

Efficacy and Safety of the Imidapril (IM) in Elderly Patients with high Cardiovascular Risk

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Summary. The antihypertensive efficacy and the safety of the novel ACE-I IM in elderly hypertensives suffering from ischemic stroke with or without diabetes mellitus (DM) or other cardiovascular risk factors was studied. Furthermore, the potential benefit of IM on proteinuria of the subgroup of diabetic patients was examined. IM was proved to be an effective antihypertensive drug in monotherapy, as well as in various combinations. A marked reduction in the microproteinuria was observed in patients with DM, suggesting a beneficial effect in this subgroup. Finally, IM was well tolerated by the elderly vascular patients of the study.

INTRODUCTION

ACE-inhibitors remain drugs of first choice in patients at high risk for cardiovascular disease or/and proteinuria. The latter is a strong marker not only of the effect of arterial hypertension on the kidney as target organ, but also an independent cardiovascular risk factor (1-6). The IM is a new ACE-I with many advantages, such as the high efficacy and the low percentage of adverse effects (especially dry cough) (7,8).

METHODS

We studied 35 patients, mean age 74.1 ± 11 years (24 females and 11 males). 26 patients had a history of DM type 2 (6 under insulin treatment). Table 1 shows the percentage of patients with DM and additional cardiovascular risk factors. Microproteinuria (30-300 mg/24h) was detected in 9 patients presenting DM. 30 patients were already under antihypertensive treatment. After monitoring and recording of the systolic and diastolic blood pressure (BP), IM was administrated in BP > 140/90 either as monotherapy (as initial

therapy in 5 patients or replacing the previous treatment in 5 patients: 2 under b-blocker, 1 under Ca^{++} antagonist and 2 under diuretic), or in combination with other drugs already administrated (25 patients: 14 following a double, 5 following a triple and 6 following a quadruple combination). The efficacy, safety and the benefit of IM in proteinuria, were evaluated in 7 days and in 2 months after the beginning of treatment.

RESULTS

- A) The mean BP was reduced, from $158 \pm 14.5/78.7 \pm 9.6$ at baseline, to $140.5 \pm 14.3/76.7 \pm 9.5$ at day 7 and to $134.1 \pm 7.1/76.2 \pm 12$ at day 60.
- B) The reduction in the BP was achieved by IM as monotherapy in 10 patients and in combined therapy in 25 patients. In double combination the IM was co-administrated with a Ca^{++} -antagonist in 8 patients, with a diuretic in 3 and with a b-blocker in 3 patients. In triple combination, it was administrated with a Ca^{++} -antagonist in 3 patients, with a diuretic in 4 and with a b-blocker in 3. Finally, as part of a quadruple combination, it was given in 6 patients with a Ca^{++} -antagonist, a diuretic and a b-blocker.
- C) Reduction of the microproteinuria was observed in all 9 diabetic patients, showing a fluctuation of the mean microproteinuria levels within a range of 259.4 ± 40 at baseline, to 229.4 ± 63.7 at day 7 and to 189.6 ± 60.7 at day 60. Among these patients, 2 were under IM as monotherapy, 2 with a Ca^{++} -antagonist, 2 as part of a triple regimen with a Ca^{++} -antagonist and a diuretic, and 3 patients were in a quadruple combination with a diuretic, a Ca^{++} -antagonist and b-blocker.

D) No adverse effects (cough, orthostatic symptoms or other) during treatment were detected.

E) No deterioration of the renal function, at the end of the two-month therapy, was observed (Table 2).

Table 1
Additional cardiovascular risk factors in the studied patients (elderly hypertensives with a history of ischemic stroke)

Cardiovascular risk factors	Percentage (%) (N=35)
Obesity	54.29 (n=17)
DM	74.29 (n=26)
Dyslipidemia	34.29 (n=12)
Coronary disease	42.86 (n=15)
Smoking	48.57 (n=17)
Heart Failure	22.86 (n=8)
Atrial Fibrillation	31.43 (n=11)
Proteinuria	25.71 (n=9)
Peripheral vascular disease	14.29 (n=5)

Table 2
Patients with abnormal values of renal function

Time	Patients with Urea>50mg/dl	Patients with Creatinine>12mg/dl
Baseline: 0 days	15	9
7 days	17	15
2 months	14	8

CONCLUSIONS

IM conferred significant benefits in the control and reduction of the blood pressure in the elderly patients suffering from ischemic stroke, with or without DM or other cardiovascular risk factors (9,10), as monotherapy, as well as in combination with different classes of antihypertensive drugs. This beneficial therapeutic result was achieved without adverse effects, already from the seventh day of treatment, with a small further reduction mainly of the systolic BP at the end of the second month. In addition, the administration of the IM decreased the degree of the proteinuria in

diabetic patients, confirming the protective effect of the IM to the renal function (5,6).

REFERENCES

- Kannel W.B.: Risk stratification in hypertension: new insights from the Framingham Study. *Am. J. Hypertens.* 13: 3-10 (2000)
- Hanson L., Lindholm L.H., Niskanen L., Lanke J., Hedner T., Niklason A., Luomanmaki K., Dahlof B., de Faire U., Morlin C., Karlberg B.E., Wester P.O., Björck J.E.: Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomized trial. *Lancet* 353: 611-616 (1999)
- Hanson L., Lindholm L.H., Ekblom T., Dahlof B., Lanke J., Schersten B., Wester P.O., Hedner T., de Faire U.: Randomized trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. *Lancet* 354: 1751-1756 (1999)
- UK Prospective Diabetes Study Group: Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. *BMJ* 317: 713-720 (1998)
- Shigikara T., Sato A., Hayashi K., Saruta T.: Effect of combination therapy of angiotensin-converting enzyme inhibitor plus calcium channel blocker on urinary albumin excretion in hypertensive microalbuminuric patients with type II diabetes: *Hypertens. Res.* 23: 219-226 (2000)
- Katayama S., Kikkawa R., Isogai S., Sasaki N., Matsuura N., Tajima N., Urakami T., Uchigata Y., Ohashi Y.: Effect of captopril or imidapril on the progression of diabetic nephropathy in Japanese with type 1 diabetes mellitus: a randomized controlled study (JAPAN-IDDM): *Diabetes Res. Clin. Pract.* 55: 113-21 (2002)
- Goldberg A.I., Dunlay M.C., Sweet C.S.: Safety and tolerability of losartan potassium, an angiotensin II receptor antagonist, compared with hydrochloriazide, atenolol, felodipine ER, and angiotensin-converting-enzyme inhibitors for the treatment of systemic hypertension. *Am. J. Cardiol.* 75: 793-795 (1995)
- Saruta T., Omae T., Kuramochi M., et al: Imidapril hydrochloride in essential hypertension: a double blind comparative study using enalapril maleate as a control. *J. Hypertens.* 13 (suppl 3): S23-S30 (1993)
- Sadoshima S., Nagao T., Ibayashi S., Fujishima M.: Inhibition of angiotensin-converting enzyme modulates the autoregulation of regional cerebral blood flow in Hypertensive rats. *Hypertension* 23: 781-785 (1994)
- Paulson O.B., Vorstrup S., Andersen A.R., Smith J., Godtfredsen J.: Converting enzyme inhibition resets cerebral autoregulation at lower blood pressure. *J. Hypertens.* 3 (Suppl.): S487-S488 (1985)