Retrospective Analysis of Real-World Efficacy of Angiotensin Receptor Blockers Versus Other Classes of Antihypertensive Agents in Blood Pressure Management

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ABSTRACT

Background: Efficacy of blood pressure (BP) lowering may differ between clinical trials and what is observed in clinical practice. These differences may contribute to poor BP control rates among those at risk.

Objective: We conducted an observational study to determine the BP-lowering efficacy of angiotensin receptor blocker (ARB) versus non–ARB-based antihypertensive treatments in a large Canadian primary care database.

Methods: We analyzed the South Western Ontario database of 170,000 adults (aged >18 years) with hypertension persisting with antihypertensive medication for ≥9 months. Routine standard of care office BP was measured using approved manual aneroid or automated devices. BP <140 mm Hg and/or <90 mm Hg ≤9 months after treatment initiation, persistence (presence of initial antihypertensive prescription at the first, second, third, and fourth year anniversary) with antihypertensive therapy, and the presence of a cardiovascular (CV) event (ie, myocardial infarction) were studied.

Results: After 9 months of monotherapy, 28% (978 of 3490) of patients on ARBs achieved target BP versus 27% (839 of 3110) on angiotensin-converting enzyme inhibitors (ACEIs) ($P > 0.05$), 26% (265 of 1020) on calcium channel blockers (CCBs) ($P > 0.05$), 21% (221 of 1050) on β-blockers ($P = 0.002$), and 19% (276 of 1450) on diuretics ($P = 0.001$). Attainment rates were significantly higher with irbesartan (38%; 332 of 873) versus losartan (32%; 335 of 1047; $P = 0.01$), valsartan (19%; 186 of 977; $P = 0.001$), and candesartan (25%; 148 of 593; $P = 0.001$). BP goal attainment rates were significantly higher when ARB was compared with non–ARB-based dual therapy (39%; 1007 of 2584 vs 31%; 1109 of 3576; $P = 0.004$); irbesartan + hydrochlorothiazide (HCTZ) was significantly higher than losartan + HCTZ (36%; 500 of 1390 vs 20%; 252 of 1261; $P = 0.001$). For patients receiving dual or tri-therapy, 48% (667 of 1390) of patients receiving irbesartan reached target BP versus 41% to 42% for losartan (517 of 1261), valsartan (194 of 462), and candesartan (168 of 401) ($P = 0.001$ for each). After 4 years, persistence rates were not statistically different among ARB, CCB, and diuretic monotherapies, but appeared somewhat higher with ACEIs and β-blockers (78%, 78%, 79%, 91%, and 84%, respectively). Persistence was not significantly different between irbesartan and losartan monotherapy (76% for both; $P > 0.05$), but was significantly higher with irbesartan + HCTZ versus losartan + HCTZ (96% vs 73%, respectively; $P = 0.001$). Patients treated with ARBs reported fewer CV events than those receiving ACEIs or CCBs (4.3% vs 7.0% and 11.0%, respectively; $P < 0.001$). Within the ARB class, the lowest rate was with irbesartan (3.0% vs 4.6%–5.0% for other ARBs; $P < 0.02$).

Conclusions: In this real-world setting, hypertensive adults treated with ARBs versus β-blockers or diuretics were more likely to have evidence-based target BP recorded. In addition, patients using ARBs versus ACEIs or CCBs had fewer reports of CV events. (*Clin Ther.* 2011;33:1190–1203)

Key words: antihypertensive, ARB, cardiovascular, hypertension, irbesartan, persistence.

INTRODUCTION

Hypertension is a major modifiable risk factor for cardiovascular (CV) disease[1,2] and the most common risk factor for death, both worldwide[3] and in Canada.[4,5]

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Numerous randomized controlled clinical trials have demonstrated that effective blood pressure (BP) control using any of the 5 conventional antihypertensive drug classes is associated with significant reductions in CV risk in people with hypertension.[6–19] Based largely on results from these and similar studies, hypertension treatment guidelines recommend lowering BP to <140/90 mm Hg in the general population and to <130/80 mm Hg in patients with diabetes and renal disease.[4,20–23] According to these guidelines, the initial choice of antihypertensive treatment strategy depends largely on patients' comorbidities and degree of hypertension. For example, people with diabetes, chronic kidney disease, and/or BP ≥20 mm Hg above the systolic BP (SBP) goal or ≥10 mm Hg above the diastolic BP (DBP) goal should be initiated on ≥2 agents; those with CKD should receive at least 1 angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) and most combination therapies should include a thiazide diuretic according to standard of care.[4]

Treatment guidelines are continuously updated to reflect the ever-increasing volume of data from clinical studies and published meta-analyses. However, clinical trial populations often do not represent those seen in real-life clinical practice.[21,24–27] Factors such as persistence with treatment tend to be artificially high in clinical trials. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), for example, persistence with any antihypertensive agent was 96% at 1 year compared with 5% to 75% in observational studies.[28–31] Such differences may lead to over-exaggerated treatment efficacy in responsive patients who may not have persisted with treatment in a real-world setting or to under-exaggerated efficacy in unresponsive patients who may have switched to a more suitable drug in clinical practice.[21] It is therefore important that guidelines should take into account results from observational real-world studies as well as those from clinical trials.[29–32]

Like randomized clinical trials, observational studies are often designed to assess treatment efficacy and tolerability in specific patient populations, such as those with hypertension and diabetes or kidney disease.[33–39] Few studies have captured treatment efficacy in the broad range of patients that are routinely seen in clinical practice. Recently, the observational The Health Improvement Network (THIN) study examined the BP-lowering efficacy of various antihypertensive drug classes in primary care in the United Kingdom.[40–42] In this study, patients prescribed ARBs, either as monotherapy or as part of a combination therapy regimen, were more likely to achieve and maintain target BP than patients using other classes of antihypertensive agents.[40–42] The aim of our study was to compare the BP-lowering efficacy and long-term persistence rates of ARB- versus non–ARB-based monotherapy, dual, and tri-therapies in a "real world" primary care population in Canada. The CV event rates associated with each treatment strategy were also assessed.

METHODS

Data Source

This retrospective observational study utilized data collected from routine primary care practices in Canada, stored in the South Western Ontario (SWO) database. The longitudinal investigation was carried out in a geographically defined area comprising rural and urban clinical practices in London, Ontario, Canada, and surrounding counties with a catchment of 1.5 million inhabitants. This retrospective study began in 2000 and, at the time of this report in 2010, included information from 53 primary care practices and >170,000 patients with hypertension through 2008. The database includes a complete record of data recorded in the clinical chart on patient morbidity and mortality, demographics, visit diagnosis, BP, medications, and consultation notes collected in a noninterventional manner during daily record keeping within primary practices. The "trigger" for a record update is a billed patient encounter and, each quarter, the cohort database is updated in terms of clinical activity, including hospitalizations, morbidity, and mortality. Data are extracted by chart abstraction at the point of care and entered in real time into a proprietary structured query language program that includes data verification. To ensure confidentiality of patient information, the data are anonymized at collection using encrypted identifiers for both the physician and the individual.

Study Design

The study design and patient flow were previously described in poster form.[43–46] Briefly, inclusion criteria included patients aged ≥18 years (able to provide informed consent) with hypertension (BP >140 and/or >90 mm Hg, a chart entry of diagnosed hypertension, or current use of antihypertensive medication), initia-