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ORIGINAL RESEARCH

Efficacy and Tolerability of Fixed-Dose Combination of Perindopril/Indapamide in Type 2 Diabetes Mellitus: PICASSO Trial

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ABSTRACT

Background: Hypertension and type 2 diabetes mellitus (T2DM) synergistically deteriorate the vascular environment, making blood pressure reduction challenging, and substantially increasing cardiovascular risk.

Methods: In the real-life, open-label, observational, PICASSO study, 9,257 hypertensive patients unsuccessfully treated with antihypertensives were switched to fixed-dose combination of perindopril 10 mg/indapamide 2.5 mg. In this subgroup analysis, we analyzed changes in blood pressure and laboratory parameters of 2,762 hypertensive patients with T2DM or pre-diabetes.

Results: After 3 months of treatment, significant decreases in office blood pressure were noted in the whole cohort ($-27.0 \pm 14.8/-12.7 \pm 9.8$ mmHg; $p < 0.001$). Significant decreases were also recorded in patients with grade 1 hypertension ($19.2 \pm 10.0/-9.4 \pm 7.9$ mmHg), grade 2 ($29.2 \pm 10.9/-13.3 \pm 8.7$ mmHg) and grade 3 ($-45.1 \pm 15.4/-21.5 \pm 11.2$ mmHg). Significant decreases in ambulatory blood pressure were also noted ($n = 93$). In patients previously treated with angiotensin-converting enzyme inhibitor ± hydrochlorothiazide or angiotensin receptor blocker ± hydrochlorothiazide, mean 24-h blood pressure decreased by $23.4 \pm 13.9/11.5 \pm 9.7$ and $22.3 \pm 8.7/10.4 \pm 13.2$ mmHg, respectively ($p < 0.001$). Treatment was well tolerated and the switch to treatment with perindopril/indapamide was associated with improvements in laboratory parameters.

Conclusions: Data from this diabetes subgroup analysis suggest that fixed combination of perindopril 10 mg/indapamide 2.5 mg should be routinely considered for the treatment of hypertension in diabetic patients who are unsuccessfully managed with other antihypertensive medications.

On behalf of the PICASSO investigators.

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Keywords: Ambulatory blood pressure monitoring; Combination treatment; Hypertension; Indapamide; Perindopril; Type 2 diabetes mellitus

INTRODUCTION

Recent epidemiologic data underscore the ongoing difficulties associated with reducing blood pressure in diabetic hypertensive patients [1, 2]. Analysis of the International Survey Evaluating Microalbuminuria Routinely by Cardiologists in Patients with Hypertension (I-SEARCH) survey, for example, showed that blood pressure control rates in diabetic patients were very low with only 19% of men and 16% of women reaching control, even though 93.5% of patients in the whole cohort were being treated and most diabetic patients were taking between two and three drugs [2]. These data suggest that the problem with blood pressure control in diabetic patients is no longer lack of treatment and that our focus needs to turn toward improving treatment strategies.

For hypertensive patients with type 2 diabetes mellitus (T2DM), recent European guidelines [European Society of Hypertension (ESH)/European Society of Cardiology (ESC) 2013] recommend that combination treatments, preferably fixed-dose combinations, be considered and that treatments include renin–angiotensin–aldosterone system (RAS) inhibitors to protect the diabetic kidney from nephropathy [3]. In line with guidelines, combination treatment with perindopril/indapamide is well suited for the treatment of diabetic patients: perindopril is a long-acting angiotensin-converting enzyme (ACE) inhibitor that has been proven to be nephroprotective [4] and indapamide is a metabolically neutral diuretic with mild natriuretic effects [5]. Treatment with perindopril/indapamide is also supported by extensive data from clinical trials [4, 6–11] and in particular this combination has been shown to reduce mortality and vascular events in patients with T2DM [12].

As roughly 30% of hypertensive patients have diabetes mellitus and 40% of newly diagnosed diabetic patients are hypertensive, the challenges associated with treating hypertension in diabetic patients are encountered regularly in general practice [2, 13]. The Perindopril Plus Indapamide Combination Blood Pressure Reduction (PICASSO) trial (No. of the Ethics Committee Approval: ETT-TUKEB-NIT 8-348/2009-1018EKU-866/PI/09) was designed to provide data that are directly relevant to everyday medical practice. It is an open-label, observational trial that included 9,257 patients with uncontrolled hypertension despite treatment. The trail evaluated blood pressure after patients were switched to treatment with fixed-dose perindopril 10 mg/indapamide 2.5 mg for 3 months [14]. In this subgroup analysis of the PICASSO trial, the blood pressure data in patients with T2DM or pre-diabetes were analyzed to determine if perindopril 10 mg/indapamide 2.5 mg should be considered regularly for the treatment of hypertension in diabetic patients.

MATERIALS AND METHODS

A retrospective analysis of the data from the PICASSO trial was performed on the subgroup of 2,762 patients with T2DM or pre-diabetes. Other risk factors, such as age, dyslipidemia, obesity, family history of early cardiovascular diseases and smoking, were also recorded. Patients with T2DM were defined as those

meeting the criteria of the European guidelines (fasting plasma glucose >7.0 mmol/L or 2-h plasma glucose test >11.1 mmol/L) [15]. Patients with pre-diabetes were defined as those with impaired fasting glucose (fasting plasma glucose of 6.1–6.9 mmol/L and a 2-h plasma glucose <7.8 mmol/L) or impaired glucose tolerance (fasting plasma glucose <7.0 mmol/L but a 2-h plasma glucose >7.8 and < 11.1 mmol/L). Materials, methods, and results of PICASSO have been described elsewhere [14]. Briefly, the PICASSO study was a 3-month, open-label, observational, study which was conducted between January 27 and August 31, 2010. The study comprised of 9,257 outpatients who had uncontrolled hypertension; blood pressure values above target levels defined by the physician (71.0%), variability in blood pressure measurements (22.6%), and poor treatment tolerability (6.4%), despite ongoing antihypertensive treatment; who had fluctuating blood pressure; or who were experiencing side effects with previous treatment, were given a fixed-dose combination of perindopril 10 mg/indapamide 2.5 mg (Coverex AS® Komb Forte, EGIS Pharmaceuticals Plc, Budapest, Hungary) for 3 months [16]. Grades of hypertension were defined according to recent 2013 ESH/ESC Guidelines [3]. To mimic real-life practice, patients were only included if treatment with perindopril/indapamide was in line with previously established therapeutic plans; therefore, exclusion criteria were not defined. Additional antihypertensive treatments (alpha-1-antagonist, beta-blocker, calcium channel blocker, centrally acting agent) could be maintained or added at the physician's discretion.

Office blood pressure and heart rate were measured at baseline, 1 month, and 3 months using validated oscillometric manometers. Blood pressure control rates for diabetic patients were defined according to the 2013 ESH/ESC guidelines as an office systolic blood pressure (SBP)/diastolic blood pressure (DBP) <140/85 mmHg [17]. Blood pressure control rates for patients with pre-diabetes were defined as office SBP/DBP <140/90 mmHg.

Baseline office blood pressure values of patients previously treated with ACE inhibitor ± hydrochlorothiazide (HCTZ) ($n = 1{,}778$), angiotensin receptor blocker (ARB) ± HCTZ ($n = 240$), enalapril + HCTZ ($n = 203$) or ramipril + HCTZ ($n = 31$) were compared to those values obtained during perindopril/indapamide treatment.

Ambulatory blood pressure monitoring (ABPM) was performed using a validated device (MEDITECH ABPM, Budapest, Hungary) in a subset of 93 patients. These patients were selected based on the presence of additional comorbidities, which prompted physicians to compare results with office blood pressure. The results of blood pressure and heart rate (HR) for 24 h, daytime (0600–2200 hours) and nighttime (2200–0600 hours) were recorded at baseline, 1 month, and 3 months. In this subset, baseline ambulatory blood pressure values of patients previously treated with ACE inhibitor ± HCTZ ($n = 67$), ARB ± HCTZ ($n = 10$) or enalapril + HCTZ ($n = 8$) were compared to those values obtained during perindopril/indapamide treatment.

Laboratory parameters [fasting plasma glucose, serum total cholesterol, high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), triglycerides, potassium, creatinine, and uric acid] were measured by routine laboratory methods at baseline and 3 months when deemed necessary by the treating physician.

Tolerability and safety of treatment with perindopril/indapamide were assessed by recording the number of patient complaints and possible side effects of drugs at all visits.

All patients had been given written information on this trial and gave informed consent. The study was approved by the Central Ethics Committee of Medical Research Council (TUKEB of ETT) of Hungary.

The analysis in this article is based on previously conducted studies, and does not involve any new studies of human or animal subjects performed by any of the authors.

Statistics

Descriptive statistics were used to summarize data. Between-group comparisons were performed using one-sample *t* tests and Chi-squared tests to compare baseline to treatment data. Baseline characteristics were summarized as mean ± standard deviations (SD) for continuous variables and numbers of patients and percentages for categorical variables, and analyses were performed on an intention-to-treat basis. Mean changes in office blood pressure were analyzed according to the grade of hypertension and pre-existing antihypertensive treatment (ACE inhibitor + HCTZ, ARB + HCTZ). A paired *t* test was used to assess whether changes in office- or ABPM-assessed SBP and DBP from baseline to 3 months were significant. The level of two-sided significance was set at 5% ($\alpha = 0.05$). Data were collected and analyzed in accordance with the European Guidelines for Good Clinical Practice/ICH guidelines. Clinical and laboratory data were analyzed by an independent statistical institute (Planimeter Kft.; Budapest).

RESULTS

Of the 9,257 patients included in the PICASSO final analysis population, 2,762 patients had type 2 diabetes mellitus ($n = 1,887$) or pre-diabetes ($n = 875$).

Mean age was 63.9 ± 10.6 years and 55.2% of patients were female (Table 1). Waist circumference was 106.2 ± 13.4 cm in males and 101.9 ± 13.8 cm in females. Dyslipidemia was recorded in 65.5% of patients, obesity [body mass index (BMI) >30 kg/m^2] in 64.9% of patients, left ventricular hypertrophy in 37.5% of patients, and microalbuminuria in 13.5% of patients (Table 1).

Mean duration of hypertension was 12.2 ± 7.7 years. Ninety-six percent of patients were being treated for hypertension at baseline. Baseline SBP/DBP was 159.3 ± 14.7/92.8 ± 9.7 mmHg and baseline heart rate was 79.5 ± 9.9 beats per minute (BPM). The distribution of patients according to baseline severity was high-normal blood pressure (3.0%; $n = 83$), grade 1 hypertension (34.7%; $n = 959$), grade 2 hypertension (48.9%; $n = 1,350$), and grade 3 hypertension (13.4%; $n = 370$). No patients were at blood pressure target at enrollment.

At baseline, 33.3% of patients were taking a diuretic: 28.7% were taking a diuretic other than indapamide and 4.6% were taking indapamide. With treatment with perindopril/indapamide, the percentage of patients taking other antihypertensive therapies decreased from 63.0% to 62.5% for beta-blockers, 28.7% to 1.2% for diuretics other than indapamide, 48.7% to 40.1% for calcium channel blockers, 8.7% to 1.0% for ARB ± HCTZ, and increased from 7.2% to 9.6% for other antihypertensive medications due to a 2.3% increase in rilmenidine. When HCTZ use

Table 1 Baseline characteristics in the enrolled population: diabetes subgroup analysis of the PICASSO trial ($n = 2,762$)

	$n = 2,762$
Demographics	
Female, %	55.2
Age (years), mean ± SD	63.9 ± 10.6
Abdominal circumference in males (cm), mean ± SD	106.2 ± 13.4
Abdominal circumference in females (cm), mean ± SD	101.9 ± 13.8
Risk factors, *n* (%)	
Age (>55 years for males; >65 years for females)	1,776 (64.3)
Dyslipidemia	1,808 (65.5)
Obesity	1,793 (64.9)
Family history of early hypertension[a]	1,114 (40.3)
Smoking	655 (23.7)
Associated disorders, *n* (%)	
Coronary heart disease	1,022 (37.0)
Cerebrovascular event	410 (14.8)
Peripheral artery disease	362 (13.1)
Heart failure	274 (9.9)
Renal disease	204 (7.4)
Subclinical organ damage, *n* (%)	
Left ventricular hypertrophy[b]	1,036 (37.5)
Atherosclerosis	935 (33.9)
Microalbuminuria[c]	372 (13.5)
Elevated serum creatinine level[d]	235 (8.5)
Grade of hypertension[e]	
High–normal	83 (3.0)
Grade 1	959 (34.7)
Grade 2	1,350 (48.9)
Grade 3	370 (13.4)
Previous antihypertensive therapy, *n* (%)	
ACE inhibitor ± diuretic	1,778 (64.4)
Beta-blocker	1,739 (63.0)
Calcium channel blocker	1,345 (48.7)
Diuretic	919 (33.3)
Angiotensin receptor blocker ± HCTZ	240 (8.7)
Other	199 (7.2)

HCTZ hydrochlorothiazide, *SD* standard deviation

[a] Males <55 years, females <65 years

[b] Left ventricular hypertrophy confirmed by electrocardiogram or electrocardiography

[c] Urinary albumin excretion of 30–300 mg/day

[d] 115–133 μmol/L in males and 107–124 μmol/L in females

[e] Grade of hypertension was defined according to the 2007 European Society of Hypertension/European Society of Cardiology guidelines [29]

was considered in monotherapy and in combination, the percent HCTZ use decreased from 20.3% to 0.9%.

Blood Pressure After 3 Months of Treatment with Perindopril/Indapamide

Mean office SBP/DBP decreased over time to 139.6 ± 11.8/83.6 ± 7.6 mmHg after 1 month and to 132.3 ± 9.7/80.1 ± 6.4 mmHg after 3 months (Fig. 1a). Changes from baseline to 3 months were statistically significant (−27.0 ± 14.8/−12.7 ± 9.8 mmHg; $p < 0.001$). After 3 months of treatment, blood pressure control was reached in 61% of patients.

Decreases in SBP and DBP were statistically significant regardless of the grade of hypertension at baseline ($p < 0.01$). Between baseline and 3 months, blood pressure decreased by −4.2 ± 10.1/−2.2 ± 7.3 mmHg in patients with high-normal blood pressure, −19.2 ± 10.0/−9.4 ± 7.9 mmHg in patients with grade 1 hypertension, −29.2 ± 10.9/

−13.3 ± 8.7 mmHg in patients with grade 2 hypertension, and −45.1 ± 15.4/−21.5 ± 11.2 mmHg in patients with grade 3 hypertension.

Office blood pressure decreased significantly in patients previously treated by a RAS inhibitor ± HCTZ ($n = 1{,}991$), from 159.5 ± 14.7/92.5 ± 9.7 to 132.3 ± 9.8/80.0 ± 6.3 mmHg ($p < 0.001$). The decrease in office blood pressure was similar for patients previously on ACE inhibitors ± HCTZ or on ARB ± HCTZ (both $p < 0.001$) (Fig. 1b).

Ninety-three patients underwent ambulatory blood pressure monitoring. In this subgroup, a

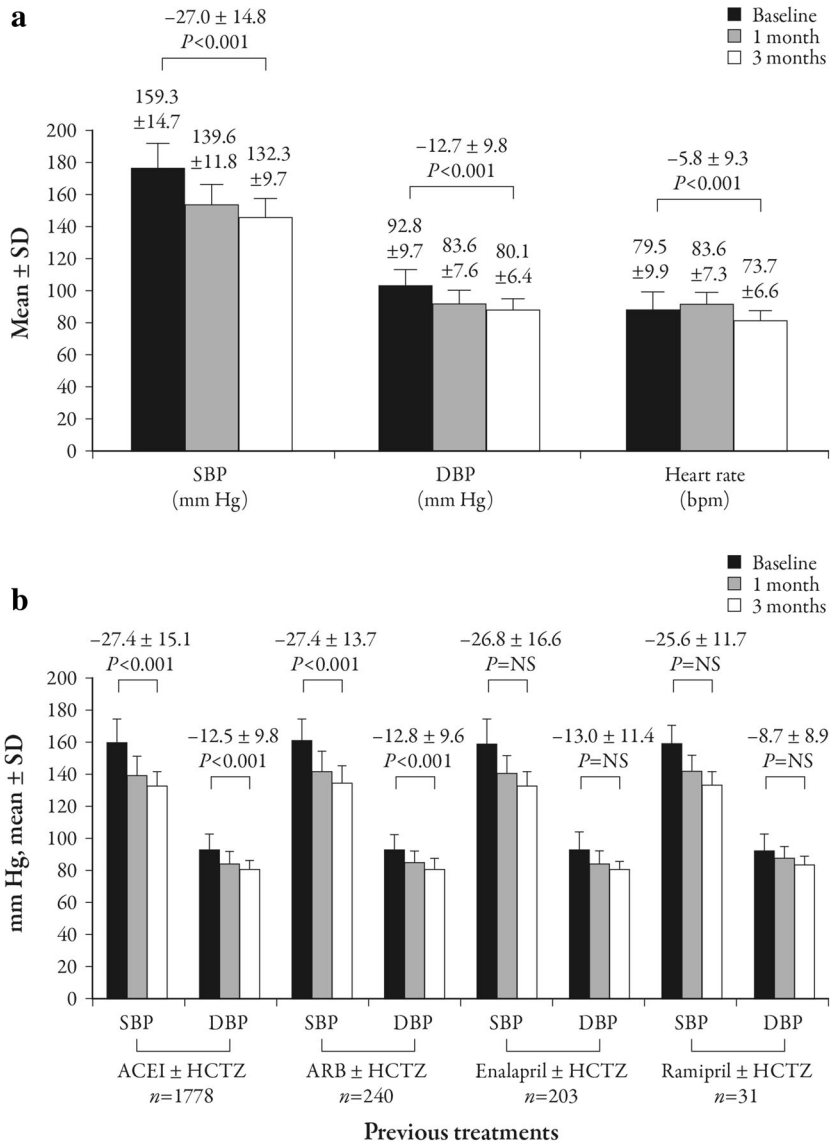


Fig. 1 **a** Change in office blood pressure ($n = 2{,}762$) after 3 months of treatment with fixed-dose combination of perindopril 10 mg/indapamide 2.5 mg: diabetes subgroup analysis of the PICASSO trial. **b** Office blood pressure according to previous treatment. *ACEI* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *DBP* diastolic blood pressure, *HCTZ* hydrochlorothiazide, *NS* not significant, *SBP* systolic blood pressure, *SD* standard deviation

higher percentage of comorbidities was recorded as compared to that of the main cohort (data not shown). Mean SBP/DBP in this cohort decreased from 159.9 ± 16.2/95.7 ± 9.5 to 130.4 ± 9.8/80.3 ± 6.2 mmHg after 3 months. Changes from baseline to 3 months were statistically significant (−29.5 ± 17.6/−15.4 ± 9.5 mmHg; $p < 0.001$; Fig. 2a, b). Mean daytime, nighttime, and 24-h blood pressure as well as mean 24-h pulse pressure, mean arterial pressure, and mean 24-h heart rate decreased significantly over the course of the 3 months of treatment ($p < 0.001$; Fig. 2a, b). In patients previously treated with ACE inhibitor ± HCTZ ($n = 67$) or ARB ± HCTZ ($n = 10$), mean 24-h blood pressure decreased by 23.4 ± 13.9/11.5 ± 9.7 and 22.3 ± 8.7/10.4 ± 13.2 mmHg, respectively ($p < 0.001$) (Fig. 2c).

Tolerability and Safety after 3 Months of Treatment with Perindopril/Indapamide

Treatment was well tolerated. Thirty-six drug-related adverse events occurred. Ankle edema occurred in 11 patients (0.4% of patients) and was reported most frequently, followed by dizziness ($n = 7$; 0.3% of patients), and cough ($n = 6$; 0.2% of patients). Seven serious adverse events occurred, none of which was treatment related: death of unspecified cause ($n = 2$), transient ischemic attack ($n = 2$), aorta stenosis diagnosed during study ($n = 1$), and worsening congestive heart failure ($n = 2$).

Between baseline and 3 months, mean changes in laboratory parameters were significant for total cholesterol (−0.7 ± 0.9 mmol/L), LDL-C (−0.4 ± 0.7 mmol/L), triglycerides (−0.4 ± 1.3 mmol/L), serum uric acid (−18.2 ± 62.9 μmol/L), fasting blood glucose (−0.6 ± 1.0 mmol/L), and serum creatinine by (−3.9 ± 14.1 μmol/L) (for all $p < 0.001$, uric acid $p = 0.004$, serum creatinine $p = 0.04$; Fig. 3). Changes were not significant for serum potassium (−0.04 ± 0.4 mmol/L), and HDL-C (+0.05 ± 0.3 mmol/L). These results were obtained against a background of stable concomitant treatment, including statins, aspirin, and antidiabetics (Table 2).

DISCUSSION

The PICASSO study was designed to provide physicians with data that are directly relevant to daily medical practice and to the challenges associated with treating hypertension. In this T2DM subgroup analysis, we analyzed blood pressure data in patients with T2DM or pre-diabetes to determine if perindopril 10 mg/indapamide 2.5 mg may offer an efficacious and well-tolerated alternative to previous unsuccessful antihypertensive treatments. Overall, these patients constitute a difficult-to-treat cohort in which 65% of patients were obese and 62% of patients had grade 2 or 3 hypertension despite ongoing treatment. Significant decreases in office blood pressure and ambulatory blood pressure were noted after 3 months of treatment and 69% of patients reached blood pressure control. As in the full PICASSO trial, treatment was well tolerated and was associated with improvements in laboratory parameters.

In this study, significant decreases in office blood pressure occurred regardless of baseline blood pressure: −19.2/9.4 mmHg in patients with grade 1 hypertension and −45.1/21.5 mmHg in patients with grade 3 hypertension. As decreases in SBP of 10 mmHg are associated with reductions in risk of diabetes-related complications (−12%), diabetes-related deaths (−15%), and myocardial infarction (−11%) [18], these data

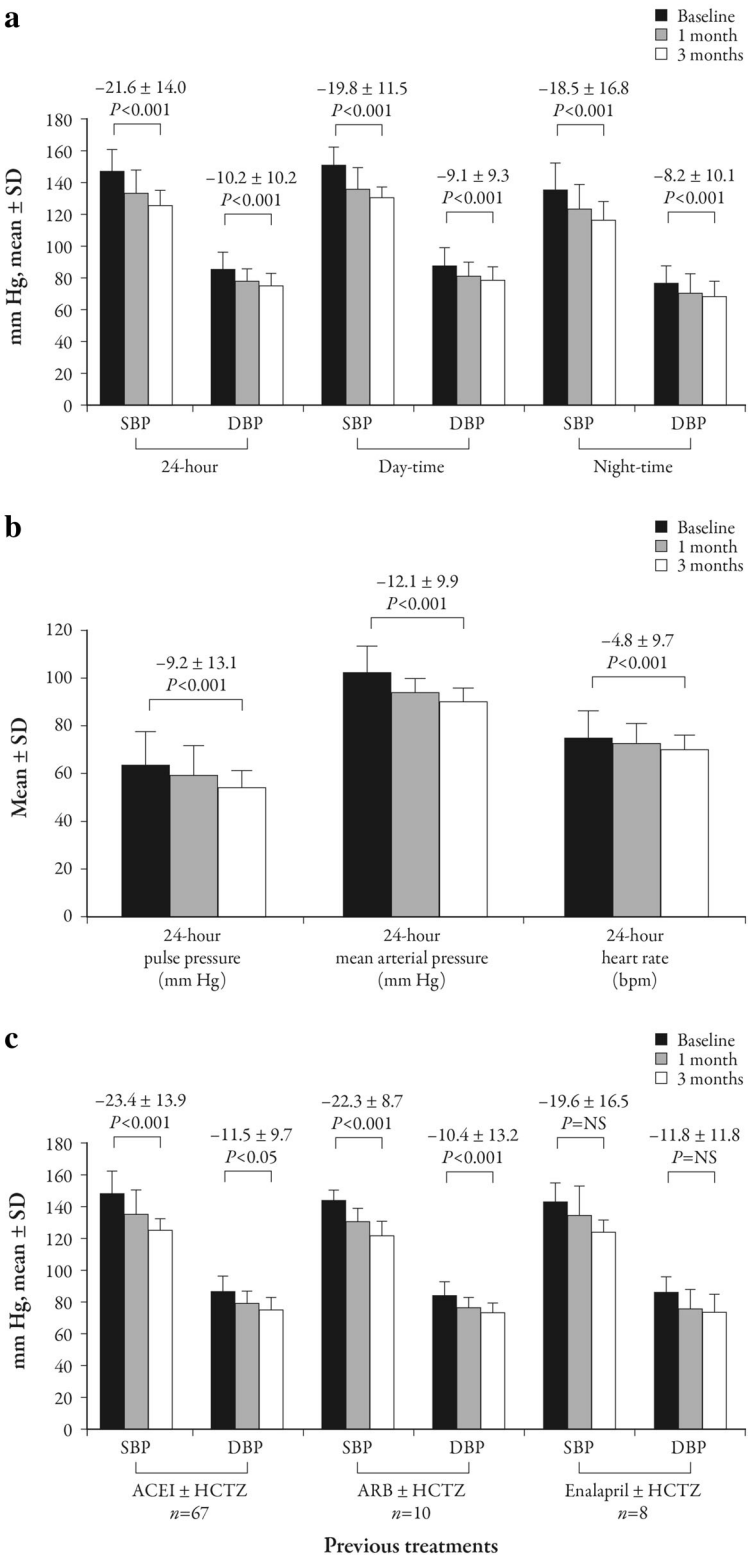
suggest that treatment with perindopril/indapamide would have a clinically meaningful long-term impact.

Ambulatory SBP and pulse pressure are independent predictors of cardiovascular risk [19, 20] and blood pressure variability over the course of a day has significant impact on target organ damage and cardiovascular risk in hypertensive patients [21, 22]. The combination of perindopril/indapamide has been shown to smooth the blood pressure curve and indapamide in monotherapy has previously been shown to reduce 24-h SBP variability [7, 23]. In this study, significant reductions in 24-h blood pressure, daytime blood pressure, nighttime blood pressure, 24-h pulse pressure, and 24-h mean arterial pressure occurred after 3 months of treatment with perindopril/indapamide. A longer-term study in a real-life setting would be needed to determine the effects on organ damage and cardiovascular risk.

For diabetic patients, treatment with ACE inhibitors is recommended due to their proven cardioprotective and nephroprotective effects. This recommendation was recently confirmed once again in a meta-analysis [24]. Combination with diuretics may help counterbalance the salt-retaining effects of diabetes and inhibit compensatory feedback loops. Within these therapeutic classes, careful choice of antihypertensive treatment is essential as drugs have different efficacy and tolerability profiles due to differences in molecular structure, pharmacokinetics, and pharmacodynamics. The British Society of Hypertension, for example, has recently highlighted the fact that diuretics differ greatly among themselves by recommending that indapamide or chlorthalidone be prescribed rather than HCTZ, which is associated with significantly poorer outcomes and an increased risk of mortality [25]. Furthermore, decreases in blood pressure presented herein support treatment with combination of perindopril/indapamide and the recommendation for combination therapy.

Fig. 2 **a**, **b** Change in ambulatory blood pressure ($n = 93$) after 3 months of treatment with fixed-dose combination of perindopril 10 mg/indapamide 2.5 mg: diabetes subgroup analysis of the PICASSO trial. **c** Ambulatory blood pressure according to previous treatment. *ACEI* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *DBP* diastolic blood pressure, *HCTZ* hydrochlorothiazide, *NS* not significant, *SBP* systolic blood pressure, *SD* standard deviation

Thiazide diuretics, due to their unwanted effects on carbohydrate, lipid uric acid, and electrolyte metabolism, are no longer the preferred choice for treatment of hypertensive patients with T2DM or pre-diabetes [25, 26]. Indapamide, however, is a thiazide-like sulfonamide and has been shown to be metabolically neutral in a wide range of patients including diabetic ones [11, 27, 28]. In this study, metabolic neutrality of indapamide is reflected in the improvement of total cholesterol, fasting glucose, and triglyceride levels that were obtained without any changes of other concomitant treatment with lipid lowering agents, or with antidiabetics. This is likely to be due to a decrease in dysmetabolic effects after discontinuation of treatments such as HCTZ or beta-blockers, e.g., atenolol. The lack of effect of treatment on serum potassium levels may reflect the fact that perindopril and indapamide have opposing action on potassium metabolism: ACE inhibitors may increase while thiazides-type diuretics decrease the plasma level of potassium by opposing action on renal excretion.


a
Baseline
1 month
3 months
−21.6 ± 14.0
P<0.001
−10.2 ± 10.2
P<0.001
−19.8 ± 11.5
P<0.001
−9.1 ± 9.3
P<0.001
−18.5 ± 16.8
P<0.001
−8.2 ± 10.1
P<0.001
mm Hg, mean ± SD
SBP
DBP
24-hour
Day-time
Night-time
b
Baseline
1 month
3 months
−9.2 ± 13.1
P<0.001
−12.1 ± 9.9
P<0.001
−4.8 ± 9.7
P<0.001
Mean ± SD
24-hour pulse pressure (mm Hg)
24-hour mean arterial pressure (mm Hg)
24-hour heart rate (bpm)
c
Baseline
1 month
3 months
−23.4 ± 13.9
P<0.001
−11.5 ± 9.7
P<0.05
−22.3 ± 8.7
P<0.001
−10.4 ± 13.2
P<0.001
−19.6 ± 16.5
P=NS
−11.8 ± 11.8
P=NS
mm Hg, mean ± SD
ACEI ± HCTZ
n=67
ARB ± HCTZ
n=10
Enalapril ± HCTZ
n=8
Previous treatments

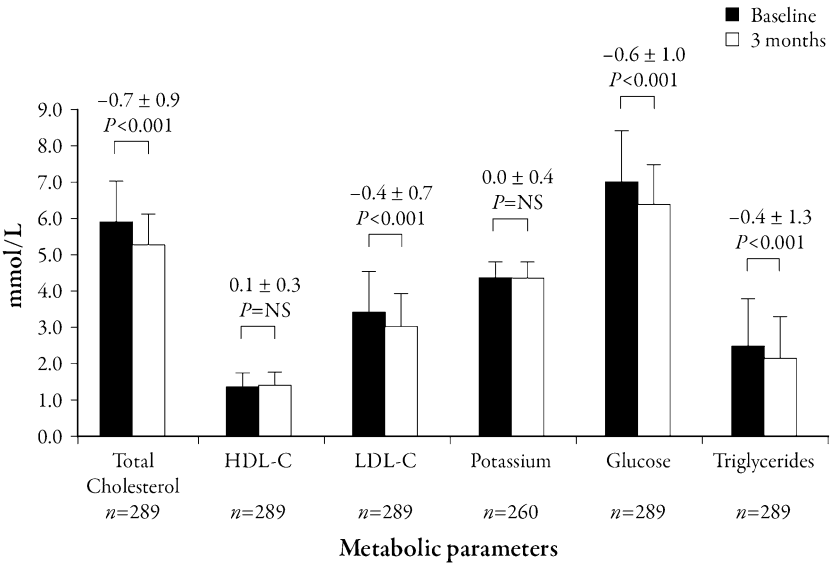


Fig. 3 Change in metabolic parameters that are most frequently affected by some antihypertensive drugs, after 3 months of treatment with fixed-dose combination of perindopril 10 mg/indapamide 2.5 mg: diabetes subgroup analysis of the PICASSO trial. Metabolic markers were measured at the physician's discretion. Means ± standard deviation are presented. *HDL-C* high-density lipoprotein-cholesterol, *LDL-C* low-density lipoprotein-cholesterol, *NS* not significant

Table 2 Concomitant treatments: diabetes subgroup analysis of the PICASSO trial ($n = 2{,}762$)

Co-prescriptions, *n* (%)	Baseline (%)	3 Months (%)
Statin	2,049 (74.2)	2,029 (73.5)
Acetylsalicylic acid	1,643 (59.5)	1,606 (58.1)
Oral antidiabetic	1,541 (55.8)	1,490 (53.9)
Insulin	366 (13.3)	343 (12.4)
Clopidogrel	214 (7.7)	210 (7.6)
Fibrate	182 (6.6)	180 (6.5)
Other	544 (19.7)	477 (17.3)

Study Limitations

The overall decrease in blood pressure observed in this trial was similar to the one observed in the whole cohort (−27/−13 mmHg) [14]. The blood pressure reduction data noted herein needs to be considered in the context of real-life everyday practice rather than that of randomized controlled studies, and need to be interpreted with the knowledge that the data most likely include some degree of placebo effect. To reflect real-life practice, specific criteria were not predefined for enrollment in the ambulatory blood pressure monitoring substudy, and as a result, the patients had, on average, more comorbidities than those in the whole cohort. These data should not be extrapolated to the whole cohort. Among limitations it has to be mentioned that no data were obtained for the duration of T2DM.

CONCLUSIONS

The PICASSO study was designed to provide physicians with data that are directly relevant to daily medical practice and to the challenges associated with treating hypertension. The data from this T2DM subgroup analysis of the main data of PICASSO study suggest that perindopril

10 mg/indapamide 2.5 mg may offer an efficacious and well-tolerated alternative to previous unsuccessful antihypertensive treatments.

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Conflict of interest. Professor Farsang discloses industry relationships (consultancy) in the last years with EGIS, Sandoz/Novartis, Sanofi-Aventis, Servier International and Richter G. In addition to Professor Farsang (principal investigator), the PICASSO investigator group included Bela Malomvolgyi, MD (medical advisor) and Norbert Habony, MD (coordinator).

Compliance with ethics guidelines. The analysis in this article is based on previously conducted studies, and does not involve any new studies of human or animal subjects performed by any of the authors.

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