

Efficacy, tolerability and safety of nebivolol in patients with hypertension and diabetes: a post-marketing surveillance study

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Abstract. – Background and Objectives: Hypertension is a widely prevalent condition of elevated blood pressure (BP) and is the leading risk factor for the development of cardiovascular disease (CVD). Many patients have additional risk factors such as diabetes mellitus (DM) or previous history of CVD. Nebivolol is a third-generation beta (β)-blockers which has been shown not to influence metabolic parameters in patients with DM. This post-marketing surveillance study aimed to collect information on the efficacy, safety and tolerability of nebivolol in hypertensive patients with concomitant DM.

Patients and Methods: Hypertensive patients with DM followed by 52 cardiologists, internal medicine specialists and general practitioners, between 24 August 2003 and 9 January 2007 in the Netherlands were included in this study. Physicians were asked to survey nebivolol treatment for 6 months.

Results: A total of 510 patients were enrolled. Overall, 93.3% of patients were diagnosed with essential hypertension and 6.7% with secondary hypertension. All patients were co-diagnosed with DM. Nebivolol therapy was associated with a significant reduction in both systolic blood pressure (BP) and diastolic BP versus baseline ($p < 0.001$ for both). These reductions were seen regardless of reason for initiation of nebivolol (i.e. first diagnosis of hypertension, resistance or intolerance to previous antihypertensive medication, or other reasons). A significant improvement in blood glucose was seen at 4 months (-0.6 mmol/L; $p = 0.021$). Significant reductions in total cholesterol (-1.45 mmol/L; $p = 0.006$), low density lipoprotein (LDL) cholesterol (-1.32 mmol/L; $p = 0.003$) and LDL/high density lipoprotein (HDL) cholesterol ratio (-0.77 ; $p = 0.011$) were observed at 2 months. No significant changes were seen in HDL cholesterol and triglycerides.

Conclusion: Nebivolol treatment was associated with a significantly reduced BP, improved blood glucose and LDL cholesterol levels and was well tolerated in hypertensive patients with concomitant DM.

Key Words:

Nebivolol, Hypertension, Diabetes, Glycaemic profile, Lipidic profile.

Introduction

Hypertension is a widely prevalent asymptomatic condition of elevated blood pressure (BP). It is a major risk factor for the development of cardiovascular disease (CVD) and is the leading cause of the global mortality according to a World Health Organisation survey¹. In 2000, it was estimated that 972 million people (26.4% of the world's adult population) were hypertensive. It has also been predicted that the total number of adults with hypertension will increase to 1.56 billion people by 2025². The current European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines define hypertension as BP $\geq 140/90$ mm Hg and recommend a treatment target of $< 140/90$ mm Hg and $< 130/80$ mm Hg in the general hypertensive population and in patients with diabetes mellitus (DM), respectively³. Guidelines also emphasise that hypertension diagnosis and management should be based on the assessment of total cardiovascular (CV) risk⁴, since only a small proportion of the hypertensive population displays elevated BP alone. The majority of patients have additional CV risk factors, such as type 2 DM: in these subjects, effective management of hypertension is essential for the reduction of total CV risk³. Patients with DM have twice the risk of myocardial infarction (MI) and stroke compared with the rest of the population and a two- to four-fold increase in risk of CVD⁵.

The classes of antihypertensive therapy available for the clinical management of hypertension include thiazide diuretics, beta (β)-blockers, calcium channel blockers (CCBs), angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs).

β -Blockers are widely used in the clinical management of hypertension^{3,6}. They provide an effective cardiovascular protection in patients with type 2 DM as a result of BP lowering. However, older β -blockers are not preferred as first-line agents, since some show less cardiovascular protection⁶ and have detrimental effects on glucose control and insulin sensitivity⁷. Third-generation β -blockers produce greater improvements in cardiovascular outcomes in patients with DM than in non-diabetics^{3,8} and do not influence glycaemic control⁹⁻¹¹. Such agents may, therefore, be particularly suitable for diabetic patients who require antihypertensive treatment. In addition, third-generation β -blockers, including labetalol, carvedilol, celiprolol, bucindolol and nebivolol, have vasodilatory effects that may offer further therapeutic benefits not provided by traditional β -blockers¹²⁻¹⁴.

The endothelium-derived vasodilator nitric oxide (NO) exerts its effects through the enhancement of cyclic guanosine monophosphate and thereby influences cardiac contractility and platelet activity¹⁵. Nebivolol is a highly selective β_1 -adrenoceptor antagonist with endothelial NO-mediated vasodilatory activity^{13,14,16,17} that is approved for the treatment of essential hypertension and chronic heart failure in Europe and in several other countries¹⁸. It is a lipophilic β -blocker, clinically administered as a racemic combination of *d*- and *l*-nebivolol, that is devoid of intrinsic sympathomimetic or membrane stabilising properties^{13,14,16,17,19}. Nebivolol exerts its endothelium vasodilatory properties via the activation of the L-arginine/NO pathway and has proven BP-lowering capability and a favourable tolerability profile^{17,20,21}. Endothelial function is improved with nebivolol treatment via the stimulation of endothelial NO-synthase (eNOS) and the reduction of oxidative inactivation of NO²².

Nebivolol has been associated with significant reductions in BP in hypertensive patients, and has been shown to be effective in lowering BP in patients with mild-to-moderate hypertension^{13,14,20}, including African American patients²³. In addition, nebivolol was associated with neutral or beneficial effects on metabolic

parameters, such as lipids and glucose^{14,24-26}. The recent Reappraisal of European guidelines on hypertension management issued by the European Society of Hypertension highlighted that nebivolol, at variance from other β -blockers, has been found to improve insulin sensitivity and oxidative stress^{27,28}. These properties may further contribute to a reduction in cardiovascular risk in hypertensive patients^{27,28}. A low incidence rate of adverse events (AEs) has been reported with this drug²⁶, and nebivolol showed a better tolerability profile than atenolol in a double-blind, randomised study²⁰.

The purpose of this post-marketing surveillance study was to evaluate the efficacy, tolerability and safety of nebivolol (Nebilet®) in the treatment of hypertension in patients with DM. A post-marketing surveillance study is a systematic surveillance of all expected and unexpected effects of a drug following introduction into the market. The study is purely observational and a physician's decision to prescribe a certain medication may not be influenced in any way, in order to describe usual daily practice. Only data collected by the physician during their daily practice were evaluated; no additional laboratory measurements or other diagnostic procedures were imposed.

Patients and Methods

Patients

Hypertensive patients with DM in the Netherlands were included in this study. There were no further inclusion or exclusion criteria except contraindications to nebivolol treatment.

Study Design

This was a prospective, open-label, multicentre post-marketing surveillance study conducted by 52 cardiologists, internal medicine specialists and general practitioners in the Netherlands between 24 August 2003 (first subject entry) and 9 January 2007 (last subject evaluation). Each physician was invited to participate and the number of patients per physician was limited to 20 patients. However, in exceptional cases the patient number could be increased. The objective of this study was to acquire information on the efficacy, tolerability and safety of nebivolol in hypertensive patients with concomitant DM in daily practice in the Netherlands. Physicians were

asked to survey nebivolol treatment over a 6-month period. Data were collected at enrolment (visit 1) and at planned follow-up visits originally scheduled for 2 months (visit 2) and 6 months (visit 3) following study inclusion. The exact timing of these follow-up visits varied according to each physician's daily practice.

Treatment

All patients received nebivolol as an oral tablet formulation, at an initial dose of 5 mg once daily. Dose was adjusted at the discretion of the physician (permitted doses were 2.5, 5 or 10 mg/day).

Measurements

Data were recorded in a database using an electronic Case Report Form (CRF). Demographic data, hypertension diagnosis (essential or secondary hypertension), co-existing diseases, existing complaints and their severity (rated as mild, moderate or severe; treatment-related or not), concomitant medications, and nebivolol dosage were recorded at enrolment (visit 1), as were systolic BP (SBP), diastolic BP (DBP), plasma glucose concentrations, urinary protein, triglycerides, total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol. The primary reason to initiate nebivolol therapy was also recorded at visit 1 and divided into 4 categories: (1) first treatment (subject had no prior antihypertensive therapy); (2) therapy resistance (subject had prior antihypertensive therapy and switched to nebivolol due to insufficient clinical response to previous therapy); (3) intolerance to therapy (subject had prior antihypertensive therapy and switched to nebivolol due to unwanted effects attributed to previous therapy); (4) other reasons (including nephropathy, changes of treatment/convenience, tachycardia, impotence, concomitant disease, other or not recorded).

SBP and DBP, nebivolol dose alterations, changes in concomitant medication, adverse events (type, severity and whether or not related to nebivolol) and, if available, plasma glucose concentration, urinary protein and lipid profile were recorded at follow-up visits. At visit 3, patients and physicians were asked to evaluate the efficacy of nebivolol using a 5-point rating scale (1 = poor, 2 = moderate, 3 = neutral, 4 = good, 5 = very good), and physicians were asked to assess the compliance of the patient, using a 3-point rating scale (1 = bad, 2 = moderate, 3 = good).

Safety

Serious adverse events (SAEs) were defined as unexpected events that resulted in death, were life-threatening, required hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, or comprised a congenital anomaly/birth defect. Other complaints were recorded in the CRF.

Statistical Analysis

Quantitative data were statistically analysed using Student's t-test or analysis of variance (ANOVA) test, as appropriate. The Cochran-Mantel-Haenszel test was used to analyse semi-quantitative data. Qualitative data were analysed using the Fishers' exact probability test. Efficacy data were analysed according to an intention-to-treat (ITT) population where last-observation-carried-forward (LOCF) was applied. Statistical significance was set at $P=0.05$ (two-tailed).

Results

A total of 510 patients were enrolled in this study. Patient characteristics at baseline are presented in Table I. Overall, 93.3% of patients were diagnosed with essential hypertension and 6.7% with secondary hypertension. All patients were co-diagnosed with DM. Insulin-dependent (type 1) DM was recorded in 21.6% of patients, while 39.8% had non-insulin-dependent (type 2) DM; the type of diabetes was unrecorded in 38.6% of patients. Although all patients were diagnosed with diabetes, anti-diabetic therapy was reported for only 57.3% of patients; 22.5% of patients used insulin and 34.7% of patients used non-insulin products. Mean body mass index (BMI) was 30.0 kg/m² and 43.3% of patients had a co-diagnosis of obesity. Concomitant diseases are presented in Table I. The most common co-diagnosis was hyperlipidaemia and nearly one third of patients had CVD.

Nebivolol was the patient's first antihypertensive medication for 19.8% of study subjects. Nearly two thirds of patients ($n=320$; 62.7%) had prior anti-hypertensive therapy and switched to nebivolol because of resistance to the previous therapy, 10.8% ($n=55$) switched to nebivolol because of unwanted side effects on their previous antihypertensive medication. 6.7% ($n=34$) were prescribed nebivolol for other reasons. During the observation period 206 (14%) of 1504 concomi-

Table 1. Patient demographic data.

Parameter	Total (n = 510)	First treatment (n = 101)	Therapy resistance (n = 320)	Intolerance to previous therapy (n = 55)
Gender (M/F) [%/ %]	265/244 [52.1/47.9]	48/53 [47.5/52.5]	172/147 [53.9/46.1]	30/25 [54.6/45.4]
Age (years)	65.0 ± 11.3	60.8 ± 13.1	66.3 ± 10.3	65.2 ± 10.6
Height (cm)	171.1 ± 9.6	171.3 ± 10.4	171.0 ± 9.2	173.0 ± 9.9
Weight (kg)	87.9 ± 17.1	85.4 ± 17.8	88.6 ± 16.8	89.1 ± 16.1
BMI (kg/m ²)	30.0 ± 5.5	29.1 ± 5.7	30.3 ± 5.5	29.7 ± 4.7
Co-diagnosis				
Type 1 DM	110	21	82	5
Type 2 DM	203	56	113	16
Type of diabetes unrecorded	197	24	125	34
Hyperlipidaemia	258	46	168	28
Asthma/COPD	12	1	6	2
Obesity**	221	39	146	23
Hyperthyroidism	7	2	4	1
CVD	144	18	96	20
Other	93	6	68	1

Baseline patient demographic data (mean±SD). BMI = body mass index; CVD = cardiovascular disease; IDDM = insulin-dependent (type 1) diabetes mellitus; NIDDM = non-insulin-dependent (type 2) diabetes mellitus; COPD = Chronic obstructive Pulmonary disease. ** Recorded as obesity and/or BMI ≥ 30.

tant therapies were discontinued: among these, 179 (87%) were antihypertensive agents, 8 (4%) were hypoglycaemic drugs, 3 (1%) were hypolipidemic drugs and 16 (8%) were other medications. In total, 27 new drugs were added during the study period: 20 (74%) were antihypertensive agents, 2 (7%) were hypolipidemic drugs and 5 (19%) belonged to other drug classes. No hypoglycaemic drugs were added. Among patients switching to nebivolol because of insufficient clinical response, the most commonly recorded previous therapies were ACE inhibitors (28.1% of medications) and ARBs (21.7%) followed by CCBs (17.3%), diuretics (15.8%), β-blockers (12.5%), α-blockers (2.4%) and other (2.2%). Among patients switching to nebivolol because of the onset of side effects, the most commonly recorded previous therapies were β-blockers (n=36; 42.4% of medications recorded) and ACE inhibitors (n=18; 21.2%), followed by ARBs (n=11; 12.9%), diuretics (n=10; 11.8%), CCBs (n=8; 9.4%), α-blockers (n=1; 1.2%) and others (n=1; 1.2%). Among the β-blockers which were associated with the onset of adverse effects, metoprolol (44.4%) and atenolol (30.6%) were the most recorded medications, followed by bisoprolol (13.9%), celiprolol (5.6%), carvedilol (2.8%) and propranolol (2.8%).

A total of 109 (21.4%) out of 510 patients withdrew from the study. Reasons for withdrawal

were loss to follow-up (1.8%), lack of efficacy (1.4%), adverse events (AEs) (1.9%), discontinued by other physician (1.0%), patient decision (0.4%) and no reason recorded (14.9%).

The majority of patients received nebivolol 5 mg/day. Nebivolol 2.5 mg/day was prescribed to 2.5%, 2.1% and 1.5% of patients at baseline, visit 2 and visit 3, respectively. Nebivolol 5 mg/day was prescribed to 96.5%, 95.0% and 94.0% of patients at baseline, visit 2 and visit 3, respectively. Only 1.0%, 2.9% and 4.5% of patients were prescribed nebivolol 10 mg/day at baseline, visit 2 and visit 3, respectively.

Overall, follow-up visits occurred at a mean of 51±28 days [≈2 months] (visit 2) and 118±58 days [≈4 months] (visit 3) after enrolment.

Efficacy

Change in Blood Pressure

Nebivolol therapy was associated with significant reductions in SBP and DBP at visit 2 and visit 3 versus baseline ($p < 0.001$ for all comparisons); these reductions were observed regardless of the reason for initiating nebivolol treatment (Figure 1). The largest reduction from baseline in BP (−21.2/−9.5 mm Hg; $p < 0.001$) was observed in newly diagnosed hypertensive patients. In all

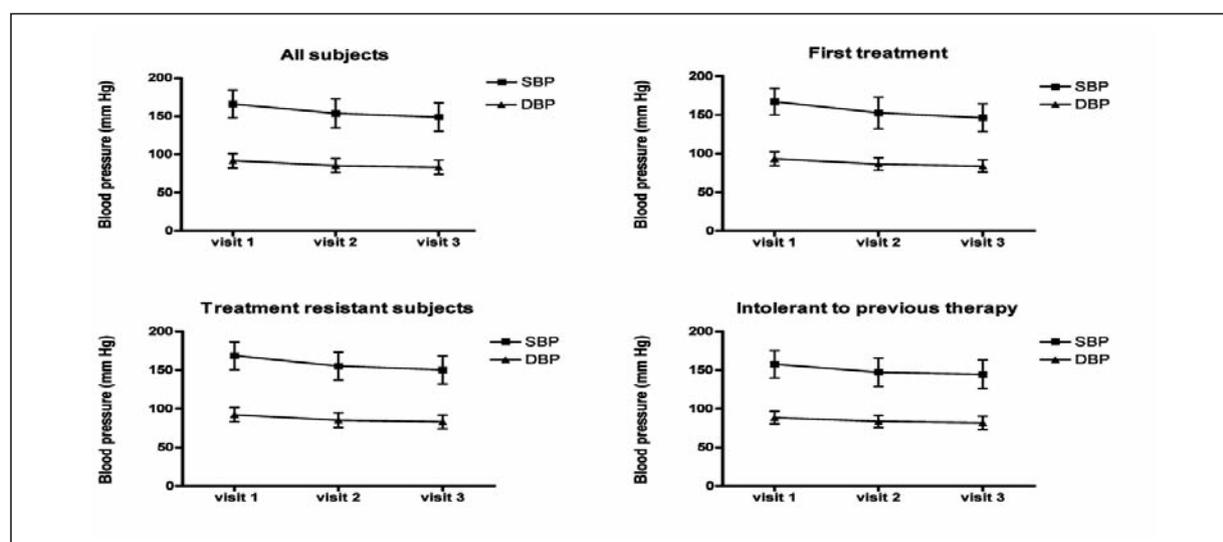


Figure 1. Effect of nebivolol therapy on systolic (SBP) and diastolic (DBP) blood pressure (BP) (mean \pm SD) before (visit 1) and during (visits 2 and 3) treatment for up to 6 months in patients with concomitant hypertension and diabetes mellitus. Results are divided for treatment reasons. Squares: SBP; triangles: DBP. * P <0.001 vs baseline for all comparisons.

patients, the mean decrease in BP was $-17.2/-8.5$ mm Hg (p <0.001 vs baseline). Corresponding values for resistant and intolerant patients were $-18.2/-9.2$ mm Hg and $-13.0/-6.6$ mm Hg, respectively (p <0.001 vs baseline for both).

Twenty-one (6.1%) patients had additional antihypertensive medications prescribed during the study; this did not significantly impact the reduction in BP achieved (data not shown).

Change in Blood Glucose and Lipid Parameters

Blood glucose concentrations and lipid parameters are shown in Table II. Note that statistical comparisons could only be made in a limited number of cases as not all parameters were recorded in all patients: for instance, blood glucose was recorded at baseline in 239 patients, in

89 subjects at visit 2 and at visit 3 in 82 subjects. A statistically significant decrease in blood glucose was observed at visit 3 (-0.6 mmol/L; $p=0.021$; $n=82$). Significant reductions in total cholesterol (-1.45 mmol/L; $p=0.006$; $n=30$), LDL cholesterol (-1.32 mmol/L; $p=0.003$; $n=28$) and LDL/HDL ratio (-0.77 ; $p=0.011$; $n=13$) were seen at visit 2. No significant changes were reported in HDL cholesterol and triglycerides.

Safety

No serious adverse events occurred. The incidence of AEs before and during the course of the study is summarized in Table III. At study enrolment, AEs were recorded in 47 patients (9.2%); of these patients, 22 (47%) were categorised as

Table II. Glycaemic and lipidic profiles during treatment.

	Visit 1	Visit 2	Visit 3
Plasma glucose (mmol/L)	8.94 \pm 5.7	8.24 \pm 3.1	8.07 \pm 2.52*
Total cholesterol (mmol/L)	5.23 \pm 1.40	4.79 \pm 1.05**	4.45 \pm 0.86
HDL cholesterol (mmol/L)	1.19 \pm 0.30	1.21 \pm 0.35	1.21 \pm 0.38
LDL cholesterol (mmol/L)	3.04 \pm 1.24	2.60 \pm 0.96†	2.33 \pm 0.95
LDL/HDL cholesterol ratio	2.62 \pm 1.04	2.32 \pm 0.95*	2.13 \pm 1.09
Triglycerides (mmol/L)	2.20 \pm 1.24	2.11 \pm 0.87	2.17 \pm 0.95

Plasma glucose concentrations and lipid measurements before and during treatment (mean \pm SD). HDL = high density lipoprotein; LDL = low density lipoprotein; * P <0.05; ** P <0.01; † P <0.005 versus visit 1.

Table III. Adverse events .

	Visit 1	Visit 2	Visit 3
Adverse events (patients)	47 (9.2%)	15 (2.9%)	12 (2.4%)
Number of adverse events	53	15	12
Mild	20 (37.7%)	10 (66.6%)	10 (83.3%)
Moderate	9 (17.0%)	4 (25.0%)	2 (16.7%)
Severe	3 (5.7%)	1 (6.2%)	0
Severity not recorded	21 (39.6%)	0	0

Adverse events before and during treatment, divided for severity [n (%)].

intolerant patients at enrolment and therefore the AEs reported in this population were considered directly related to previous therapy.

The rate of treatment-emergent AEs was low. At visit 2, 15 patients reported a total of 15 AEs, of which 66.6% were considered mild; for 13 of these patients the complaint was of a new AE not present before the start of the study. At visit 3, 12 patients reported 12 AEs, 83.3% of which were mild; for 11 of these patients the complaint was of a new AE. Only one severe AE (fatigue) was reported during the treatment period and was classified as unlikely to be treatment-related.

Overall Patient Experience and Investigator Opinions of Nebivolol Treatment

The overall experience was rated as “good” or “very good” by 86.5% of evaluable patients (n=407), while investigators rated the experience as ‘good’ or ‘very good’ in 84.6% of patients. Patient and investigator opinions of nebivolol were highest in patients intolerant to previous therapy (93.2% and 95.5% reported a good to very good experience). Treatment compliance was rated by physicians as ‘good’ in 78.6% of all patients and ‘bad’ in only 3.3% (Figure 3).

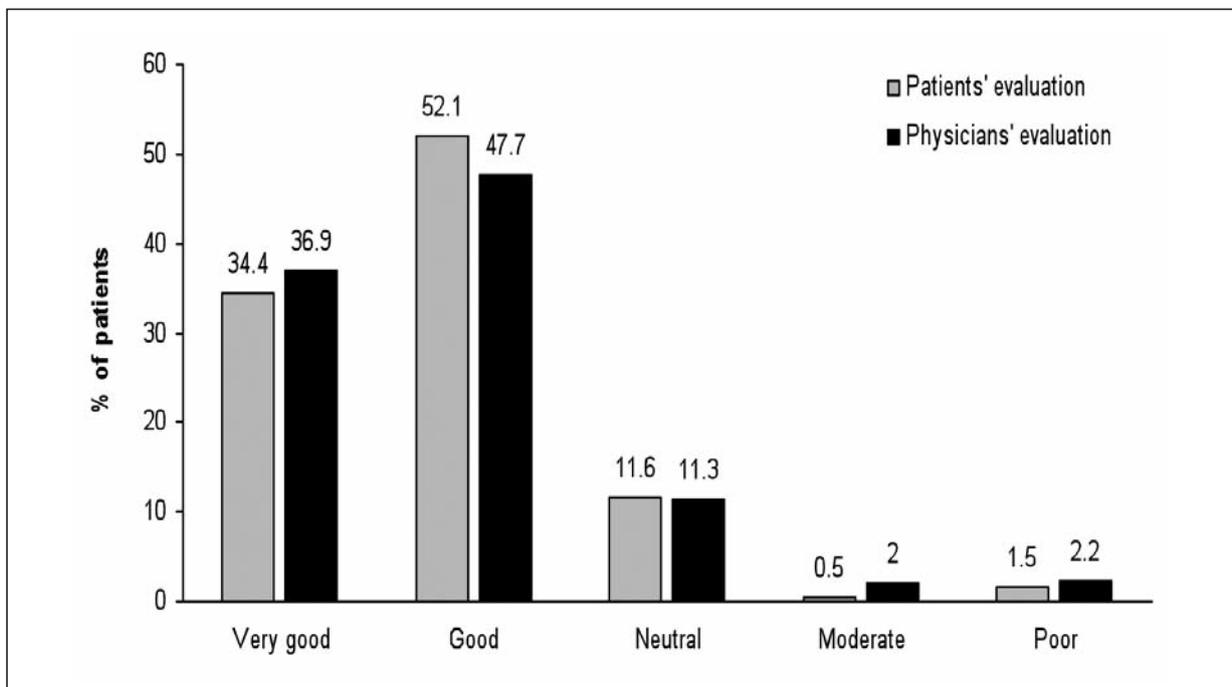


Figure 2. Overall patient experience with treatment and physician opinion of nebivolol treatment rated on a five-point scale. Grey bars: patients' evaluation; black bars: physicians' evaluation,

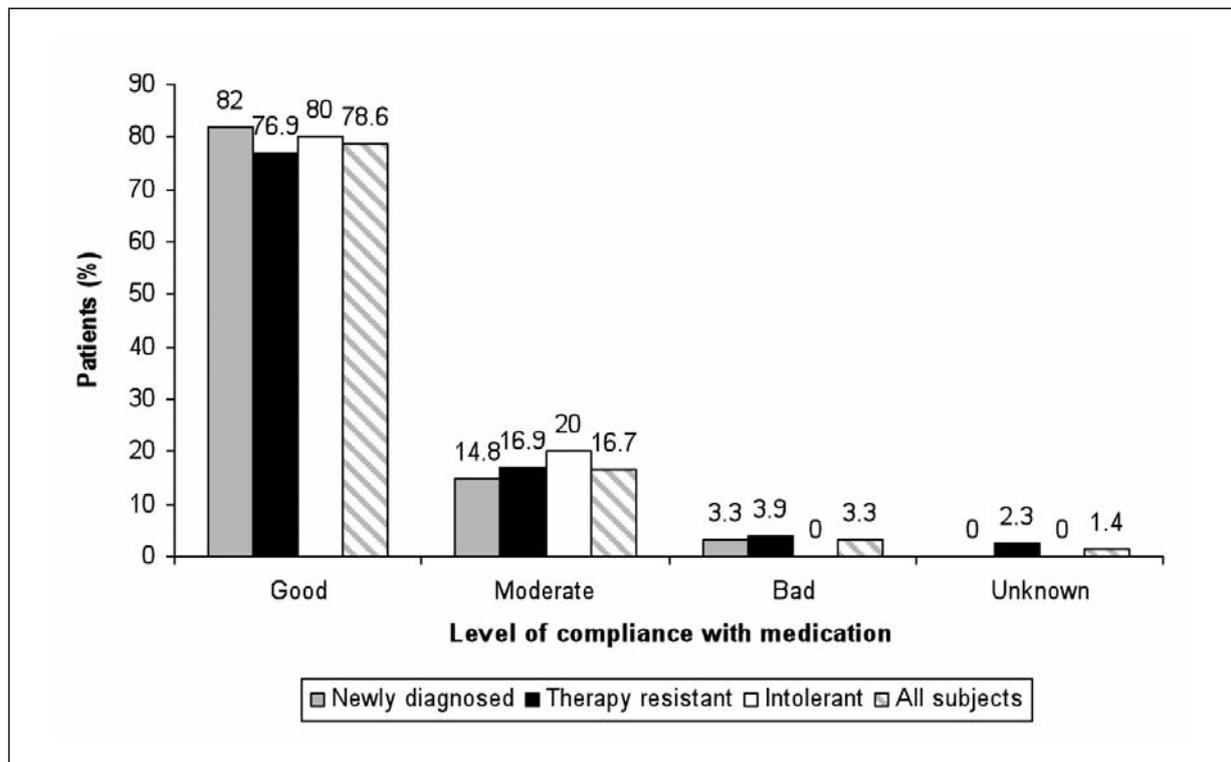


Figure 3. Compliance with medication at visit 3 as evaluated by the physician on a 3-point scale (good, moderate or bad). Results are divided for treatment reasons. Grey bars: newly diagnosed patients; black bars: therapy resistant patients; white bars: intolerant patients and hatched bars: all subjects.

Discussion

This was a multicentre, prospective observational study that aimed to evaluate the efficacy, safety and tolerability of nebivolol in hypertensive patients co-diagnosed with DM. Nebivolol treatment significantly lowered both SBP and DBP from baseline in hypertensive patients with concomitant DM. In particular, a significant decrease of $-21.2/-9.5$ mm Hg was seen in newly diagnosed patients, which suggests considerable protection against the cardiovascular risks associated with hypertension. Another post-marketing surveillance study involving nebivolol reported that the mean decreases in SBP were -14.9 and -21.1 mm Hg after 2 weeks and 3 months, respectively, and DBP decreased by -7.8 and -10.9 mm Hg, respectively²⁶.

Interestingly, a significant BP reduction observed in patients resistant to previous therapy suggests that nebivolol may be a suitable alternative in situations where previous antihypertensive therapy has failed to effectively manage elevated BP. Studies have shown that nebivolol treatment

is associated with BP reductions similar to those seen with lisinopril²⁹, amlodipine³⁰ and losartan³¹. A recent meta-analysis reported that nebivolol treatment produced antihypertensive response rates (percentage of patients achieving target BP levels or a defined DBP reduction) that were higher than those of ACE inhibitors (Odds Ratio [OR] = 1.92; $p=0.001$) and all antihypertensives combined (OR= 1.41; $p=0.001$), and were similar to those of β -blockers, CCBs, and losartan²¹. Likewise, a higher proportion of patients achieved BP targets with nebivolol compared with losartan (OR= 1.98; $p=0.004$), CCBs (OR =1.44; $p=0.024$) and all antihypertensives combined (OR= 1.35; $p=0.012$)²¹.

In the group of patients intolerant to previous therapy in the current study, intolerance was greatest among β -blockers (42.4%), with metoprolol (44.4%) and atenolol (30.6%) being the least well tolerated. Nebivolol was subsequently well tolerated, suggesting that nebivolol may be better tolerated than other β -blockers.

Despite the fact that all study patients were diagnosed with diabetes, antidiabetic therapy was

not always recorded. Although not always statistically significant, improvements in blood glucose concentration, total cholesterol and LDL cholesterol were reported during nebivolol treatment. In particular, a significant decrease in blood glucose was observed after 17 weeks of treatment, and LDL and total cholesterol were significantly reduced after 7 weeks of treatment. These findings support the results of previous studies, which have demonstrated that nebivolol does not have deleterious effects on metabolic parameters, including insulin sensitivity, in hypertensive patients with concomitant type 2 DM^{24-28,32}.

During nebivolol treatment, the incidence of AEs was relatively low. Following 7 weeks of nebivolol treatment, the incidence rate was 3.3% and, after 17 weeks, a rate of 3.0% was recorded. Schmidt et al reported a lower incidence rate of AEs (0.3%) with nebivolol treatment²⁶. Other studies have also reported a low incidence of AEs in patients treated with nebivolol.

The overall experience with nebivolol treatment was “good” to “very good” in 86.5% of patients according to the patients’ rating and in 84.5% of patients according to the physicians’ rating. The experience of the patient is important, since adherence to BP lowering therapy is notoriously low over the long term, with adverse events being a major cause of non-compliance^{33,34}. Therefore, a positive experience with a well tolerated therapy might well increase the compliance of the patient.

Even though physicians were asked to survey nebivolol treatment for 6 months, the average follow-up time was 4 months. The lack of adherence to scheduled assessment times (2 and 6 months) was probably due to the fact that follow-up visits took place according to daily practice and the interval between visits differed according to the physician’s practice since this was an observational study conducted in a real-life scenario.

Study Limitations

The present study was an observational study which is by definition only able to identify associations, and not causal relationships.

Although the number of patients enrolled is high, the results pertaining to the effects of nebivolol on metabolic profiles are limited to 82 subjects for glycaemic control and to 30 individuals for lipidic profile. As such, the tolerability results from this limited sample size may not be representative of the total study population.

Lipid lowering and hypoglycaemic therapies were slightly more recorded as discontinued than as added during the observation period. However, data on dose changes in these medications were not recorded as well we did not record the concentration of glycated haemoglobin, which may further clarify the metabolic profile of nebivolol in diabetic patients. Moreover, we did not collect data on lifestyle modifications (diet, physical exercise, etc.). Therefore, we cannot exclude that the observed effects of nebivolol on lipidic and glycaemic profiles could have been affected by such changes.

Finally, as we did not record data on the difference between “prescribed” and “assumed” daily dose of nebivolol (e.g. by applying the method of “pill count”), we based the assessment of patients compliance only on a semi-quantitative analysis. Although the accuracy of information on patient compliance from self-reporting data is limited, it remains a frequently-used method for the estimation of patients’ compliance³⁵.

Conclusion

In a real-life setting, nebivolol was associated with a significant reduction in BP in hypertensive patients with concomitant DM, including patients intolerant of previous therapy and in those for whom previous antihypertensive therapy had failed. Nebivolol was most effective as first-line therapy in diabetic patients with newly diagnosed hypertension, who represented approximately 20% of the study population. Nebivolol treatment was also associated with significant improvements in blood glucose and LDL cholesterol levels supporting its lack of deleterious effects on metabolic parameters in patients with concomitant DM. Nebivolol was well tolerated, with the majority of patients rating their overall experience as good to very good, which is likely to result in improved adherence with therapy. Thus, this third-generation β -blocker appears suitable in routine clinical practice for hypertensive patients with concomitant DM.

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