

NEWS LETTER

Egyptian Hypertension Society



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THE PRESIDENT'S MESSAGE

RENIN ANGIOTENSIN SYSTEM (RAS) INHIBITION IN HYPERTENSION

Drugs that inhibit the renin-angiotensin-system (RAS), namely angiotensin-converting enzyme-inhibitors (ACE-I) and angiotensin receptor antagonists (ARBs) are gaining increasing popularity as initial medications for the management of hypertensive patients. In the year 2002, ACE-I were the most commonly prescribed drugs for the treatment of hypertension in USA. Though their antihypertensive efficacy as monotherapy is similar to other antihypertensive agents, they have the advantage of better tolerability, limited side effects and a favorable metabolic profile. When compared to other antihypertensive agents (diuretics, beta-adrenergic blockers and calcium antagonists) in large clinical trials, ACE-I and ARBs provided no additional advantages regarding improvement in cardiovascular and total mortality. With the exception of the superiority of ARBs in prevention of stroke, RAS inhibitors have no advantage over other agents in prevention of other cardiovascular morbid events namely, heart failure (though ACE-I are superior to calcium antagonists), coronary heart disease and total cardiovascular events.

However, there is the possibility that these agents have other benefits beyond blood pressure lowering. At equal degrees of blood pressure reduction RAS inhibitors prevent or delay the development of diabetes mellitus and provide better end organ protection, kidneys, blood vessels and the heart when compared with other antihypertensive agents. The combined use of ACE-I and ARBs is particularly useful in organ protection.

RAS inhibitors are specifically indicated in treatment of hypertension in patients with impaired left ventricular systolic function, diabetes, proteinuria, impaired kidney function, myocardial infarction, multiple cardiovascular risk factors and possibly elderly patients. The main limitation of the ACE-I is cough and rarely allergic reactions. Elderly patients or those who are volume depleted or receiving large doses of diuretics or in heart failure are liable to develop hypotensive reaction and/or deterioration in kidney function.

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President of The Egyptian Hypertension Society.

SCIENTIFIC PREDICTIONS

Prediction of which CV disease event [*stroke, congestive heart failure (CHF), coronary heart disease (CHD), CV vs nonCV-death, end-stage renal disease, & all cause mortality*] would happen first to people with newly diagnosed HYPERTENSION, in hope to optimize their prevention strategies, was sought in 12 years follow up data from Framingham Heart Study. Though the study did show that newly diagnosed hypertensives would experience a CV event rather than non-CV death, first, yet it did not clearly answer which of the events is likely to occur first as they seem to vary according to age and gender. Thus women and elder witnessed stroke & CHF more, while men younger than 60 would experience CHD more, as first event, emphasizing on the use of statins and aspirin in younger age groups.

Hypertension 2005; 45: 39-45.

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TURNING CONCEPTS

STATINS LOWER BP !!!

The vasodilatory potentialities of statins and their possibility to lower BP is clinically emerging. For instance, analysis of the lipid-lowering arm of ASCOT [10,305 patients without CHD, but with hypertension] demonstrated a significant SBP & DBP lowering [6 w.-2.5 y. after randomization of placebo vs 10 mg atorvastatin] despite more placebo-treated patients tended to receive anti-hypertensive agents than atorvastatin-treated ones. The same was clear in a double blind, randomized, placebo-controlled study at the University of California, San Diego (UCSD), showing the impact of 6 months statins [pravastatin 40 mg or simvastatin 20 mg on BP reduction.

The posed logistic mechanisms of BP lowering beyond cholesterol-lowering effects of statins, is via mediation of vascular reactivity by reducing superoxide production, increasing the bioavailability of nitric oxide, and decreasing angiotensin II type I receptor density.....etc. Clinical evidence confirming this pleiotropic effects of statins was highlighted at 77th annual Scientific Sessions of AHA, when comparing a two cholesterol lowering agents; statins and ezetimibe; the former being the only one capable of improving endothelial vasodilator function. This could also help to explain why several studies have reported that statins can reduce the risk of stroke, despite cholesterol not being an important risk factor for cerebrovascular disease while hypertension is.

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LOOKING UP IN THE GUIDES

The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents has cleared that **primary hypertension is now detectable in the young** and occurs commonly. The long-term health risks for hypertensive children and adolescents can be substantial; therefore, it is important that clinical measures are taken appropriately. Once hypertension is confirmed, **clinical evaluation** should be conducted according to the **following guides** :

Additional evaluation could enroll, ambulatory BP monitoring, plasma renin, plasma & urine steroid or catecholamine determination, if indicated.

Furthermore, renovascular imaging isotopic scintigraphy, duplex doppler flow studies, 3-dimensional CT, arteriograph: DSA or classic can be also requested upon demand.

Beyond this, evaluation for comorbidities and for target organ involvements should follow with one objective in mind; reducing risks, securing appropriate life style modification, and justifying optimal pharmacotherapy to all in all optimize health outcomes.

N.B.

R/O: rule out
: as diabetes mellites, kidney disease...etc.

Pediatrics 2004; 114: 555-576.

Study or Procedure	Purpose	Target Population
Evaluation for identifiable causes History, including sleep history, family history, risk factors, diet, and habits such as smoking and drinking alcohol; physical examination	History and physical examination help focus subsequent evaluation	All children with persistent BP \geq 95th percentile
BUN, creatinine, electrolytes, urinalysis, and urine culture	R/O renal disease and chronic pyelonephritis	All children with persistent BP \geq 95th percentile
Complete blood BC	R/O anemia, consistent with chronic renal disease	All children with persistent BP \geq 95th percentile
Renal U/S	R/O renal scar, congenital anomaly, or abn. renal size	All children with persistent BP \geq 95th percentile
Evaluation for comorbidity Fasting lipid panel, fasting glucose	Identify hyperlipidemia, identify metabolic abnormalities	Overweight patients with BP at 90th–94th percentile; all patients with BP \geq 95th percentile; family history of hypertension or CVD; child with chronic renal disease
Fasting lipid panel, fasting glucose	Identify hyperlipidemia, identify metabolic abnormalities	Overweight patients with BP at 90th–94th percentile; all patients with BP \geq 95th percentile; family history of hypertension or CVD; child with chronic renal disease
Drug screen	Identify substances that might cause hypertension	History suggestive of contribution by substances or drugs.
Polysomnography	Identify sleep disorder with hypertension	History of loud, frequent snoring
Evaluation for target-organ damage Echocardiogram	Identify LVH and other indications of cardiac involvement	Patients with comorbid risk factors* and BP 90th–94th percentile; all patients with BP \geq 95th percentile
Retinal exam	Identify retinal vascular changes	Patients with comorbid risk factors and BP 90th–94th percentile; all patients with BP \geq 95th percentile



WHAT'S NEW!!!

HYPERTENSION PREVENTION

Fibers, at an average dose of 11.5 g/day lowered SBP by 1.13 mmHg and DBP by 1.26 mmHg [reduction tending to be largest over 40 years of age]. This was clear in a meta-analysis from 24 randomized, placebo-controlled trials published between 1999 and 2003, investigating the effect of fiber supplementation on BP. This is less than AHA recommendation of 25-30 g/day fiber intake in general population which may contribute to hypertension prevention.

Arch Intern Med 2005; 165: 150-156.

Folate consumption [1000 µg/day] helps prevent the development of hypertension, particularly younger women as analysed from data of 93,803 young women [27-44 y.] in the Nurses' Health Study II vs 62,260 older women [43-70 y.] in the Nurses' Health Study I. Though precise mechanism of this benefit is not clear yet it seems in part mediated through improvement of endothelial function.

JAMA 2005; 293: 320-329.

Baked or broiled fish, significantly reduced the risk of stroke in the elderly, while conversely, eating fried fish increased its risk. This was cleared in a 12 years follow-up study examining the association between different types of fish consumption and stroke risk, in 4775 people aged 65 years and over, who completed a food questionnaire between 1989 and 1990. Thus, n-3 fatty acid content or preparation methods pose impact on CV protection.

Arch Intern Med 2005; 165: 200-206.

Maternal midgestational calcium supplementations during pregnancy may lower offspring BP, thus helping to prevent hypertension in next generations. This was based on realizing intrauterine aside genetic and environmental factors in shaping the hypertensive phenotype.

Circulation. 2004 Oct 5; 110(14):1990-5.

Whole-grain intake is inversely while refined-grain intake is positively associated with the risk of having metabolic syndrome. *Eur J Clin Nutr. 2004.*

MOLECULAR REASONINGS;

CHRONOBIOLOGY AND CHRONOTHERAPY IN CVD

Abdel Moniem Ibrahim Ahmed, MD., Prof. CV physiology, Cairo University.

Biological functions, exhibit significant circadian variations. For instance, this could account to 15-25 mmHg change in the 24-hour peak to trough SBP & DBP. This nocturnal BP changes track sympathetic NS activity that: down regulate during nocturnal sleep, that is enhanced on awakening "sympathoadrenal branch", and is activated with subsequent orthostasis "noradrenergic branch".

Chronobiology, is the science concerned with biological rhythms and their underlying mechanisms. The external expression of an internal timing system is mediated via entrainment (synchronization) pathways, circadian clock, that output to effector systems. Entrainment (synchronization) pathways may be photics 'light-dark cycle' and/or nonphotics as melatonin (inhibitory) and locomotor activity. These transduce to the circadian clock [located in the suprachiasmatic nucleus] whereby the oscillations of gene expression within, are translated to periodic rhythmic electrical activities. These latter mainly project to the hypothalamus, that translates oscillations into diurnal variations of anterior pituitary secretions, sympathetic NS activity, and melatonin secretion. Aside this, a peripheral circadian oscillation system in aorta & VSMCs exists whereby Ang II modulates gene expression (mPer2) through AT₁ receptor, a phenomenon that is abolished by ARBs.

In most hypertensive patients, some chronobiological variations are heightened as demonstrated by ambulatory BP monitoring. Thus they show a marked rise in BP upon awakening "morning or 'am' surge", which comprise a critical risk for angina, AMI, stroke & subarachnoid haemorrhage, specially if these patients are old, with underlying atherosclerotic or vascular disease. Also, the regular decline of BP from mid-afternoon to reach its nadir between midnight & 3:00 a.m. [dipping] is dampened in hypertensives i.e they would become non dipper. This means that their decline in BP > 10% below the day time BP is blunted or absent. As a consequence, non dipper patients are more liable to LVH, stroke, and renal impairment.

Chronotherapy; links the biological effects of a disease associated with time and the timing of drug delivery. A vivid example to this is Controlled Onset Extended Release-verapamil COER-verapamil, with "novel delivery system". It is the first chronotherapeutic agent for HT and angina. COER-verapamil in a nearly dose-dependent manner controls the rapid morning rise and daytime excess of BP; exerts significant effect at night in non dipper patients; and minimizes the risk of excessive dipping of BP during night in non dipper patients. The delivery of the COER-verapamil has been tailored to the typical circadian rhythms of BP & HR. This calls for more chronotherapeutics to be on the way to cope with our circadian variations.

- *Circulation 1989; 79 (4): 733-743*

- *Annu. Rev. Physiol. 2001. 63:647-676*

- *Circulation 2001 Oct 9; 104 (15): 1746-8*

- *Am J Cardio. 1995; 76: 375-380*

- *Am J Cardio. 1997; 88: 469-47*

- *Am J Cardio. 1998; 81: 422-431*

DIAGNOSTIC CONSIDERATIONS;

RECOMMENDED DIMENSIONS FOR BP CUFF BLADDERS

Age Range	Width, cm	Length, cm	Max. arm circumference, cm*
Newborn	4	8	10
Infant	6	12	15
Child	9	18	22
Small adult	10	24	26
Adult	13	30	34
Large adult	16	38	44
Thigh	20	42	52

* : Calculated so that the largest arm would still allow the bladder to encircle arm hv at least 80%.

Pediatrics 2004; 114: 555-576.



LATE-BREAKING TRIALS ▶

GEMINI: Carvedilol-Metoprolol Comparison in Hypertensive (GEMINI) trial; is the first large-scale randomized trial to evaluate the addition of beta-blockade to ACE inhibition to achieve the recommended BP target of <130/80 mmHg for patients with Type 2 diabetes. Results cleared that the combination was well tolerated and effective in achieving BP target. However, carvedilol resulted in [better] maintenance of glycemic control and improvement in parameters related to the metabolic syndrome relative to metoprolol.

Read more → JAMA 2004;292:2227–2236.

RIO-NA: is part of the phase III RIO program that includes RIO-Lipids, RIO-Europe, and RIO-diabetes – including over 6,600 patients in all that test the efficacy of Rimonabant; the first selective blocker of cannabinoid type 1 (CB1) receptors of the endocannabinoid system. This ubiquitous system plays a key role in the control of food intake in the brain, but is also important in peripheral regions such as adipose tissue, where it is involved in regulating caloric expenditure.

Read more about this system → Am J Physiol Regul Integr Comp Physiol 2003;284: R343-344. Look up the trials → proceedings of ESC congress in Munich, Germany, Sept. 2004 & of AHA Scientific Sessions in New Orleans, Louisiana, USA, Nov. 2004.



* The Arabic Corner for the Public and the Patients, issued by the EHS Web-site is achieving great success. This is because this site is concerned with patient self education and methods of patients assistance and aid from their surrounding. This aside raising different preventive approaches to life threatening habits, toxic consumptions...etc. as well as raising public awareness to global health problems relevant to hypertension and other CV diseases.

* The 7th Scientific meeting of Egyptian Hypertension Society CARDIOVASCULAR PROTECTION FORUM, was held on Friday, October 22, 2004 / 8th Ramadan 1425 h at Cairo Conrad Hotel. Dyslipidemias, RAS targeting and several technical aspect of hypertension diagnosis, assessment,... etc were all discussed.

The forum also arranged a mini course for practitioners on "Chest Pain" on Friday- January 14, 2005 at Le Meridien Luxor. The course centered on ischemic vs nonischemic cardiac pains, non-cardiac pain and chest pain in women. The diagnostic biomarkers, imaging techniques and managements strategies of acute chest pain where all covered.



CALENDAR:

LOCAL MEETINGS		
32 nd Annual Scientific Meeting of the Egyptian Society of Cardiology	Intercontinental Heliopolis Hotel, Cairo, Egypt. 22 nd -25 th Feb. 2005	International Center for Organization & Marketing Tel. (203) 4204849 - Fax (203) 4204849 E-mail: icom@dataxprs.com.eg
9 th Annual Meeting of EHS & WHL Regional Meeting	Marriot Hotel, Cairo, Egypt. 6-9 th April, 2005.	Secretary; Mrs Amany Kandeel Tel (202) 794-8877 - Fax (202) 794-8879
EHS Cardiovascular Protection Forum "Hypertension Evaluation"	Conord Hilton Hotel, Cairo, Egypt. 20 th May, 2005.	Secretary; Miss Rehab Mohamed Tel (202) 794-8877 - Fax (202) 794-8879
INTERNATIONAL MEETINGS		
International Stroke Conference 2005	New Orleans, LA, USA. 2 nd -4 th February, 2005.	AHA National Center, Dallas, TX, USA. Tel. +1 214 706 1543 – Fax +1 214 706 5262
ACC Annual Scientific Session 2005	Orlando, FL, USA. 6-9 th March, 2005	Heart House, 9111 Old Georgetown Road Bethesda, MD, USA. Tel. +1 800 253 4636 – Fax +1 301 897 9745