Friday, May 17, 6:30 AM - 8:00 AM  
Sunrise Seminar Series: Angiotensin II Blockade in the Management of Cardiovascular Disease*  
ANGIOTENSIN II BLOCKADE IN THE MANAGEMENT OF CARDIOVASCULAR DISEASE  
James R. Sowers, SUNY Downstate, Brooklyn, NY, United States.

Angiotensin 2 plays a key role in the pathogenesis of hypertension and CV and renal disease. Randomized controlled trials shown that ACE inhibitors provide cardiovascular and microvascular benefits and may also improve insulin resistance and prevent the development of diabetes. Furthermore, ACE inhibitors provide considerable benefits in diabetic patients with heart failure, and reduced left ventricular mass and left ventricular dilation and significantly reduced mortality and hospitalization for heart failure. Thus, ACE inhibitors are currently recommended as a first line treatment for patients with hypertension and diabetes particularly those with proteinuria as well as those with heart failure. Data from randomized controlled trials in patients with type 2 diabetes suggest that ARBs may be considered equal to ACE inhibitor for renal protection. For example, the Reduction of Endpoints in NIDDM with the Angiotensin Losartan (RENEAL) trial demonstrated that angiotensin II receptor blocker combined with conventional antihypertensive treatment as needed confers significant renal protection in patients with type 2 diabetes and nephropathy. The risk of the primary end point (a composite of doubling of serum creatinine, end stage renal disease or death from any cause) was reduced by 16% with losartan. The risk of doubling of serum creatinine was reduced by 25% and the risk of end stage renal disease was reduced by 28% over a follow up period of 3.4 years. The study also documented reduction in the initial hospitalization for heart failure. These benefits were above and beyond those attributable to BP reduction alone, suggesting that ARBs, like ACE inhibitors, have special beneficial cardiovascular/renal benefits in diabetic patients.

Key Words: Angiotensin Therapy, Diabetes Mellitus

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BEYOND BLOOD PRESSURE EFFECTS OF ALL BLOCKADE  
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Research on the development of atherosclerotic plaque and the mechanisms of acute coronary syndromes has identified multiple levels of input from the Renin Angiotension System. Drugs that block the Type I receptor for ANG II have joined ACE inhibitors as effective strategies to protect patients with atherosclerotic vascular disease as well as hypertensive and diabetic renal disease.

This vascular protection may be attributable to inhibition of the mitogenic effects of Angiotensin II, thus reducing ventricular and vascular hypertrophy. Yet many authorities now attribute this benefit to the improvement in endothelial dysfunction. The prime mechanism may be inhibition of NADH and NADPH oxidases, which then curtails production of reactive oxygen species. Thus preventing activation of transcriptional factors such as NF-kB and initiation of the inflammatory cascade, (an obligatory part of the plaque development as well as its eventual destabilization). Recent reports have examined the independent effects of Type I and Type II Angiotensin receptors on inflammatory cytokines and plaque development and confirmed the role of the Type II receptor. Clinical studies have validated the antihypertensive effects of blocking the type I receptor for angiotensin II. By also reversing left ventricular hypertrophy, this therapeutic intervention has impacted a formidable risk factor for stroke and myocardial infarction. The data from ValHeFT is a further indication of the benefit that can be expected from incorporating ANG II receptor blockade in the treatment of patients with left ventricular dysfunction. We have also learned of the benefit of Angiotensin II blockade in hypertensive patients with Type 2 DM and renal insufficiency. Studies presented last year at these meetings documented a renal protective effect that had not been validated in primary outcome studies with ACE inhibitors.

The potential of coming ACEI’s and ARB’s in patients with atherosclerotic risk is now under active investigation, along with studies on the interdependence of receptors for ANG II and oxidized LDL. This talk will focus on the newer aspects of Angiotensin II inhibition.

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Saturday, May 18, 6:30 AM - 8:00 AM  
Compliance With Antihypertensive Therapy: Is it Time for Chronotherapy?  
IS IT TIME FOR CHRONOTHERAPY?  
Janice G. Douglas, Case Western Reserve University, University School of Medicine, Cleveland, Ohio, United States.

Blood pressure and heart rate follow a circadian rhythm, peaking between the hours of 6:00 AM and 12:00 noon. The early morning surge in blood pressure has been linked to an increased occurrence of acute myocardial infarction, sudden cardiac death, silent ischemia, and stroke during these critical hours. Specifically, there is a 40% higher risk of heart attack, a 29% increased risk of cardiac death, and a 49% increased risk of stroke during this period. From a clinical standpoint, optimal antihypertensive therapy includes a renal protective effect that had not been validated in primary outcome studies with ACE inhibitors. As these agents offer 24-hour blood pressure control and provide improved blood pressure control during the early morning BP surge, Antihypertensive regimens that provide improved control of blood pressure during high-risk periods may reduce adverse outcomes and sequelae, particularly in high-risk patients. It is critical for specialist to evaluate the role of chronotherapy in hypertension management, thereby enabling them to make informed treatment decisions, and advocate to primary care providers, based upon their assessment of the body of evidence in the professional literature. Furthermore, selecting drug treatments that correlate with specific circadian variations in BP may provide alternative treatment options for improving the management of hypertensive patients.

1. Elliot WJ. Cyclic and circadian variations in cardiovascular events. AJH. 2001; 14:291S-295S
2. Glasser SP, Neutel JM, Albert KS, et al. Efficacy and safety of diltiazem HCl extended release (GG9) dosed at nighttime (10PM) compared to placebo and to morning dosing (8AM) in moderate to severe essential hypertension [abstract]. AJH. In press.

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Saturday, May 18, 1:30 - 3:30 PM  
Combination Drug Therapy for High Risk Hypertensive Patients*  
DIABETES MELLITUS: EVIDENCE-BASED RATIONALE FOR COMBINATION THERAPY  
Murray Epstein. Dept. Medicine, University of Miami School of Medicine, Miami, FL, United States.

Recent data from the United States Renal Data System (USRDS) indicate that despite attempts to control blood pressure, the incidence of end stage