Persistence and adherence to antihypertensive treatment in relation to initial prescription: diuretics versus other classes of antihypertensive drugs.

BACKGROUND:

- The use of thiazide diuretics in the treatment of hypertension is widely considered as a first-line treatment, given the efficacy and low cost of this class of drugs.
- This indication is not unanimous, because thiazides can cause metabolic alterations, and other side effects that reduce compliance and persistence on treatment.

OBJECTIVE:

- To compare adherence and persistence to therapy of chlorthalidone versus other treatments, as a first-line antihypertensive therapy.

METHODS:

- **Design:** Multicentre, parallel, open-label randomized study; Duration: 2 years.
- **Inclusion criteria:** age 18–75 years and stage I or II essential hypertension, previously untreated or poorly controlled.
- **Exclusion criteria:** Women in fertile age not using recognized contraceptive methods, or pregnant or nursing, were excluded from the study. Exclusion was established for patients with documented coronary or cerebrovascular events during the previous 6 months, evidence or history of congestive heart failure or ejection fraction less than 45% at the baseline echocardiographic exam, secondary hypertension, cancer disease, chronic renal disease (serum creatinine >2 mg/dl), liver cirrhosis, or any other health problem that may interfere with the projected 2-year follow-up.
- **Primary Outcome Measure:** Adherence to treatment that is based on control visits by the practitioners, prescription records, and adherence questionnaires. Persistence was also a primary outcome measure, measures as continuing treatment for the prescribed duration.
- **Secondary Outcome Measure:** Safety and efficacy of the study groups. Measured by effect on blood pressure and adverse effects.
- 2409 patients were recruited with indication to anti-hypertensive therapy. 1205 were randomized to receive chlorthalidone and they were placed into group D, and 1204 were randomized into group A which contained all other antihypertensives besides diuretics.
- 90% power to detect equivalence with a two-tailed alpha error of 0.05 and a confidence interval of 90%.
- Data handling method was exclusion of subjects.

RESULTS:

- 1051 patients in the chlorthalidone arm and 1026 in the other anti-hypertensive group completed the study.
- **Primary Outcome Measure:** There were no significant differences recorded between group D and A. Although in 3 individual areas, there were statistically significant differences. Group D, the chlorthalidone arm, had greater amount of patients changing therapy due to poor BP control (P < 0.001), side effects (P < 0.001), and drug intolerance (P < 0.001) when compared to group
A. Adherence to treatment measured as ‘adherence score’ showed no significant differences between the two study groups.

- **Secondary Outcome Measure:** Both treatment arms, individually, showed statistically significant reductions in decreasing systolic blood pressure, diastolic blood pressure, and heart rate. Although, no statistically significant differences between the two groups exists when comparing efficacy.

- **Author’s Conclusion:** The recommendation to start anti-hypertensive therapy with diuretics, when no compelling indications are present, is not supported by the evidence that this strategy produces more rapid and better control of BP.

**STRENGTHS:**

- The study not only included adherence to treatment, but also measured efficacy and adverse effects, as these could play major roles in usefulness of these anti-hypertensive drugs.
- Duration of the study was of sufficient length.

**LIMITATIONS:**

- The study was open-label, not double blinded.
- Many of the patients were lost to follow up which could have dropped the power below 80%.
- The study did not provide information on the patients’ previous uncontrolled blood pressure therapies and what they were prescribed.
- The study did not include the percentage of patients that were started on each different class of antihypertensives.

**CONCLUSION:**

- The correct outcomes were measured for this study; however, the results were not interpreted appropriately by the authors. The study did not provide sufficient background information on each patient and also did not provide which antihypertensives were being used and in what proportion.
- This therapy has been proven as appropriate first-line antihypertensive therapy as long as no compelling indications are present. Until further research concludes in favor of all other antihypertensive medications, diuretics such as thiazides should remain as first-line therapy.
- Future research: In the future, it would be beneficial to conduct this study with thiazide diuretics versus specific antihypertensive drug classes, initially. Without the study providing data including the specific drugs used, as well as proportions used, it is extremely difficult to accurately assess the usefulness of either therapy.

Todd Picklesimer, PharmD Candidate