and other neuroimaging techniques play an important role in the definition and detection of VCI and provide evidence that subcortical forms of VCI with white matter hyperintensities and small deep infarcts are common. In many cases, risk markers for VCI are the same as traditional risk factors for stroke. These risks may include but are not limited to atrial fibrillation, hypertension, diabetes mellitus, and hypercholesterolemia. Furthermore, these same vascular risk factors may be risk markers for Alzheimer disease.

Currently, no specific treatments for VCI have been approved by the US Food and Drug Administration.

However, detection and control of the traditional risk factors for stroke and cardiovascular disease may be effective in the prevention of VCI, even in older people.

CONCLUSIONS:

Vascular contributions to cognitive impairment and dementia are important.

Understanding of VCI has evolved substantially in recent years, based on preclinical, neuropathologic, neuroimaging, physiological, and epidemiological studies. Transdisciplinary, translational, and transactional approaches are recommended to further our understanding of this entity and to better characterize its neuropsychological profile. There is a need for prospective, quantitative, clinical-pathological-neuroimaging studies to improve knowledge of the pathological basis of neuroimaging change and the complex interplay between vascular and Alzheimer disease pathologies in the evolution of clinical VCI and Alzheimer disease. Long-term vascular risk marker interventional studies beginning as early as midlife may be required to prevent or postpone the onset of VCI and Alzheimer disease.

Studies of intensive reduction of vascular risk factors in high-risk groups are another important avenue of research.

Arch Intern Med. 2011;17:1542-1550, 1550-1551
September 26, 2011

More Frequent Office Visits Lead to Faster Diabetes Control

Patients with diabetes mellitus who visited their primary care physicians once every 1 to 2 weeks were more likely to achieve clinical goals than patients who visited less frequently, according to a study published in the September 26 issue of the Archives of Internal Medicine.

Elevated levels of hemoglobin A1c, blood pressure (BP), and low-density lipoprotein cholesterol level (LDL-C) are associated with greater risk for diabetes complications, but most patients have not achieved target levels for these factors.

Patients who interact more frequently with their providers are believed to gain faster control of hemoglobin levels, BP, and LDL-C levels, but there are no existing guidelines for provider visit frequency.

Patients who interact more frequently with their doctors are believed to gain faster control of hemoglobin levels, BP, and LDL-C levels, but there are no existing guidelines for doctors visit frequency.

Fritha Morrison, MPH, from the Division of Endocrinology, Brigham and Women's Hospital, Boston, Massachusetts, and colleagues conducted a retrospective cohort study that included 26,496 patients with diabetes at 2 teaching hospitals between 2000 and 2009. The participants had elevated hemoglobin A1c levels, BP, and/or LDL-C levels. The

researchers determined the association between frequency of provider visits and the length of time it took patients to control their hemoglobin A1c levels, BP, and LDL-C levels.

Patients were separated into groups based on the frequency of physician visits. Among patients with an encounter frequency of every 1 to 2 weeks, it took a median time of 4.4 months to achieve hemoglobin A1c levels of less than 7.0% in patients not receiving insulin (compared with 24.9 months for those who saw their physicians every 3 to 6 months; $P < .001$). Among patients receiving insulin, the difference was 10.1 months vs 52.8 months ($P < .001$).

With respect to BP, the group with a higher frequency of physician visits achieved a BP lower than 130/85 mm Hg in 1.3 months (vs in 13.9 months for those with less frequent physician visits; $P < .001$). The median time to achieving LDL-C levels less than 100 mg/dL was 5.1 months (vs 32.8 months; $P < .001$).

Multivariate analysis revealed that for every doubling of the time between physician visits, the median time to achieving hemoglobin A1c targets increased, including a 35% increase ($P < .001$) in patients not receiving insulin, and 17% ($P < .001$) in patients who did receive insulin. Similar trends were seen in BP (87%; $P < .001$) and LDL-C (27%; $P < .001$).

The study has limitations, including its retrospective nature. A randomized prospective study is needed to better understand optimal visit frequency, according to Allan H. Goroll, MD, MACP, from Medical Service, Massachusetts General Hospital, and Harvard Medical School, Boston, Massachusetts, the author of an accompanying commentary. According to Dr. Goroll, little information is available about the nature of the visits, or what transpired that caused a change in patient behavior.

"Understanding how best to deliver...care and change patient behavior, especially in primary care settings, is going to be as important as knowing what care to prescribe," he writes.

The study was supported by grants from the Agency for Healthcare Research and Quality, the National Library of Medicine, and the Diabetes Action Research and Education Foundation. The study authors and the editorialist have disclosed no relevant financial relationships.

"Understanding how best to deliver care and change patient behavior, especially in primary care settings, is going to be as important as knowing what care to prescribe," he writes.

EndocrPract. 2011;17(Suppl 2):1-53.

American Association of Clinical Endocrinologists (AACE) 20th Annual Meeting and Clinical Congress

Diabetic patients... Are they getting a comprehensive care?

April 28, 2011 (San Diego, California) — In an effort to address the dangerous comorbid conditions that often accompany diabetes, as well as the symptoms of the disease itself, the American Association of Clinical Endocrinology (AACE) has released new clinical practice guidelines that emphasize individualized, comprehensive healthcare for patients with diabetes. Until now, that comprehensive care has been a missing piece in the healthcare that patients with diabetes receive, said 2 experts here at the AACE 20th Annual Meeting and Clinical Congress.

"When you look at comorbid conditions that commonly affect those with diabetes, such as heart attack, congestive heart failure, and chronic kidney disease, statistics show us that diabetic patients suffer these complications at a rate 3 to 7 times greater than those without diabetes," said Yehuda Handelsman, MD, president of AACE and medical director of the Metabolic Institute of America. Unfortunately, many patients with diabetes do not have the most common complications of the disease — high lipids and high blood pressure, in addition to high blood sugar — under control, Dr. Handelsman said.

Only 7% to 13% of patients with diabetes have good cholesterol, blood sugar levels, and blood pressure that are under control and also take aspirin to reduce the risk for heart attack, according to Dr. Handelsman.

"Diabetics are not getting comprehensive care, and with the new guidelines, we hope to address that problem," he added.

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"Diabetics are not getting comprehensive care, and with the new guidelines, we hope to address that problem," he added.

"This is the first year that our guidelines have been so comprehensive," said Daniel Einhorn, MD, immediate past president of AACE and clinical professor of medicine at the University of California–San Diego. The new guidelines address not only high blood sugar and comorbid conditions such as heart and kidney disease but also underrecognized problems affecting patients with diabetes, such as depression and sleep apnea, he said. They also provide modified diagnostic criteria for diabetes and new diagnostic criteria for gestational diabetes. There is also a new emphasis on decreasing obesity through lifestyle, medications, and surgery, including with laparoscopic-assisted gastric banding or Roux-en-Y gastric bypass for patients with diabetes with a body mass index higher than 30 or 35 kg/m2.

The new guidelines for type 1 and type 2 diabetes are written in a question-and-answer format and were developed by 23 of the nation's leading diabetic experts. The guidelines were first announced in early April and discuss the importance of achieving a treatment plan that avoids hypoglycemia, which is now thought to be a continual and pressing concern for many patients with diabetes. The guidelines recommend a blood glucose target of an HbA1c level of 6.5% if it can be achieved safely — a level more stringent than that recommended by the American Diabetes Association, which recommends 6.9% or below. "The majority of diabetics can achieve 6.5% safely, and this target helps avoid possible complications," Dr. Handelsman said.

The new AACE guidelines are published in supplement 2 of the March/April issue of the association's official medical journal, Endocrine Practice.

The guidelines emphasize a personalized approach to controlling diabetes and achieving blood glucose targets with care plans that take into account patients' risk factors for complications, comorbid conditions, expected life span, and psychological, social, and economic status. Although the guidelines recommend a blood glucose target of HbA1c level of 6.5% if it can be achieved safely, a treatment plan should take into account a patient's risk for development of severe hypoglycemia. The new guidelines also provide information on appropriate use of new technologies such as insulin pumps and continuous glucose monitoring.

In the guidelines, AACE recommends comprehensive diabetes lifestyle management education at the time of diagnosis, as well as throughout the course of diabetes. The importance of medical nutrition therapy, physical activity, avoidance of tobacco products, and adequate quantity and quality of sleep should be discussed with patients who have prediabetes as well as type 1 and type 2 diabetes, according to the new guidelines.

The guidelines also address healthcare for special populations, such as children, those with gestational diabetes, patients in hospitals, and people with prediabetes.

Although providing patients with diabetes with comprehensive care can demand more of health clinicians, the guidelines also provide support for using treatment approaches for diabetes that are truly evidence-based, Dr. Handelsman noted. "The guidelines are a result of consensus and consideration of the scientific evidence by the best minds in endocrinology in the United States," Dr. Handelsman said.

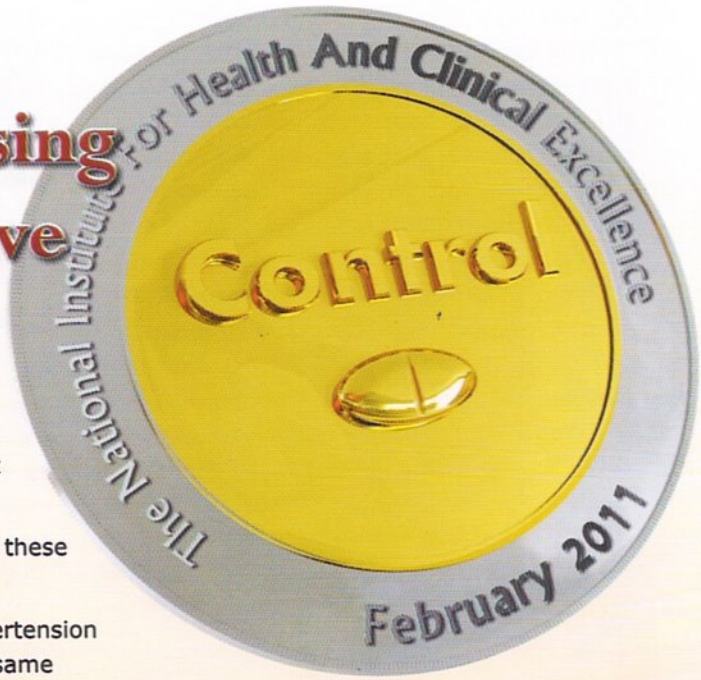
Yet it may take time for the new guidelines to be disseminated throughout the health clinician community, Dr. Einhorn said.

"We hope that the guidelines are transformative for both diabetic patients and their clinicians," Dr. Handelsman added.

Dr. Handelsman and Dr. Einhorn have disclosed no relevant financial relationships.

American Association of Clinical Endocrinologists (AACE) 20th Annual Meeting and Clinical Congress. Presented April 15, 2011.

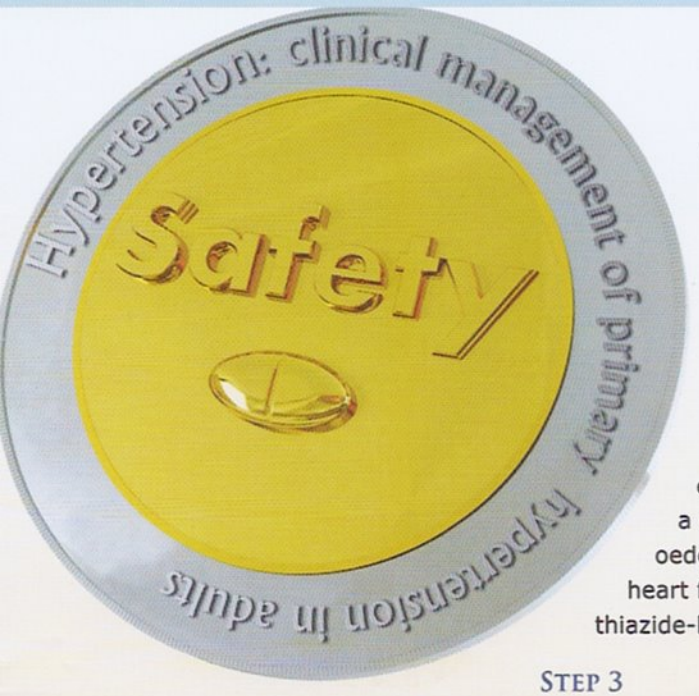
Criteria of choosing antihypertensive agents



- Where possible, recommend treatment with drugs taken only once a day.
- Prescribe non-proprietary drugs where these are appropriate and minimise cost.
- Offer people with isolated systolic hypertension (systolic BP 160 mmHg or more) the same treatment as people with both raised systolic and diastolic blood pressure.
- Offer people older than 80 years the same antihypertensive drug treatment as people aged 55–80 years, taking into account any comorbidities.
- Offer antihypertensive drug treatment to women in line with recommendations 'Hypertension in pregnancy' (NICE clinical guideline 107).

STEP 1

- Offer step 1 antihypertensive treatment with an angiotensin-converting enzyme (ACE) inhibitor or a low-cost angiotensin-II receptor blocker (ARB) to people aged under 55 years. If an ACE inhibitor is not tolerated, offer an ARB.
- Do not combine an ACE inhibitor with an ARB to treat hypertension.
- Offer step 1 antihypertensive treatment with a calcium-channel blocker (CCB) to people aged 55 years and older and to black people of African or Caribbean descent of any age. If a CCB is not suitable, for example because of oedema or intolerance, or if there is evidence of heart failure or a high risk of heart failure, offer a thiazide-like diuretic.
- If a diuretic is required, choose a thiazide-like diuretic.
- Beta-blockers are not a preferred initial therapy for hypertension. However, beta-blockers may be considered in younger people, particularly:
  - those with an intolerance or contraindication to ACE inhibitors and angiotensin-II receptor antagonists or
  - women of child-bearing potential or
  - people with evidence of increased sympathetic drive.



- In these circumstances, if therapy is initiated with a beta-blocker and a second drug is required, add a calcium-channel blocker rather than a thiazide-type diuretic to reduce the person's risk of developing diabetes.

Step 2

If step 2 antihypertensive treatment is required, offer a CCB in combination with either an ACE Inhibitor or a low-cost ARB. If a CCB is not suitable, for example because of oedema or intolerance, or if there is evidence of heart failure or a high risk of heart failure, offer a thiazide-like diuretic

Step 3

- If treatment with three drugs is required, the combination of ACE 363 inhibitor (or angiotensin-II receptor blocker), calcium-channel 364 blocker and thiazide-like diuretic should be used.

Step 4

- Regard clinic blood pressure that remains higher than 140/90 mmHg with the optimal or best tolerated doses of an ACE inhibitor or an ARB plus a CCB plus a diuretic as resistant hypertension and consider adding a fourth antihypertensive drug and/or seeking expert advice.
- For treatment of resistant hypertension at step 4, consider further diuretic therapy with low-dose spironolactone (25 mg once daily) if blood potassium levels are lower than 4.5 mmol/l and estimated
- Glomerular filtration rate is higher than 60 ml/min/1.73m2. If blood potassium levels are higher than 4.5 mmol/l, consider higher-dose thiazide-like diuretic treatment.
- When using further diuretic therapy for resistant hypertension at step 4, monitor blood sodium and potassium and renal function within 1 month and repeat as required thereafter.
- If further diuretic therapy for resistant hypertension at step 4 is not tolerated, contraindicated or ineffective, consider an alpha- or beta-blocker.
- If blood pressure remains uncontrolled with the optimal or maximum tolerated doses of four drugs seek expert advice if it has not yet been obtained.

Low zinc intake during pregnancy and its association with preterm and very preterm delivery

Among the urban poor, a marginal zinc intake during pregnancy may play an important role in the duration of gestation and is associated with increased risk of preterm and very preterm delivery.

Theresa O. Scholl, etal.

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Abstract

Zinc affects growth, development, and reproduction. However, the effect of poor maternal zinc nutriture, usually measured as plasma zinc, on poor pregnancy outcome has not been consistent. The influence of dietary zinc on pregnancy outcome was examined in a cohort of 818 pregnant girls and women from a poor urban community in Camden, New Jersey (1985–1990). Zinc intake in this sample was 11.1 mg/day, a level ascertained from averaged 24-hour dietary recalls during pregnancy. Gravidas with low zinc intake (≤6 mg/day, amounting to 40% of the recommended dietary allowance for pregnancy) had lower caloric intake and multivitamin usage as well as a higher incidence of inadequate weight gain during pregnancy and iron deficiency anemia at entry to prenatal care compared with those with higher intakes. A low zinc intake was associated with approximately a twofold increase in the risk of low birth weight (<2,500 g) after controlling for calories and other confounding variables. The risk of preterm delivery (<37 completed weeks) was also increased, particularly when rupture of the membranes preceded the onset of labor (adjusted odds ratio = 3.46, 95% confidence interval 1.04–11.47). A low intake of dietary zinc earlier in pregnancy was associated with a greater than threefold increase in the risk of very preterm delivery (<33 completed weeks). In conjunction with iron deficiency anemia at entry to prenatal care, the adjusted odds ratio for very preterm delivery with low zinc intake was 5.44 (95% confidence interval 1.58–18.79). Among the urban poor, a marginal zinc intake during pregnancy may play an important role in the duration of gestation and is associated with increased risk of preterm and very preterm delivery.