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IRB Protocol: Rates of Practitioner Use of Aldosterone Antagonists for Resistant Hypertension in an Academic Quaternary Referral Ambulatory Clinic Setting

A. Study Purpose and Rationale

The purpose of this study is to determine the incidence of resistant hypertension in an ambulatory clinic population and assess the state of current practice among practitioners for the treatment of resistant hypertension. Resistant hypertension is defined by blood pressure above goal (140/90 in most patients or 130/80 in patients with diabetes or chronic kidney disease) despite treatment with three antihypertensive agents belonging to different classes (including a diuretic) or at or above goal on four or more antihypertensive agents. [1] The prevalence of resistant hypertension is unknown, but according to the most recent report of the National Health and Nutrition Examination Survey (NHANES) it is estimated to be 8.9% of all US adults with hypertension while other studies put the figure at 10% to 15%. [2, 3, 4]

One proposed mechanism of resistant hypertension that has been is termed “aldosterone escape.” Approximately 30-40% of patients taking an angiotensin-converting-enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) are observed to have increasing aldosterone levels despite upstream blockade of the rennin-angiotensin-aldosterone-system (RAAS). [5 ] Several studies have demonstrated the effectiveness of aldosterone antagonists for lowering blood pressure in resistant hypertension including the Addition of Spironolactone in Patients with Resistant Arterial Hypertension (ASPIRANT)—a large randomized, double-blind, placebo-controlled trial which demonstrated the effectiveness of 25 mg of spironolactone in lowering blood pressure among patients with resistant hypertension. [6-12]

There are other compelling reasons to use aldosterone antagonists to treat patients with resistant hypertension. Aldosterone works in the collecting duct to promote the retention of sodium and water increasing extracellular volume and thus blood pressure. However, aldosterone also has non-epithelial, profibrotic, and proinflammatory effects which are independent of its effect on volume and blood pressure. These effects are particularly pronounced in obese individuals who live in an effective hyperaldosterone state. [13]

The most recent data on treatment of resistant hypertension comes from NHANES 2003-2008. In those years only 3% of patients with resistant hypertension were treated with an aldosterone receptor blocker. [1] The intent of this study is to determine the incidence of resistant hypertension in an outpatient setting and assess the current state of practice in the treatment of resistant hypertension. This data will be valuable in assessing the need for further practitioner education in the management of resistant hypertension.

B. Study Design and Statistical Analysis

This study will be a retrospective observational cohort study consisting of chart reviews of sequential clinic visits. The data will be gathered irrespective of clinic attendance at the time of the appointment and will be based on the latest available data. Patients will only be excluded if there is no data available or if the patient is under 18. Demographic data will be obtained from chart review including age, gender, and ethnicity. Vital statistics will be gathered including blood pressure, height,

and weight. In addition, all antihypertensive medications the patient is on will be recorded. Laboratory data including sodium, potassium, and creatinine levels will be recorded. The chart will be assessed by the investigator to assess for any contraindications or adverse reactions to aldosterone antagonist therapy including hyperkalemia, renal failure, or gynecomastia. Finally, the chart will be assessed for possible secondary causes of resistant hypertension such as sleep apnea, primary aldosteronism, chronic kidney disease, and renal artery stenosis.

From this data the rate of practitioner prescription of aldosterone antagonist for resistant hypertension will be determined. The best estimate of rate of use of aldosterone antagonists in this setting is 10%. Using chi-square analysis in order to show a difference from the best data available on the national average use of 3% with power of 95%, approximately 120 patients with resistant hypertension must be enrolled. The best prevalence data suggests persons with resistant hypertension make up 3% of the population. Thus, a total of 3600 charts will need to be reviewed. Given that there are 200 patients per day in the outpatient clinic in question, the study can reasonably be completed in 1 month.

Given the prevalence of poor socioeconomic hardship and psychiatric comorbidity, it can reasonably be expected that the study participants will have higher than average rates of medication non-compliance. The chart review will include examiner assessment of practitioner records for mention of medication non-compliance. However, this is not expected to be a source of error as the patient should be a candidate for treatment with an aldosterone receptor antagonist if the physician suspects they have resistant hypertension irrespective of whether the patient is compliant with the medications. If the physician suspects non-compliance, the patient does not have resistant hypertension.

C. Study Procedure

As noted above, this is a retrospective cohort study. Data will be gathered from patient charts from sequential clinic visits irrespective of clinic attendance. The expected completion time for this project is 1 month.

D. Study Drugs

Not applicable.

E. Medical Device

Not applicable.

F. Study Questionnaires

Not applicable

G. Study Subjects

Subjects will consist of sequential clinic patients enrolled based on the clinic visit schedule.

H. Recruitment of Subjects

Subjects will be recruited sequentially from the clinic visit schedule.

I. Confidentiality of Study Data

The patients' identities will be decontextualized by assigning a unique identifier at the time of recruitment. A spreadsheet linking these identifiers to medical record numbers will be kept on a secure computer at the New York Presbyterian campus following standard data security protocols. The subjects' individual data will be accessed using the secure electronic medical record (EMR) already in place. Only individuals who are HIPAA certified will access protected health information (PHI). No PHI will be included in the study data.

J. Potential Conflict of Interest

None of the researchers have any potential conflicts of interest to declare. This IRB has been prepared as part of the requirements for completion of a residency for internal medicine.

K. Location of the Study

Associates of Internal Medicine (AIM) outpatient clinics located on the second floor of the Vanderbilt Clinic Building at 622 West 168th Street New York, NY 10032 part of the New York Presbyterian Hospital – Columbia University Medical Center.

L. Potential Risks

None.

M. Potential Benefits

None.

N. Alternative Therapies

Not applicable.

O. Compensation to Subjects

None.

P. Costs to Subjects

None.

Q. Minors as Research Subjects

Not applicable.

R. Radiation or Radioactive Substances

Not applicable.

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