Population-Based Studies Improve Outcome in Hypertensive Patients

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In a population-based study, three groups of individuals were examined: 334 hypertensive subjects (group 1) received 7 years of intervention therapy by a Hypertension Team (HyT); 418 subjects (group 2) were simply observed with blood pressure (BP) measurement on demand and given lifestyle advice; and 437 subjects (group 3) had no contact with HyT. Hypertension intervention therapy was then withdrawn, leaving patients to their general practitioners. After phase A, BP was significantly lower than baseline in group 1 (14.2%, P < .01) and group 2 (12.4%, P < .01), whereas it was unchanged in group 3. Cerebrovascular (but not coronary) events were observed less in group 1 (fatal 2.7%, nonfatal 3.7%) than in group 2 (7.2% and 5.2%, respectively, both P < .001 v group 1) or group 3 (8.3% and 6.9%, respectively, both P < .001 v group 1). During a further 7 years of observation (phase B), no between-group differences in mortality were observed. We conclude that simple observation improves BP control, but that intervention is needed to reduce the incidence of stroke. Am J Hypertens 2002;15:605–608 © 2002 American Journal of Hypertension, Ltd.

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In Europe, specific updating on arterial hypertension reaches general practitioners (GP) mainly through the educational programs of pharmaceutical companies. The impact of this information on the clinical behavior of GP is, however, scarce. Hypertension therefore remains largely underestimated and undertreated.1,2 Only in 10% to 26% of hypertensive patients is blood pressure (BP) normalized, mainly as a consequence of a conservative approach by GP.1,3

It has been suggested that a direct involvement of GP and patients in observational studies, as well as in clinical trials, might help to improve this situation.

The aim of the present work was to analyze the impact of the presence of a team of experts, acting in addition to the conventional care granted by the National Health System, on BP control and on cardiovascular mortality and morbidity trends in an Italian population.

Methods

Study Population

This study included 1189 Italian elderly hypertensive patients recruited at a population level in the frame of the Cardiovascular Study in the Elderly.4–7 Study protocol and selection criteria have been described elsewhere.5 Briefly, 3282 subjects aged ≥65 years were called from the Register Office. Of these, 73% agreed with the study protocol, gave informed consent and were recruited, while the remaining 27% did not answer or did not accept the study protocol (this is the usual acceptance rate in North Italian epidemiological studies). No significant age and sex differences existed among those subjects who were included versus not included in the study.

The protocol was carried out in accordance with the Declaration of Helsinki of the World Medical Association and approved by the local ethics committees. Procedures were followed in accordance with institutional guidelines.

According to the guidelines of the time when the study was started, 1189 subjects were considered to be hypertensive; that is, systolic BP was ≥140 mm Hg or diastolic BP was ≥90 mm Hg in the absence of any antihypertensive treatment.

Data Collection

Sphygmomanometric supine BP and heart rate were measured in triplicate at 15-min intervals by trained doctors, who repeated this procedure three times at 1-month intervals; the average of the last two of the nine measurements (diastolic Korotkoff phase 5) was taken into consideration for the analysis of data to reduce any white-coat effect. Historical data were recorded by means of a Rose’s questionnaire.8 All subjects underwent physical and laboratory examinations.
Definitions and Cut-Off Values

Body mass index (BMI) was calculated as the ratio of the weight (in kilograms) to height (in meters squared). Subjects were labeled as diabetic if their fasting blood glucose was repeatedly $>7$ mmol/L, if they had a history of diabetes, or if they were receiving treatment with antidiabetic drugs.9

Subjects with total cholesterol $>5.2$ mmol/L were labeled as hypercholesterolemic, and those with triglycerides $>1.7$ mmol/L as hypertriglyceridemic.

Subjects with one of the following items were labeled as having coronary artery disease (CAD): Minnesota code $^9$ equal to 1.1 or 1.2 or 1.3 (if absent 6.4.1) or 4.1 or 4.4 (if absent 6.4.1, 7.1.1 and 7.2.1) or 5.1 or 5.2 or 5.3 or 5.4 (if absent 6.4.1, 7.1.1, 7.2.1 and 7.4), positive myocardial scintigraphy, positive stress test, history of myocardial infarction confirmed by hospital files, history of angina pectoris confirmed by hospital or physician files, or appropriate antianginal chronic treatment.

Subjects with clear neurological signs or a positive history of stroke confirmed by hospital or physician files were considered to have had a stroke. Subjects with calf pain during waking or a positive arterial duplex were considered to have peripheral artery disease.

Study Plan

Two distinct phases were considered.

Study Phase A  During this phase, the 1189 subjects (425 men and 764 women) who were found to be hypertensive at the initial screening were divided into three groups, as described below.

Group 1 patients ($n = 334$) received a 7-year direct intervention, performed by experts in hypertension from Padua University, acting as a Hypertension Team (HyT) organized in the rural northeast Italy. These patients were invited to attend medical appointments at 4-month intervals; they underwent to periodic blood tests and received pharmacologic treatment that was decided according to international guidelines and administered at each visit by the specialists. The GP had no voice in deciding the therapy and, according to the preliminary agreement, were advised not to interfere in any way with the management of hypertension without approval by the HyT. Drugs administered by the GP were in general the same as those used by the HyT (clonidine, slow-release nifedipine or other dihydropiridininic calcium channel blockers, slow-release verapamil, atenolol or other $\beta$-blockers, hydrochlorothiazide or other thiazide diuretics, and converting enzyme inhibitors), sometimes combined.

Group 2 patients ($n = 437$) were deliberately excluded from any contact with the HyT apart from the initial screening. They were left for 7 years to the care of GP, without any direct or indirect intervention or even observation. They received only the care granted by the Italian National Health Service.

The three groups were homogeneous with regard to age and sex. Age at initial screening was $73.4 \pm 5.0$ years in group 1, $73.7 \pm 5.1$ years in group 2, and $74.3 \pm 5.3$ years in group 3. The male/female ratio was 0.34, 0.35 and 0.36, respectively. All differences were nonsignificant.

At the end of phase A, a second field examination was performed that was similar to the first one carried out 7 years before.

Study Phase B  At the end of phase A, the HyT ceased any activity in that area, having completed the period of intervention that had previously been planned. All 848 survivors were left to the care of their physicians independently of the group to which they had previously been assigned. However, mortality was continuously monitored for another 7 years.

Mortality

Mortality was monitored and double-checked for causes of death by referring to hospitals, retirement homes, or physicians’ files. Deaths due to ischemic or hemorrhagic stroke (diagnosed through computed tomography, clinical picture, physician or hospital files, or autopsy) were labeled as stroke mortality. Deaths due to myocardial infarction (diagnosed through electrocardiogram, cardiospecific enzymes, troponin, or autopsy) or to fatal angina pectoris (diagnosed on the basis of the clinical picture) were labeled as CAD mortality.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ SD. Analysis of variance was used to compare grouped continuous variables, and the $\chi^2$ test was used to compare the prevalence of categoric variables, including 7-year and 14-year mortality. Univariate annual mortality in the three groups was compared with the Mantel-Haenszel approach after generating cumulative survival curves. The analysis was performed separately for phases A and B. Multivariate stepwise Cox analysis was used to identify the variables with a prognostic role in mortality. Relative risk (RR) adjusted for confounders with 95% CI was calculated for each categoric item.
Results

At the end of phase A, BP had decreased as follows: group 1, from 183 ± 22/98 ± 11 to 157 ± 24/85 ± 13 mm Hg (P < .01); group 2, from 185 ± 21/98 ± 11 to 162 ± 21/86 ± 11 mm Hg (P < .01); and group 3, from 185 ± 18/98 ± 10 to 186 ± 27/99 ± 13 mm Hg (nonsignificant).

In group 3, BMI had significantly increased by 3.4% (P < .01), along with total cholesterol (3.4%, P < .01) and LDL cholesterol (2.8%, P < .01), but not in group 1 or 2. Triglycerides decreased in groups 1 and 2 (6.7%, P < .001; and 11.6%, P < .001), whereas it was unchanged in group 3.

During phase A, cumulative stroke mortality (Fig. 1) was lower (P < .001) in group 1 than in group 2 or 3; it significantly diverged in the three groups starting from year 4. At the end of phase A, stroke mortality rate was 2.7% in group 1, 7.2% in group 2 (P < .001 vs group 1), and 8.3% in group 3 (P < .001 vs group 1). Seven cases of nonfatal stroke were recorded in group 1 and 2 (−6.7%, P < .01; and −11.6%, P < .001), whereas it was unchanged in group 3.

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During phase A, there were 22 CAD events in group 1 (18 fatal), 34 in group 2 (25 fatal), and 42 in group 3 (17 fatal) (nonsignificant). The cumulative incidence of CAD at the end of phase A was 6.6% in group 1, 8.1% in group 2, and 9.7% in group 3 (nonsignificant). The item group did not enter logistic regression of CAD events.

Discussion

A professional approach to hypertension (namely, that furnished by a HyT) gives better results in terms of BP control and prevention of stroke than a conventional approach granted by a National Health System. In fact, in this study, the HyT not only improved BP values and decreased stroke incidence and mortality in patients under direct intervention (given drugs under strict control), but it also produced positive results in those under more liberal active observation (given advice and answers and being near the hypertensive patients). The direct intervention gave positive results because of the more aggressive therapeutic protocol aimed at reaching values of BP as close as possible to normalization, the active observation probably because of the exchange of information among HyT, GP, and patients. Patients probably became more sensitive to their condition and felt the atmosphere created by the HyT. A poor therapeutic compliance is in fact a major cause of insufficient hypertension control, and even a single educational meeting on hypertension seems sufficient to improve patients’ knowledge.11

Although a better control of BP is a positive result, the modern view is that improvement of outcome is the real aim of antihypertensive treatment. A direct intervention performed by a HyT actually reduced stroke mortality, with 4 years of intervention being necessary to enable the
mortality curves to diverge. A mere observation by the HyT improved BP control but was less effective on patient outcome. This may be explained by the fact that in these patients, SBP remained 5 mm Hg higher than that in group 1, and even slight reduction in BP may have an important impact on prognosis. However, the mechanisms involved in the reduction of mortality and morbidity in hypertensive patients are many-sided, and are not limited to a simple BP lowering effect. In group 3 patients, on whom GP probably exerted a milder psychologic pressure, a less evident improvement of lifestyle was obtained: lipids and BMI were found to worsen at the end of phase A. When the HyT left the field (phase B), stroke mortality dramatically increased in the former intervention group. One year was sufficient to make the stroke survival rate suddenly approach that of the other two groups.

Both the direct intervention and the active observation in this study had little effect in preventing CAD. This is in agreement with previous observations, suggesting a limited effect of antihypertensive treatment in the prevention of CAD, especially in the elderly.

References