Journal of Human Hypertension (2008) 22, 295–297

www.nature.com/jhh

RESEARCH LETTER

Prescribing practices and morning blood pressure control: results of a large-scale, primary-care study conducted in Germany

Journal of Human Hypertension (2008) **22**, 295–297;
doi:10.1038/sj.jhh.1002326; published online 17 January 2008

Using a questionnaire, data were collected by 2934 general practitioners on 64 644 patients regularly being monitored because of hypertension ($n = 55\,165$) or the presence of cardiovascular risk factors. In patients prescribed antihypertensives ($n = 52\,469$), 46.9% received monotherapy, but morning blood pressure was normalized (<140/90 mm Hg) in only 23.3%. Monotherapy with angiotensin receptor blocker provided the best normalization (30.1%), and angiotensin-converting enzyme inhibitors provided the worst (22.3%). Normalization occurred in 21.8% of patients after receiving combination therapy.

Wolf-Maier *et al.*[1] showed that awareness, treatment and control of hypertension in Germany is poorer than in other European and North American countries.[1] Typically, blood pressure (BP) is highest during the day and lowest at night, with a morning surge on arousal.[2] The incidence of many cardiovascular events reaches a peak during the post-awakening hours, coincident with the morning surge in BP.[2] Hence, control of BP is particularly important in the morning. This large-scale study evaluated the management of morning BP by German general practitioners (GPs).

Data were collected on patients (age ⩾18 years) with hypertension (>140/90 mm Hg) or who had cardiovascular risk factors (coronary heart disease, diabetes mellitus, obesity and/or sleep apnoea) when they came for a morning consultation between January and October 2001 for routine monitoring. Patient characteristics, initial diagnosis, antihypertensive medication, time of last dose and morning (0600 to 1200 hours) BP measured in the GP's office using a standard procedure[3] were recorded in the questionnaire; ambulatory BP and home BP measurements were excluded. Descriptive statistical analysis was performed on the data.

Information on 64 644 patients was collected by 2934 GPs, with morning BP readings available for 55 165 hypertensive patients (average age 63.0 ± 12.6 years, average body mass index 27.9 ± 4.5 kg m^{-2}). Obesity, coronary heart disease, diabetes, sleep apnoea and other risk factors were present in 37.2, 25.9, 27.4, 2.7 and 18.3% of the patients, respectively. Antihypertensive medication was received by 95.1% of hypertensive patients. A total of 69.9% patients reported that the medication had been taken that morning before BP measurement.

Overall, 44.6% received antihypertensive monotherapy. Among the 27 555 patients receiving combination therapy, 62.3% were prescribed two drugs. However, 2292 patients were treated with four to six different agents. β-Blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blocker (ARBs), calcium channel blockers and diuretics (in decreasing order) were the most common antihypertensives to be prescribed as monotherapy; α_1-blockers or α_2-agonists were QJ;prescribed to only 220 patients as monotherapy and to 467 as part of combination therapy. The most frequently used combination therapies were an ACE inhibitor plus a diuretic (7.1%), a β-blocker plus an ACE inhibitor (5.7%), an ACE inhibitor plus a calcium channel blocker (3.4%), an ARB plus a diuretic (3.1%) and a β-blocker plus a diuretic (3.0%). In 59.7% of the patients, the antihypertensive therapy was administered once daily, although in about 20% of those treated with β-blockers, ACE inhibitors or calcium channel blockers, the dosing was twice daily.

In the majority of patients, BP was recorded between 0800 and 1000 hours, with little variation in BP depending on the time, in the morning, it was measured. Mean morning BP was lower in those who had taken their medication in the morning (146.5/85.0 mm Hg) as opposed to other times of day (152.8–154.1/87.5–90.0 mm Hg). Using the German Hypertension Society classification, 23.2% were classified into normotensive (<140/90 mm Hg), 17.7% mildly hypertensive (140–159/90–99 mm Hg), 17.7% moderately hypertensive (160–179/100–109 mm Hg) and 7.6% severely hypertensive (⩾180/110 mm Hg). Isolated systolic hypertension (⩾140/<90 mm Hg) was present in 33.9%. Systolic BP was similar irrespective of the presence of an additional diagnosis in all classes of hypertensive patients.

Morning BP normalization was achieved in 25.6% on monotherapy, with distinct differences between treatments (Figure 1). For combination therapy, the best BP normalization was achieved with a β-blocker plus an ARB and the poorest using an ACE inhibitor plus an ARB (Figure 1).

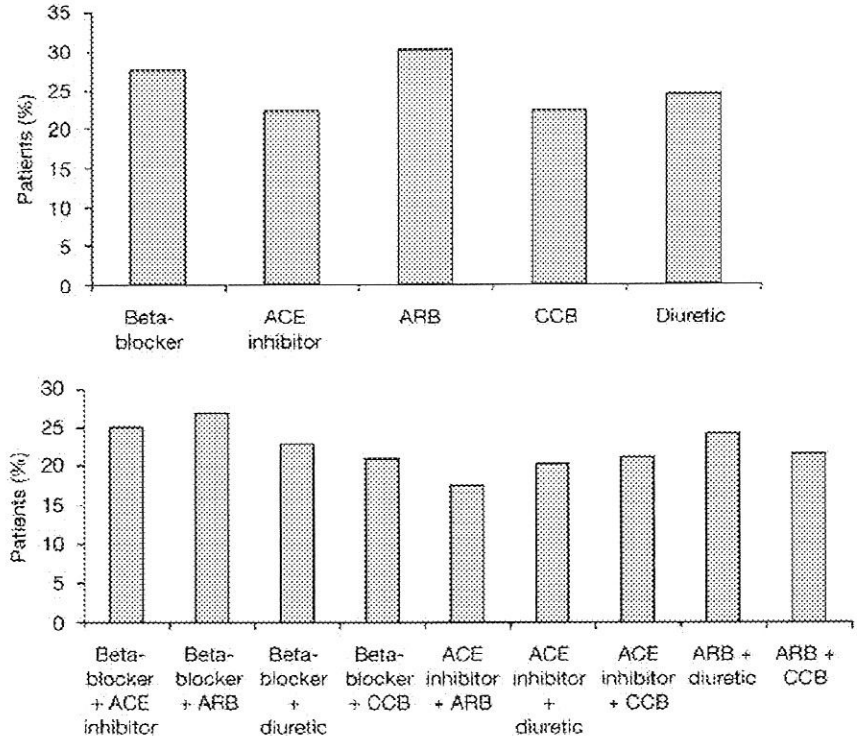

Figure 1 Normalization of blood pressure by monotherapy or combination therapy. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

The findings of this survey clearly demonstrate that the treatment of German hypertensive patients is not ideal; the control of morning BP is inadequate in many and, consequently, patients' long-term cardiovascular prognosis may be compromised.[4] The multinational study by Wolf-Maier *et al.*[1] highlighted Germany's poor track record in the management of hypertension, compared with other European countries. The Hypertension and Diabetes Risk Screening Awareness (HYDRA) study drew attention to the inadequacy of hypertension control in the primary-care setting within Germany, without specifically examining the control of morning BP when cardiovascular risk is elevated.[5,6]

One alarming observation from our study is that approximately 5% of patients were not receiving antihypertensives despite having evidence of high BP; no explanation was provided for this.

In our survey, BP was measured using recommended procedures and with exclusion of home BP measurement that may be less accurate in the morning between 0600 and 1200 hours, in the majority, after receipt of antihypertensive medication. Thus, despite most patients having already taken their antihypertensive medication for the day, BP was normalized in less than one-quarter with considerable variations according to agents prescribed.

In the majority of patients, a single agent was prescribed. This deficiency in prescribing practice has also been identified by the HYDRA study, with many GPs following outdated guidelines.[6] Doses of monotherapy may need to be increased, but GPs may be hesitant because of a possible increase in side effects. For many patients, however, it may be more appropriate to introduce a more aggressive BP control using an appropriate combination of agents.[7] In our survey, we found that some patients were clearly receiving inappropriate combinations, such as a β-blocker plus an ARB, β-blocker plus an ACE inhibitor, α-blocker plus an ARB, calcium channel blocker or diuretic,[8] and treating patients with four or more agents may even have been counterproductive by hindering compliance.

In our study, morning BP normalization was better with monotherapy than with combination therapy. This is surprising at first glance. This observation may be partly attributed to use of inappropriate combinations, but also to the fact that the patients receiving combination therapy had more severe hypertension. Our findings do suggest that BP levels were not greatly dependent on the class(es) of antihypertensive agent(s) prescribed. However, under monotherapy, the proportion of patients treated with an ARB achieving BP normalization was higher than that of patients treated with ACE inhibitors. Possible explanations could be side effects, resulting in patient nonadherence, or an insufficient dosing regimen.

Recent evidence suggests that target organ protection is not simply a matter of reducing BP. The Heart

Outcomes Prevention Evaluation (HOPE)[9] and Losartan Intervention For Endpoint reduction in hypertension study (LIFE)[10] demonstrate that agents that target the renin–angiotensin–aldosterone (RAA) system may confer additional benefits that are independent of their antihypertensive activity. It is encouraging, therefore, to see that agents targeting the RAA system were relatively frequently prescribed.

A frequent problem in the treatment of hypertension is patient persistence with medication.[11] Compliance was assumed in this study; inevitably, GPs were reliant on the information provided by their patients. However, we may presume that patients were sufficiently conscientious to attend their monitoring consultation and thus more likely to be compliant.

We conclude that there are still lessons to be learnt about the care of hypertensive patients in primary care in Germany, with a clear need for more effective BP control in the morning to reduce cardiovascular risk.

What is known about the topic

- Management of hypertension by German GPs is suboptimal, often adhering to out-of-date guidelines.

What this study adds

- Not all hypertensive patients who are regularly evaluated are receiving antihypertensive therapy.
- Less than one-quarter of hypertensive patients had their morning BP normalized.
- A combination of a β-blocker plus either an ACE inhibitor or an ARB or an ARB plus a diuretic was the most effective combination.

B Lemmer[1], M Middeke[2], B Schaaf[3] and L Eckes[4]

[1]*Institut für Experimentelle und Klinische Pharmakologie und Toxikologie, Ruprecht-Karls-Universität Heidelberg, Heidelberg, Germany;*

[2]*Blood Pressure Institute, Munich, Gemany;*

[3]*Gesellschaft für Statistik, wissenschaftliche Information und Kommunikation mbH, Offenbach, Germany and*

[4]*Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany*

E-mail: bjoern.lemmer@pharmtox.uni-heidelberg.de

Published online 17 January 2008

References

1 Wolf-Maier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR *et al.* Hypertension treatment and control in five European countries, Canada, and the United States. *Hypertension* 2004; **43**: 10–17.

2 Lemmer B. The importance of circadian rhythms on drug response in hypertension and coronary heart disease—from mice and man. *Pharmacol Ther* 2006; **111**: 629–651.

3 American Society of Hypertension. Recommendations for routine blood pressure measurement by indirect cuff sphygmomanometry. *Am J Hypertens* 1992; **5**: 207–209.

4 Lemmer B, Portaluppi F. Chronopharmacology of cardiovascular diseases. In: Redfern PH, Lemmer B (eds). *Physiology and Pharmacology of Biological Rhythms*. Springer: Heidelberg, 1997, pp 251–298.

5 Sharma AM, Wittchen HU, Kirch W, Pittrow D, Ritz E, Göke B *et al.* High prevalence and poor control of hypertension in primary care: cross-sectional study. *J Hypertens* 2004; **22**: 479–486.

6 Stecklings UM, Stoppelhaar M, Sharma AM, Wittchen HU, Krause P, Küpper B *et al.* HYDRA: possible determinants of unsatisfactory hypertension control in German primary care patients. *Blood Press* 2004; **13**: 80–88.

7 Hansson L, Zanchetti A, Carruthers SG, Dahlöf B, Elmfeldt D, Julius S *et al.* Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the hypertension optimal treatment (HOT) randomised trial. *Lancet* 1998; **351**: 1755–1762.

8 ESH-ESC Task Force on the Management of Arterial Hypertension. 2007 ESH-ESC practice guidelines for the management of arterial hypertension. *J Hypertens* 2007; **25**: 1751–1762.

9 Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000; **342**: 145–153.

10 Dahlöf B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U *et al.* Cardiovascular morbidity and mortality in the Losartan intervention for endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002; **359**: 995–1003.

11 Hasford J, Schröder-Bernhardi D, Rottenkolber M, Kostev K, Dietlein G. Persistence with antihypertensive treatments: results of a 3-year follow up cohort study. *Eur J Clin Pharmacol* 2007; e-pub ahead of print 14 August 2007.