# Plasma Renin Activity as a Guide for Medical Management of Essential Hypertension

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## A. Study Purpose and Rationale

The medical management of essential hypertension is relatively variable due to the availability of a wide spectrum of drug classes with demonstrated benefit. In clinical practice some patients seem to respond better to certain classes than others, however, until recently there was no subdivision of primary hypertension guiding therapy towards certain classes over others. Over the last 5 years the idea of high-renin vs. low-renin hypertension has been popularized by researchers like Laragh, whose clinical pearls for treating hypertension have been published in the American Journal of Hypertension. The argument is that 70% of essential hypertension is secondary to high plasma renin activity (PRA > 0.65 ng/ml/h), the so-called "high-renin hypertension", and therefore responds best to ant-renin drugs such as ace-inhibitors, angiotensin receptor blockers, or beta-blockers. The remaining 30% of low-renin or salt-mediated hypertension does not respond to anti-renin therapy and is best controlled with natriuretic drugs such as diuretics, calcium-channel blockers, or alpha-blockers.

This study will look at the differential effects of metoprolol, a beta-blocker and anti-renin or R type drug, and amlodipine, a calcium-channel blocker and natriuretic or V type drug, in high-renin hypertensives vs. salt-mediated hypertensives to determine if therapy directed by PRA has merit. Up until this point, there is virtually no data examining this interesting and somewhat revolutionary method of categorizing and treating essential hypertension.

## B. Study Design and Statistical Analysis

Randomized, double-blind, parallel-arm trial comparing the effectiveness of metoprolol, an R-drug, and amlodipine, a V-drug, in achieving goal BP in high-renin vs. low-renin hypertensives (see Study procedure). Multiple logistic regression analysis will be used, with independent variables initial PRA and initial BP.

## C. Study Procedure

Patients presenting to AIM Clinic with an elevated BP (SBP> 120, DBP > 90) will be identified as potential subjects. BP will be recorded and PRA measured. On visit 2, the follow-up visit, BP will again be recorded and if again high the patient will meet criteria for the diagnosis of HTN and the patient is eligible for the study (see Inclusion/Exclusion criteria). At this point patients will be consented and enrolled. Based on the PRA from visit 1, patients will be sorted into the high renin or low renin arm of the study and randomized this visit to metoprolol XL 25 mg po qd or amlodipine 2.5 mg po qd. The patient will then be followed in clinic for 12 weeks from visit 2, with each study medication titrated up as necessary to achieve SBP < 120, DBP < 90. The final BP will be the BP measured at the end of the 12 weeks or, in the event that a second agent is required for further BP reduction, the last BP measured on the study drug alone.

## D. Study Drugs

Both metoprolol XL and amlodipine are FDA-approved for the management of hypertension.

**E. Medical Device**

n/a

**F. Study Questionnaire**

n/a

**G. Study Subjects**

Inclusion criteria for the study will be patients over the age of 21 with newly diagnosed hypertension followed at AIM Clinic, on no hypertensive medication, with no contraindication to metoprolol or amlodipine

Exclusion criteria will be: diabetes mellitus, ischernic cardiomyopathy or CHF

**H. Recruitment of Subjects**

Patients will be recruited by informed physicians at the AIM Clinic. Any patient with newly diagnosed, not medically managed hypertension will be identified, and the AIM physician will ascertain from the patient that he/she is willing to discuss the study with the research team. If after that discussion the patient is agreeable, the patient will be consented for the study and enrolled.

**I. Confidentiality of Subject Data**

Each study subject will be assigned a unique coding number by which all data will be recorded. These data will be stored in a secure location accessible only to the investigators.

**J. Potential Conflict of Interest**

None of the investigators has a proprietary interest in either drug under investigation.

**K. Location of the Study**

The study will be conducted at the Associates in Internal Medicine Clinic at Columbia University Medical Center.

**L. Potential Risks**

Given that both medications are within the realm of standard treatment for hypertension, it is not felt that subjects will be placing themselves at increased risk by being randomized to either as part of this study versus being treated per the discretion of the primary care provider.

**M. Potential Benefits**

Subjects may or rnay not benefit from participation in this study since both drugs would otherwise be available to them were they not part of the study.

**N. Alternative Therapies**

Both study medications are within the realm of standard treatment for hypertension.

**O. Compensation to Subjects**

There will be no monetary compensation to subjects, although since the study medication will be provided participants will be spared the cost they would otherwise incur for medical. treatment.

**P. Costs to Subjects**

There will be no additional cost to subjects for participation in the study.

**Q. Minors as Research Subjects**

n/a

**R. Radiation or Radioactive Substances**

n/a

**S. References**

1. Bisognano J. Incremental effectiveness of amlodipine besylate in the treatment of hypertension with single and multiple medication regimens. Am J Hypertens. 2004 Aug 7(8):676-83,

2. Jamerson KA. Initial angiotensin-converting enzyme inhibitor/calcium channel blocker combination therapy achieves superior blood pressure control compared with calcium channel blocker monotherapy in patients with stage 2 hypertension. Am J Hypertens. 2004 June, 17(6):495-501.

3. Kubik M. Metoprolol with and without chlorthalidone in hypertension. CAM Pharmacol Ther. 1979 Jan;25(l):25-32.

4. Materson, BJ. Single-drug therapy for hypertension in men. A comparison of six antihypertensive agents with placebo. NEJM 1993-1328:914.

5. Neaton, JD. Treatment of Mild Hypertension Study: Final results. JAMA 1993; 270: 713.

6. Staessen, JA. Cardiovascular prevention and blood pressure reduction. J Hypertens 2003; 21:1055.

7. Tuomilehto J. A comparison between metoprolot and pindolol in the treatment of essential hypertension. Ann Clin Res. 1978 Feb; 10(l): 24-9.

8. Turnbull, F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed over-views of randomized trials. Lancet 2003 -1 3621527.

9. Wu SC. Prospective and randomized study of the antihypertensive effect and tolerability of three antihypertensive agents, losartan, amlodipine, and lisinopril, in hypertensive patients. Heart Vessels. 2004 Jan; 19(l); 13-8.