Hypertension Management in the Elderly Has Improved Ontario Prescribing Trends, 1994 to 2002

Karen Tu, Norman R.C. Campbell, Minh Duong-Hua, Finlay A. McAlister

Abstract—To examine whether the treatment of elderly hypertensives had become more aggressive over the past decade, we evaluated: (1) the frequency of new prescriptions for hypertension treatment, adjusted by age and gender; (2) the frequency with which multiple antihypertensives were prescribed concurrently within 2 years of initial diagnosis; and (3) discontinuation rates for antihypertensive therapy. We linked 4 administrative databases and a province-wide clinical database in Ontario, Canada, to derive a cohort of patients ≥66 years of age who were newly started on an antihypertensive agent between July 1, 1994, and March 31, 2002, without another indication for the agent (all patients were followed for 2 years after their initial antihypertensive prescription). Our cohort consisted of 196 451 people newly started on antihypertensive therapy, 30 433 of whom also had diabetes mellitus. The population-adjusted rate of new antihypertensive prescriptions increased by 30% between 1994 and 2002. Whereas 21% of patients newly diagnosed with hypertension in 1994 were prescribed multiple antihypertensives concurrently within 2 years of diagnosis, this proportion had increased to 40% by 2002 (P<0.0001). In the cohort of patients first prescribed an antihypertensive in 1994, 36% were not taking any antihypertensive within 2 years; only 21% of patients first prescribed an antihypertensive in 2002 had discontinued all therapy within 2 years (P<0.0001). Our data provide evidence that the physician management of hypertension in elderly Canadians became more aggressive between 1994 and 2002. (Hypertension. 2005;45:1113-1118.)

Key Words: hypertension, essential ■ drug therapy ■ prospective studies ■ elderly

Despite a plethora of guidelines for the treatment of hypertension, studies consistently demonstrate suboptimal rates of blood pressure treatment and control.1-9 In response to this, the Canadian Hypertension Education Program (CHEP) was formed in 1999 in the hope of improving hypertension management in Canada.10 CHEP consists of 2 components: (1) an annual, rigorously evidence-based update of hypertension diagnosis and treatment recommendations, and (2) an extensive implementation process that includes passive dissemination strategies (such as journal publications, wall posters, and pocket cards) as well as more active strategies (such as workshops run by local opinion leaders in a variety of locales and academic detailing of physicians about key CHEP recommendations).

Since 1999, the CHEP guidelines have placed less emphasis on the choice of specific antihypertensive classes for patients with uncomplicated essential hypertension (all 5 major antihypertensive classes: thiazide diuretics, angiotensin-converting enzyme [ACE] inhibitors, calcium channel blockers [CCBs], angiotensin receptor blockers, and β-blockers are listed as appropriate choices for initial monotherapy) and instead have chosen to emphasize the importance of attaining target blood pressures in hypertensive individuals. Because attaining target blood pressures often requires ≥1 antihypertensive agent,11,12 a key message in the implementation of the CHEP guidelines has been the need for multiple agents to adequately control hypertension in most patients. The CHEP guidelines have also specifically advocated the prescribing of ACE inhibitors or β-blockers concurrently with either CCBs or thiazide diuretics (the ABCD recommendation)13 when using multidrug therapy to manage hypertension.

To evaluate the impact of the CHEP program, a national health survey incorporating blood pressure measurements in randomly selected adults is required. However, because no such study is planned in Canada for at least another 3 years, we designed this study to examine trends in antihypertensive prescribing for elderly patients in Ontario from mid-1994 to the first quarter of 2002 to explore the aggressiveness of hypertension management over time. A priori, we did not expect to find any changes in the relative proportions of initial antihypertensive drug classes prescribed (because the
CHEP recommendations endorse all 5 major classes but were more interested in exploring 3 proxies for judging the aggressiveness of hypertension management over time: (1) the frequency of new prescriptions for antihypertensive agents without other indications, (2) the frequency with which ≥2 drugs were prescribed concurrently, and (3) the frequency with which patients were maintained on antihypertensive therapy after initiation.

Methods
We used the Ontario Drug Benefit (ODB) prescription drugs database to identify all Ontario residents ≥66 years of age who had received a new prescription for an antihypertensive agent (list available from corresponding author on request) between July 1, 1994, and March 31, 2002. The ODB database records all drugs prescribed from a minimally restricted formulary for patients ≥65 years of age in Ontario. We prespecified a 1-year washout period to ensure that our cohort comprised all newly treated patients and thus excluded patients with a first claim date within 12 months of the beginning of the study or within 12 months of their entry into the ODB. We linked this cohort to the Ontario Health Insurance Plan (OHIP) physician claims database, the Canadian Institute for Health Information (CIHI) hospitalization database, and the Registered Persons Database using a unique encrypted Ontario health card number that preserved the exact identification of individuals but allowed for the examination of individuals across the 3 administrative databases.

The OHIP database records all fee-for-service billings for physician services rendered in Ontario, including the most responsible diagnosis at each visit. The CIHI database records the primary responsible and up to 15 secondary diagnoses for all discharges from acute care hospitals. Studies on the validity of these administrative databases confirmed their high degree of accuracy and comprehensiveness (>95% for both).14 Finally, we cross-linked with the Ontario Diabetes Database to identify those patients with diabetes mellitus.

We created a cohort of newly treated hypertensives by excluding any patients who had another condition for which an antihypertensive may be prescribed (full list of conditions, International Classification of Diseases, 9th Revision [ICD-9] codes, and medications used as “markers” for nonhypertension diagnoses available from corresponding author on request). In brief, we excluded patients with OHIP claims within 3 years or CIHI claims within 4 years (or marker medications prescribed in the ODB within 1 year) for myocardial infarction or angina, heart failure, arrhythmias, renal disease, liver disease including esophageal varices, transient ischemic attack, or stroke, hyperthyroidism, or migraines before their initiation of the event. Combination agents that consisted of agents from 2 different subclasses were counted as 1 prescription in each respective subclass when assessing concurrent use.

We followed prescriptions filled by our cohort of newly treated hypertensive patients for 2 years after their initial antihypertensive prescription and examined rates of concurrent use, switching to other antihypertensive classes, and discontinuation of antihypertensives altogether. We restricted these analyses to patients without diabetes because we were trying to examine blood pressure control strategies, and it is conceivable that physicians may use an ACE inhibitor or angiotensin receptor blocker with another antihypertensive agent in a diabetic patient for treatment of microalbuminuria rather than for the primary purpose of improving hypertension control. Concurrent use was defined as the addition of another antihypertensive drug class within 100 days of the date of the last prescription of the initially prescribed antihypertensive drug class. A switch was defined as a prescription filled from a different antihypertensive drug class after 100 days from the date of the last prescription of the initially prescribed antihypertensive drug class (if the initially prescribed agent was no longer prescribed). We also examined concurrent use and switching with prescribing window definitions of 30 and 60 days in sensitivity analyses. Patients were deemed to have discontinued antihypertensives if they were not given a prescription for any antihypertensive drug within 180 days of the date of the last prescription (but we also conducted sensitivity analyses with 100, 120, and 150 daytime windows). Patients who died or were hospitalized during the 2-year follow-up period were censored at the time of the event. Combination agents that consisted of agents from 2 different subclasses were counted as 1 prescription in each respective subclass when assessing concurrent use.

Prescribing rates were calculated using Statistics Canada yearly intercensal population estimates for Ontario. To assess whether changes in prescribing rates over time were different between genders, we used a Poisson model, adjusting for age and sex, and examined the interaction between year and gender. Time series analysis was conducted using intervention auto-regressive, integrated, moving average (ARIMA) models to assess the impact on antihypertensive prescribing of the CHEP process that began in 1999 and the presentation or publication of a priori–defined “landmark” hypertension trials during the study period.16–24 Autocorrelation, partial autocorrelation, and inverse autocorrelation functions were assessed for model-parameter appropriateness and seasonality. Stationarity was assessed using the autocorrelation function and the augmented Dickey-Fuller test. The presence of “white noise” was assessed by examining the autocorrelations at various lags, using the Ljung-Box χ² statistic.25 Two-sided P values are reported. Kaplan-Meier curves were used to assess concurrent use, switching, and discontinuation rates, and trends in rates across years were assessed using the Cochran–Armitage test; differences between genders were assessed with the log-rank χ² test.

Results
From July 1994 through March 2002, we identified 196 451 newly treated elderly hypertensives in Ontario (30 433 of whom also had diabetes mellitus). The population-adjusted rate of new prescriptions demonstrated an annual increasing trend (Table), with a 30% increase from the beginning to the end of the study period. The incidence of new antihypertensive prescriptions increased by 20% in elderly women (from 20.1 per thousand in 1994 to 24.1 per thousand in 2002), whereas initiation of antihypertensives in previously untreated elderly men increased by 50% (from 15.8 per thousand to 23.6 per thousand) over the same time period (Table; P<0.0001 comparing the rate of increase over time in men versus women).

The 2 most frequently prescribed classes of antihypertensives were ACE inhibitors and diuretics in both men and women (Table). Between 1994 and 2002, prescribing rates increased by 81% for ACE inhibitors, 10% for diuretics, and 27% for β-blockers, whereas CCBs decreased by 22% (Table). Although diuretic prescriptions decreased by 34% in hypertensive diabetic patients, diuretic prescriptions increased by 21% in nondiabetic hypertensive patients (ACE inhibitor prescriptions increased by 118% and 63% in both groups, respectively; Figures 1 and 2).

Although prescribing rates for all antihypertensive drug classes changed over time, of the landmark trials we defined a priori,16–24 only the Heart Outcomes Prevention Evaluation (HOPE) trial21 was associated with a statistically significant change in prescribing (P=0.002 for the increase in ACE inhibitor prescribing after presentation of HOPE in August 1999). Of note, although total antihypertensive prescribing (even after adjustment for changing population rates) increased over time, the greatest increase was seen in 1999 (a
period that included the initiation of the implementation strategies associated with the CHEP process).

The number of patients prescribed antihypertensives from >1 class concurrently increased steadily over time (from 21% within 2 years of diagnosis in those patients first diagnosed in 1994 to 40% within 2 years of diagnosis in the 2002 cohort; \( P \leq 0.0001; \) Figure 3). Very few patients were initiated on multiple antihypertensive agents on the first day of observation, and most patients had a second (or more) class added within 6 to 9 months of the initial agent prescription. Overall, 75% of the 2 drug class combinations were compatible with the ABCD recommendations of the Canadian Hypertension Society guidelines, with no appreciable change over time.

In addition to the increasing population-adjusted rates of antihypertensive prescribing and the increasing proportion on \( \geq 2 \) antihypertensives concurrently, there was a decreasing trend (36% in 1994% to 21% in 2002; \( P < 0.0001 \)) in the number of patients discontinuing all antihypertensive therapy within 2 years of starting. Overall, the discontinuation rate in our cohort was 25%, with no clinically meaningful differences between genders. There was an increasing trend (26% in 1994 to 32% in 2002; \( P < 0.0001 \)) in the number of patients switching from the initial antihypertensive drug class prescribed to a different antihypertensive drug class within 2 years.

Sensitivity analyses confirmed that imputing different prescription durations had little impact on the rates of concurrent use, switching, or discontinuation and the time trends outlined above. For example, the concurrent antihypertensive drug use rates in the 2002 cohort were 40.3% within 2 years if a 30-day prescribing window was used, 40.0% if a 60-day

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*Data for 1994 are from the third and fourth quarters, and for 2002, the first quarter only.

ARB indicates angiotensin receptor blocker.

Figure 1. Annual population-adjusted rates of initial antihypertensives prescribed for newly treated hypertension in the elderly in Ontario without diabetes. Note that these rates are adjusted per 1000 elderly Ontario residents, including those with and without hypertension, and thus do account for underlying population changes.
window was used, and 39.6% if 100 days was used. Similarly, switching rates in the 2002 cohort ranged from 30.8% for the 30-day prescribing window to 31.4% for the 60-day window to 31.9% for the 100-day window. Finally, discontinuation rates were most affected by changes in drug-prescribing windows (as expected, defining “discontinuation” as not getting a repeat prescription within 100 days led to higher “discontinuation rates” [26.6% in 2002] than using the 180-day prescribing window [21.3% in 2002]). However, it should be noted that the time trends for discontinuation rates (and indeed concurrent use and switching) were identical regardless of the chosen prescribing window because the window was applied in all years in the same fashion. For example, between 1994 and 2002, discontinuation rates decreased by 41% (from 36% to 21%) if lack of a prescription within 180 days was used to define discontinuation, 41% (from 38% to 22%) if 150 days was chosen as the window, 40% (from 41% to 24%) if 120 days was used, and decreased by 38% (from 43% to 27%) if lack of a prescription within 100 days was used to define discontinuation.

Discussion

In summary, we found that new antihypertensive prescriptions in elderly Ontario residents increased steadily from 1994 to 2002, even after adjusting for population changes over time. Antihypertensive prescribing increased over time for all drug classes except CCBs; however, ACE inhibitors were the most commonly prescribed drug class in diabetics, and diuretics were the most commonly prescribed drug class in nondiabetic patients. Our data suggest that physicians are being more aggressive in their treatment of hypertensive patients over time as: (1) the population-adjusted rates of antihypertensive-prescribing increased by 30% between 1994 and 2002, (2) patients newly treated in the latter years of our study were nearly twice as likely to be treated with multiple antihypertensive drugs concurrently within 2 years of diagnosis (40% versus 21%), and (3) patients newly treated in the latter years of our study were 40% less likely to stop all antihypertensive therapy within 2 years than patients treated in the mid-1990s (19% versus 32%). Further, three fourths of the concurrent 2-drug prescribing combinations were consistent with the ABCD recommendations endorsed by CHEP.

Although a study on national Canadian prescribing data in Canada did find statistically significant changes in all antihypertensive drug classes in 1999 (after the introduction of the CHEP program), we were unable to isolate the specific impact of CHEP in our data set given our a priori approach of adjusting for the myriad of landmark hypertension trials published in the same time frame. Although the increases in

**Figure 2.** Annual population-adjusted rates of initial antihypertensives prescribed for newly treated hypertension in the elderly in Ontario with diabetes. Note that these rates are adjusted per 1000 elderly Ontario residents, including those with and without hypertension, and thus do account for underlying population changes.

**Figure 3.** Kaplan-Meier curve for use of concurrent antihypertensive drug classes within 2 years for elderly patients in Ontario without diabetes initiating on antihypertensive therapy, by year. Probability of being prescribed 2 (or more) antihypertensive drugs concurrently over time (up to 2 years after initial medication start); each curve represents the cohort of patients first started on antihypertensive therapy in each year.
thiazide diuretics and β-blockers in the late summer/early fall of 1999 are most likely attributable to CHEP; it is impossible to determine to what extent the CHEP process contributed to the marked increase in ACE inhibitor prescribing that occurred after presentation of the HOPE trial. Certainly, other studies have suggested that virtually all of the increase in ACE inhibitor prescribing in Canada and the United States after the HOPE trial was driven by ramipril prescriptions,27,28 raising the possibility that this change in prescribing habits was driven more by trial data than the CHEP recommendations.

Our data showing relatively high discontinuation rates for patients started on antihypertensive drugs are consistent with other studies that have used different methods for monitoring, different definitions, or different durations of follow-up.29–32 However, the steady decrease in discontinuation rates we documented provides some encouragement that patients may be more compliant with their antihypertensive medications in recent years.

The use of administrative databases in the evaluation of hypertension treatment is subject to a number of limitations. Administrative databases do not contain information on actual blood pressures, and therefore, we can only use changes in prescribing frequency and patterns of antihypertensive use as proxy measures for changes in detection and control of hypertension. Although our study was limited to the elderly because of the limitations of our databases, a high proportion of hypertensives are elderly. Because exact duration of prescriptions was not available, we had to arbitrarily define each prescription as lasting 100 days (the maximum allowable prescription duration on ODB) for determining concurrent use and switching to other antihypertensive drug classes. Although this may have led to overestimates of concurrent use at the expense of underestimates of switching, our sensitivity analyses using 30- and 60-day prescription durations revealed that the differences were <1% and consistent across all years of the study (which would have systematically biased our time trends toward the null and thus serves to reinforce the validity of our findings). Although our study is the largest to date that has examined contemporary antihypertensive prescribing, it is limited to those patients that actually fill out a prescription for an antihypertensive and thus does not give information on the true incidence and prevalence of hypertension in the population because only one third of hypertensive Canadians are actually on therapy.1

Finally, although ACE inhibitor prescriptions increased most markedly during our study period, we do not believe that this is just because of an “expansion of indications” for ACE inhibitors as a result of the HOPE Trial; indeed, patients with overt atherosclerotic disease or diabetes mellitus were excluded from our analyses of concurrent drug use, switching, and discontinuation rates for this very reason.

Perspectives

Although some studies have suggested that physicians are not as aggressive enough in their management of hypertensive patients,1–9 our data suggest that prescribing practices for hypertensive elderly patients have improved substantially since implementation of the CHEP program in Canada. Specifically, we found that even after adjusting for changes in population demographics, antihypertensive prescribing to patients without other indications for these agents had increased by one third, discontinuation rates had declined by nearly half, and newly treated patients were more than one third as likely to be treated with multiple antihypertensive drugs concurrently in 2002 than 1994. Although the full impact of these changes in prescribing patterns on blood pressure control rates cannot be assessed until a nationally representative physical measures survey is done, we believe our data provide some encouragement that, at least in those elderly hypertensive Ontarians who have been started on treatment, management has become more aggressive over the past decade.

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References


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