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INSIDE

Blood Pressure Control: A Marathon or a Sprint?

BLOOD PRESSURE CONTROL: A MARATHON OR A SPRINT?

This symposium took place on 27th August 2016 as a part of the European Society of Cardiology (ESC) Congress 2016 in Rome, Italy

Chairpersons

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MEETING SUMMARY

This symposium discussed several recent initiatives used around the world to improve the management of hypertensive patients and achieve better blood pressure (BP) control. The key objectives of the symposium were to review the current position with regards to BP control in Europe, to discuss the initiatives used in Italy, France, and Canada to improve hypertension management and their outcomes, and to assess how single-pill fixed-dose combinations of antihypertensive drugs have improved adherence. Some of the key barriers to BP control were discussed and measures to overcome these presented, so that further improvements in hypertension management can be achieved going forward.

Prof Anthony Heagerty opened the meeting by discussing the key causes of suboptimal BP control and the results of the SPRINT study. Prof Massimo Volpe presented the initiative to achieve 70% BP control and assessed its success to date in Italy. Prof Jean-Jacques Mourad discussed the results of the PAssAGE 2014 study and French League Against Hypertension Survey (FLAHS) in 2015, following the initiative to achieve 70% BP control in France by the end of 2015. Prof Raj Padwal presented the Canadian Hypertension Education Program (CHEP) and the improvements in the management of hypertensive patients in Canada. Finally, Dr Julian Segura bought the meeting to a close by discussing how fixed-dose combinations have improved adherence in clinical practice.

Introduction: Issues in Hypertension Management Related to Blood Pressure Goal Achievement

Professor Anthony Heagerty

Despite our best efforts at an individual level, rates of BP control (systolic BP/diastolic BP [SBP/DBP] <140/90 mmHg) are suboptimal in the majority of countries across Europe, with numerous countries having control rates of <50%.[1-3] The key causes of poor BP control, as identified in the 2013 European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines, include physician inertia, low patient adherence to complex regimens, and healthcare system deficiencies in the management of chronic disease, with a focus on short-term cuts instead of long-term gains.[4] In 2015, a European working group suggested five key actions to improve BP control: identification of the BP treatment target <140/90 mmHg for the majority of patients; simplification of treatment strategies by encouraging pill reduction; decreasing therapeutic inertia; improving patient empowerment; and involving healthcare systems to reduce the focus on drug costs.[5] These diverse actions demonstrate that the responsibility for the improvement of BP control in hypertensive patients is shared between physicians, caregivers, authorities, pharmacists, patients, scientific societies, and industry.[5]

The SPRINT study compared the effects of lowering SBP to <140 mmHg with standard therapy or to <120 mmHg with intensive therapy in hypertensive patients ≥50 years of age.[6] The primary composite outcome was myocardial infarction (MI), other acute coronary syndromes, stroke, heart failure, or death from other cardiovascular (CV) causes. A total of 9,361 hypertensive patients aged ≥50 years, with a SBP of 130–180 mmHg and an increased risk of CV events, were randomised. Intensive BP therapy significantly reduced the number of patients with the primary outcome (1.65% versus 2.19% of patients per year for intensive treatment and standard treatment, respectively, p<0.001), and the hazard ratio (HR) for intensive treatment was 0.75 (95% confidence interval: 0.64–0.89, p<0.001). Intensive treatment significantly reduced the risks of heart failure (HR: 0.62, p=0.002), death from CV causes (HR: 0.57, p=0.005), and death from any cause (HR: 0.73, p=0.003). However, rates of emergency department visits or serious adverse events were significantly higher in the intensive treatment group than the standard treatment group. The percentage of patients with hypotension was significantly higher in the intensive treatment group than the standard treatment group (3.4% versus 2.0%, p<0.001), with rates of acute kidney injury or acute renal failure significantly higher for the intensive treatment group (4.4% versus 2.6%, p<0.001).[6]

Currently, rates of BP control are suboptimal across Europe and there remains room for improvement in the management of hypertensive patients. Data from the SPRINT study has shown that lowering the target SBP for BP control reduces the risk of CV events and death. However, we need to balance the gains in BP control from lowering the treatment target with the increased frequency of adverse events observed in the intensively treated patient group.[6]

Have Initiatives to Achieve 70% Blood Pressure Control Among Treated Hypertensives in Italy Changed the Situation?

Professor Massimo Volpe

In Italy, a 2012 study reported that 39.7% of hypertensive patients had suboptimal BP control (SBP/DBP <140/90 mmHg); a figure in keeping with the rates of BP control across Europe.[3] An analysis of a large database from Italian general practitioners (GPs) (N=893,879), reported an overall prevalence of hypertension of 25.1% in patients >15 years of age, with a high prevalence in both males and females.[7] Two large analyses of hypertensive patients have been performed in Italy, the first from 2001–2005 included 52,715 patients, and the second from 2005–2011 comprised 158,879 patients.[3,8,9] Although these two analyses have demonstrated some improvement in the percentage of treated hypertensive patients with BP control over time, from 18.4% of patients in the first assessment to 39.7% in the second, there remains significant room for improvement (Figure 1).[3,8,9]

In 2012, an objective was set by the Italian Society of Hypertension (SIIA) that 70% of hypertensive patients should have controlled BP by the end of 2015, with interventions targeted both at patients and healthcare professionals to achieve this goal.[10] The key points of the SIIA strategy were the implementation of home BP measurement in partnership with patients, simplification of antihypertensive therapy to single-pill combinations,

the development of a network of Italian hypertension centres nationwide, involvement of healthcare institutions, increase in the use of new technologies including smartphones and the SIIA app for BP monitoring and control by patients, and finally the analysis of new large databases to measure the outcome of these interventions.[10-13]

To enable the simplification of treatment to a single-pill therapy, an angiotensin II receptor blocker (ARB)-based hypertension treatment platform was developed, identifying the correct therapy for individual patients based on clinical evidence and experience, guidelines, and best practice.[14] The treatment platform takes the grade of hypertension, patient risk factor (such as renal damage, diabetes, age), and comorbidities (including atrial fibrillation, heart failure, coronary artery disease, previous stroke) into account. For practicality, the platform was based on the ARB olmesartan medoxomil which is available as monotherapy and in single-pill formulations with the calcium channel blocker amlodipine and/or the diuretic hydrochlorothiazide.[14]

Since the implementation of the SIIA strategies in Italy an improvement in the rates of BP control has occurred. In an analysis of adult outpatients in the GP database, 43.2% of hypertensive patients had controlled BP in 2009, rising to 60.6% of patients in 2013 and 60.2% of patients in 2014.[7,15] Similarly, data from a real-world assessment on World Hypertension Day in Italy showed that 50% of hypertensive patients had their BP controlled under treatment from 2004–2010, rising to 55.5% of patients in 2011–2012 and 57.6% of patients in 2013–2014.[16] In the same study, an increase in hypertension awareness from 62.7% of patients in 2011–2012 to 64.7% of patients in 2013–2014 was also observed.[16]

Hypertension remains a significant problem in Italy, affecting >25% of Italian adults with an approximately 60% awareness rate observed.[16] Encouragingly, two independent analyses have demonstrated marked improvements in the rates of BP control since the SIIA objective to achieve BP control in 70% of hypertensive patients, which will result in a significant improvement in hypertension-related burden of disease in Italy.[7,15-17]

PAssAGE 2015: Final Impact of the Initiative to Achieve 70% Blood Pressure Control at the End of 2015 in France

Professor Jean-Jacques Mourad

In 2012, a campaign was launched by the FLAH with the objective of achieving BP control in 70% of hypertensive patients by 2015, to reduce the rates of MI, stroke, and premature death, and costs to the healthcare system.[17,18] Seven key actions for this objective were identified, based on what were considered traditional barriers to BP control:

- Confirmation of high BP outside the GP office environment
- Screening patients for poor therapy adherence
- Switching from monotherapy to combination therapy when initial therapy did not achieve BP control
- Prescription of three-drug therapy in patients not controlled by two-drug therapy
- Screening for causes of uncontrolled hypertension
- Organising a standardised healthcare course for patients with access to specialists if required
- An evaluation of the performance of treatment management[17,18]

A French national study from 2006–2007 showed that 41.8% of males and 58.5% of females aged 18–74 had controlled BP with treatment (N=2,266).[2] The PAssAGE study, conducted from the end of 2013 to 2014, approximately a year after the introduction of the French campaign to achieve control in 70% of hypertensive patients, included a total of 24,849 hypertensive patients identified at GP visits. The mean age of the study population was 67 years with 14.2% of patients aged >80 years. Almost a quarter of patients (23.6%) practised home BP monitoring. Half of the patients in the study (48.9%) were on monotherapy, 32.1% on two drugs, and 16.4% were receiving ≥3 drugs.

PAssAGE reported that 53.8% of all patients had controlled BP with no significant difference between males and females, and 73% of patients >80 years had controlled BP. A significant association between the number of drugs received and the BP outcome was observed; 48.4% of patients on monotherapy had controlled BP versus 62.5% of patients on two drugs. The mean number of antihypertensive therapy classes received was significantly higher in patients

with BP control than those with uncontrolled BP (1.8 versus 1.5, p<0.001). Interestingly, no significant difference in the percentage of patients using home BP monitoring was reported between those achieving BP control and those with uncontrolled BP (24.1% versus 23.2%). Other statistically significant predictive factors for BP control were age, BMI, active smoking, and history of MI.[19]

The FLAHS 2015 was conducted to evaluate BP control nationwide in 1,724 hypertensive patients using home BP monitoring, who were questioned by mail. Data were adjusted according to region, category of urban area, sex, and age. A FLAHS was conducted every 2–5 years from 2004–2015, and comparison of the data from these studies showed an increase in the proportion of hypertensive patients with BP control over time, from 38% of patients in 2004 to 61% of patients in 2015 (Figure 2). In the FLAHS 2015, 46% of patients were receiving monotherapy, 36% of patients were on two drugs, and 14% on three drugs. However, of the patients on triple therapy only 22% were on recommended triple therapies (an ARB or an angiotensin converting enzyme inhibitor, plus a calcium channel blocker and a diuretic), with 66% receiving beta blockers.[20]

In conclusion, significant improvements in the rates of BP control have been observed since the 70% BP control initiative was introduced in France in 2012, and the majority of elderly patients with hypertension are now at the BP control goal.

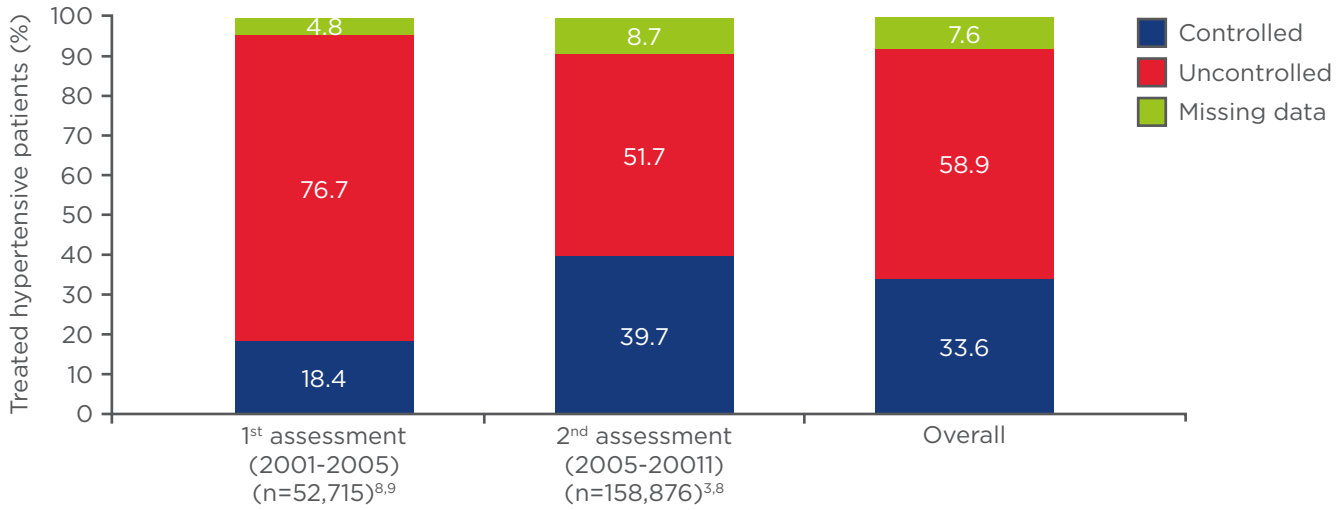
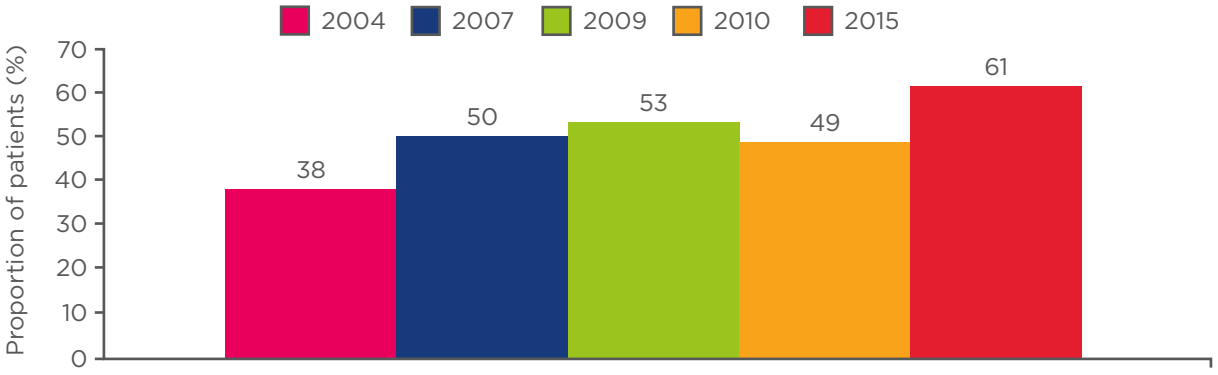


Figure 1: Blood pressure control rates in outpatients included in hypertension surveys performed in Italy from 2001–2011.[3,8,9]

*Systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg.



558 patients in 2004, 424 in 2007, 537 in 2009, 596 in 2010 (>35 years old), 882 in 2015 (>55 years old)

Figure 2: Evolution of blood pressure control in French hypertensive patients from 2004–2015.

Home BP: <135/85 mmHg at 55–79 years of age; <145 at mmHg ≥80 years of age.

BP: blood pressure.

However, there is an urgent need to conduct repetitive and homogeneous evaluations of BP control to evaluate the efficiencies of different initiatives to inform future strategies.

Canadian Hypertension Education Program: Improving the Management of Hypertension

Professor Raj Padwal

The CHEP was launched in 1999 to improve the management of hypertension in Canada.[21,22] It includes annually updated evidence-based recommendations with the goal of improving hypertension prevention, detection, assessment, and management in Canada.[23] In the first 4 years of the programme, a large increase in the diagnosis and treatment of hypertension was observed,[18] and hypertension control has improved from 13.2% in 1992 to 68.1% in 2012–2013.[24,25] Improved management of hypertension has been associated with greater use of antihypertensive drugs and significant reductions in the number of deaths from MI from 1996–2003 (16%, p<0.0001), and stroke mortality (6%, p<0.0001), although other factors may have also contributed to these improvements.[21]

The CHEP Task Force comprises topic subgroups of experts that perform annual systematic reviews of the literature and appraisal of the relevant studies. Members of a central review committee of methodological experts, who are free of potential industry-related conflicts, vet all new recommendations. The CHEP Task Force votes on new recommendations with a requirement of 70% approval before they are added to the guideline paper. Current recommendations are then disseminated via extensive knowledge translation initiatives. The outcomes research committee exists to evaluate the outcomes of new recommendations and identify knowledge gaps in the literature.[26]

CHEP 2016 identified a number of key messages to improve BP control in Canada.[27] Several of these messages were summarised in the diagnostic algorithm for hypertension published by Leung et al.[23] in 2016: all adults should have their BP assessed at all appropriate clinical visits with automated measurement preferred, multiple automated measurements are recommended, and out of office measurement should be performed to confirm the initial diagnosis of hypertension.

To address the key message of identifying the appropriate threshold of therapy initiation for each patient, the Canadian guidelines list the threshold SBP and DBP values by risk factor for the initiation of pharmacological treatment, such as diabetes, high risk of total organ damage or CV risk factors, SPRINT eligibility, and age.[23] Similarly, recommended SBP and DBP treatment targets are provided based on the patient's age and whether the patient has diabetes. The CHEP 2016 key messages also cover the effectiveness of health behaviour modification in preventing and treating hypertension, and reducing CV risk, and the importance of health behaviour modification alongside antihypertensive drugs in the effective treatment of hypertension.[27]

In 2009, the STITCH study, conducted in Eastern Canada, showed that more hypertensive patients achieved BP control when treated using a simplified treatment algorithm (STITCH) compared with usual care based on the CHEP guidelines (64.7% versus 52.7% of patients), highlighting the importance of simple treatment protocols in achieving BP control.[28] This simplified algorithm directed physicians to initiate treatment with a half-strength angiotensin converting enzyme inhibitor and diuretic, or ARB and diuretic combination therapy. If BP remained uncontrolled, the combination preparation was maximised before adding a calcium channel blocker and subsequent agents.

The treatment and control of hypertension in Canada has markedly improved in recent years, with CHEP being instrumental in its success. However, the challenges to achieving BP control remain: simplifying the guidelines and increasing their uptake.

Conclusions: Have Fixed Dose Combinations Improved Adherence in Clinical Practice?

Doctor Julian Segura

In Spain, trends in treatment and BP control over time have been observed in the multicentre cross-sectional studies PRESCAP 2002, PRESCAP 2006, and PRESCAP 2010 conducted in primary care.[29] Over time, an improvement in the rates of BP control was observed from 36.1% of patients with hypertension in 2002, to 41.4% of patients in 2006 and 46.3% in 2010.[29] In addition, a significant reduction over time in the proportion of patients

receiving monotherapy (p<0.001) and significant increases in those prescribed two drugs, three drugs, or more than three drugs (p<0.001) have been observed.[29]

In an analysis of patient dosing histories, the number of patients persisting with their antihypertensive treatment regimen decreased over time and adherence to treatment also dropped due to poor execution of the dosing regimen.[30] The pill burden had a significant impact on adherence, with 87.3% adherence reported when patients were prescribed a single-pill fixed-dose combination for two concomitant drugs, in comparison with 73.6% for separate pills (p<0.0001).[31] Patient compliance decreased as the pill burden increased, with 73.7% adherence reported with a single drug in comparison with 65.6% when ≥7 drugs were given concomitantly.[31] Single-pill fixed-dose combinations were associated with significantly greater adherence (55.3%) than two (40.4%) or three pill (32.6%) combinations (p<0.0001).[32] Hence, the ESH and ESC guidelines recommended the use of fixed-dose combinations of antihypertensive drugs to improve patient adherence.[4]

A recent meta-analysis of 20,451 patients with hypertension showed that the combination of angiotensin system blockade agents with calcium channel blockers was superior to other combinations, as patients demonstrated a lower incidence of CV events and adverse events. However, the effects of different combinations of agents on lowering BP and preserving renal function was similar.[33] A longitudinal database study showed that the initiation of therapy with the combination treatment resulted in more patients achieving target BP, which was associated with reduced risk of CV events.[34] A 2013 study demonstrated greater adherence for patients receiving a fixed-dose combination of olmesartan medoxomil and amlodipine in comparison with a free combination of ARBs with amlodipine (63.0% versus 34.0%, p<0.001), and fewer CV events (5.9% versus 16.9%, p<0.001).[35]

There is now significant evidence that BP control is improving across Europe, with improvements in France, Italy, Spain, and Canada in particular demonstrating that it is possible to achieve BP control goals for more patients. A number of studies have shown that utilising single-pill fixed-dose combinations improves patient adherence and leads to improved BP outcomes, and this approach has been included in a number of the initiatives to date. Whilst great progress has been made with these initiatives in France, Italy, and Canada, further initiatives are required to improve BP control in all countries.

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