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A comparison of intervention with losartan or captopril in acute myocardial infarction

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Abstract

Aim of study: Angiotensin-converting enzyme (ACE) inhibitors prolong life, lower the progression of heart failure, and decrease the need for hospitalizations in patients after myocardial infarctions. It is still unclear whether these effects could also be achieved by blocking the angiotensin II (ATII) type 1 receptor. *Methods and results*: We randomized 201 patients with acute myocardial infarction treated with either direct angioplasty, thrombolysis, or heparin alone to the ACE inhibitor captopril or the ATII antagonist losartan. The primary endpoints were safety, tolerability, and left ventricular parameters. The patients were followed for at least 15 days. The incidence of severe adverse events was similar in both groups, although cough presented less often in the losartan group. Captopril failed to prevent an increase in end-diastolic volume and did not influence left ventricular end-systolic volume. This effect led to an increase in the left ventricular ejection fraction ($P < 0.001$) without a change in wall-motion index. Losartan did not affect end-diastolic volume but decreased end-systolic volume ($P < 0.001$), resulting in a significant increase in left ventricular ejection fraction ($P < 0.001$) and a decrease in wall-motion index ($P < 0.001$). *Conclusion*: This study suggests that losartan is safe and well tolerated in patients after myocardial infarction. ATII antagonists seem to have a more pronounced effect on left ventricular remodeling than ACE inhibitors.

Keywords: Losartan; Angiotensin II receptor; Myocardial infarction; Captopril

1. Introduction

Recently, direct angioplasty and wide use of thrombolytic therapy have markedly improved the treatment of acute myocardial infarction (MI), with recanalization achieved in nearly 80% of patients [1,2]. Early restoration of blood flow to the myocardium contributes to the maintenance of function and improvement of survival [3].

Experimental and clinical evidence suggest that the use of the angiotensin-converting enzyme (ACE) inhibitor captopril in the early phases of MI lowers the incidence of arrhythmias [4,5]. Use of ACE inhibitors in patients with reduced left ventricular ejection fraction following the acute phase of MI improves ventricular function by reducing diastolic and systolic ventricular expansion [6]. Moreover, there is strong evidence that the use of an ACE inhibitor improves the prognosis and long-term outcome in both patients

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with a low ejection fraction [7] as well as those with signs and symptoms of heart failure and preserved ejection fraction [8]. ACE inhibitors have been shown to be safe even when administered within the first 24 h of symptom onset, [9,10] with the most pronounced effect on mortality occurring within the first days [9]. ACE inhibitors are now regarded as standard treatment for patients with left ventricular dysfunction after MI.

ACE inhibitors have, in fact, become cornerstones in the treatment of heart failure of various etiologies and severity [11]. Early clinical trials with angiotensin II (ATII) antagonists have shown effects similar to ACE inhibitors on both hemodynamics [12] and exercise performance [13] in patients with heart failure. Although the Evaluation of Losartan in the Elderly (ELITE) study was designed as a comparison of captopril vs. losartan on renal function, an unexpected significantly lower mortality rate was observed in the losartan group in analysis of the study's secondary endpoints [14]. The ELITE II trial was, therefore, designed to confirm this result with all-cause mortality as the primary endpoint.

The present study was based on the assumptions of comparable hemodynamic effects of losartan and captopril and a probable benefit of losartan over captopril on mortality, with a lower incidence of adverse events [15]. The primary objectives included assessment of the efficacy of both drugs, as measured by attenuation of left ventricular volume expansion, and improvement in systolic function of the left ventricle; the tolerability of both drugs was also assessed. The study enrolled patients with confirmed MI admitted to hospital within 24 h after onset of chest pain.

2. Methods

This was a prospective, randomized, parallel-group, single-blind study with double-blind evaluation of echocardiographic parameters. A total of 201 patients were enrolled in two intensive care units at St. Anne's University Hospital, Brno, Czech Republic. The study was controlled and supervised by two study directors. All echocardiographic examinations were recorded on videotape and evaluated by two independent echocardiographers without any knowledge of the treatment allocation. All laboratory tests were performed in the laboratory of St. Anne's University Hospital. The study was approved by the Institutional Ethics Committee, and all patients gave informed consent.

2.1. Study objectives

The primary objectives of our study were: (1) assessment of the tolerability and safety of captopril and losartan; and (2) comparison of the efficacy of captopril and losartan with regard to preservation of left ventricular volumes, ejection fraction, and wall-motion index as measured by repeated two-dimensional echocardiography.

Secondary objectives of the study were: (1) assessment of infarct size estimated from peak creatine phosphokinase (CPK); (2) evaluation of the use of concomitant medications; and (3) chest X-ray evaluation (cardiothoracic ratio, signs of pulmonary congestion).

2.2. Eligibility of patients

Patients were considered eligible for enrollment if they were admitted to hospital and treatment (e.g. direct percutaneous transluminal coronary angioplasty, thrombolysis) was started within 24 h after the onset of symptoms of MI. The type of treatment given was left to the discretion of the attending physician. Study drug had to be started within 24 h after hospital admission. Direct PTCA or thrombolysis was preferred, but if the patient did not fulfill criteria for thrombolysis (typical chest pain and ST elevation) or arrived more than 12 h after chest pain, only heparin was given. The diagnosis was based on the presence of characteristic symptoms of acute MI, ECG changes, and/or coronary enzyme elevation. Patients were excluded if there was a known intolerance to ACE inhibitors, renal insufficiency, systolic blood pressure < 90 mmHg, and diastolic blood pressure < 50 mmHg. Additional exclusion criteria were: the need for continuous infusion of catecholamines; severe valvular heart disease; serious systemic or metabolic diseases except diabetes mellitus; second- or third-degree atrioventricular block; need for temporary cardiostimulation; or repeated defibrillation for ventricular fibrillation or tachycardia.

2.3. Treatment protocol

Immediately after admission to the intensive care unit, the patients were treated by direct percutaneous transluminal coronary angioplasty, or alternatively, 1 500 000 international units of streptokinase was administered over 45 min, or 10 000 international units of heparin was administered over 5 min, followed by a continuous heparin infusion for at least 48 h. Nitrates were allowed when indicated for hypertension or severe angina. Aspirin (400 mg) was given to all patients on admission, followed by 100–200 mg aspirin/day. The protocol did not exclude the use of β blockers, nitrates, digitalis, or any other drugs, except for other ACE inhibitors or ATII antagonists.

Calcium-channel blockers were not recommended because there is no clear indication for these agents after MI.

Study medication was initiated orally within 24 h after hospital admission. The initial dose of captopril was 6.25–12.5 mg, while the initial dose of losartan was 25 mg. Captopril (12.5–25.0 mg) was administered after 8, 16, and 24 h. Losartan (25 mg) was administered after 24 h. Dose titration was continued if systolic blood pressure, measured immediately before the next scheduled dose of study medication, was >90 mmHg. The recommended maintenance doses were 12.5–25.0 mg captopril three times daily, and 25–50 mg losartan once daily.

2.4. Measurements

2.4.1. Echocardiography

Apical two- and four-chamber views were used for evaluation of left ventricular volumes and ejection fraction. Parasternal short- and long-axis views and apical two- and four-chamber views were used for wall-motion index calculation. Recordings were obtained at the end of expiration and stored on videotapes. All recordings were evaluated off-line by two independent echocardiographers without knowledge of patients' medication or clinical status. End-diastolic and end-systolic frames were traced from both apical views using the KONTRON 2000 analysis system (Munich, Germany). Left ventricular volumes and ejection fractions were calculated by the biplane Simpson's rule. The mean of three measurements of consecutive cycles was taken for each examination. A 14-segment model was used for the calculation of wall-motion index. A normokinetic segment was given the score 1, hypokinetic 2, akinetic 3, and dyskinetic 4. Wall-motion index was calculated as the sum of all segments divided by 14. The initial echocardiographic evaluation was performed immediately before the first study drug administration and repeated at day 5 ± 2 and day 15 ± 5 after randomization; echocardiography always took place in the morning before the next scheduled dose of study drug.

2.4.2. Enzymatic infarct size

Infarct size was estimated from the cumulative release of CPK activity per liter of plasma, measured every 6 h during the first 48 h, then every 12 h during the next 48 h.

2.4.3. Chest X-ray

Chest X-ray was performed at day 5 ± 2 in the standing position. Cardiothoracic ratio was calculated and signs of lung congestion were evaluated using a four-point classification system (0 = normal, 1 = lung congestion, 2 = interstitial edema, 3 = alveolar edema) [16].

2.5. Clinical events

Clinical events, including death, development or worsening of heart failure, angina pectoris, reinfarction, need for balloon angioplasty, or coronary artery bypass grafting, were noted in patient records. Patients were excluded from the study if death, reinfarction, or the need for discontinuation of study drug for >24 h occurred before final evaluation. Reinfarction, defined as new chest pain, ECG changes, and cardiac enzyme elevation, was an exclusion criterion because of the potential influence on echocardiographic parameters. The patients were monitored for arrhythmias for at least 72 h using the Space Lab monitoring system (Space Lab, USA). The severity of heart failure was assessed at day 5 and at discharge by the New York Heart Association criteria.

3. Statistics

If not otherwise indicated, variables were compared using Student's *t*-test and categorical variables using χ^2 test. Results were considered significant if the *P* values were $=0.05$, using the two-sided level of significance. Left ventricular volume, ejection fraction, and wall-motion index data are expressed as means $\pm$ S.D. The changes over time were evaluated by analysis of variance for repeated measurements.

4. Results

There were 201 patients randomized, 101 to captopril and 100 to losartan. All patients are included in the safety and tolerability analysis. Thirteen patients in the captopril group and 12 in the losartan group were withdrawn because of death or serious adverse events (reinfarction or other events that led to withdrawal of study medication). Main adverse events and reasons for discontinuation are summarized in Table 1.

All reasons for discontinuations occurred within the first 5 days, except for one death in the captopril group and one reinfarction in the losartan group. There were no non-cardiac deaths.

Thus, 176 patients completed the study with all three echocardiographic examinations. These patients are included in the concomitant medication evaluation and clinical outcome evaluation. Their baseline characteristics are shown in Table 2.

Twenty-one (24%) patients in the captopril group

Table 1
Baseline characteristic and adverse events in randomized patients[a]

	Captopril ($N = 101$)	Losartan ($N = 100$)	P
Age (years)	65.9 ± 12.1	65.7 ± 11.4	NS
Gender (no.)			
Female	31	29	NS
Male	70	71	NS
All serious adverse events	13 (13)	12 (12)	NS
Death	6 (6)	4 (4)	NS
Reinfarction	4 (4)	5 (5)	NS
Cough	26 (0)	12 (0)	< 0.05
Hypotension	7 (2)	6 (1)	NS
Renal failure	2 (1)	2 (1)	NS
Allergy	0	1 (1)	NS

[a]Numbers in parentheses indicate number of patients withdrawn from the study because of serious adverse events.

and 16 (18%) in the losartan group were treated with direct coronary angioplasty (NS); 20 (23%) patients in each group were treated with thrombolysis (NS); while 47 (53%) patients in the captopril group and 52 (59%) patients in the losartan group were initially treated only with heparin (NS). No significant differences between the groups were found in concomitant medications at day 1, day 5, or at discharge.

Forty-eight (55%) infarctions in the captopril group and 51 (60%) in the losartan group were classified as anterior or anterolateral; 23 (26%) in the captopril group and 18 (20%) in the losartan group as posterior or posterolateral; 8 (9%) in the captopril group and 10 (11%) in the losartan group as lateral; and 9 (10%) in each group as anteroposterolateral (all NS). New pathologic Q waves indicating Q-wave MI appeared in 57 (65%) patients in the captopril group and in 61 (69%) in the losartan group (NS).

There were no significant differences between the groups in cardiothoracic ratio or signs of pulmonary congestion at day 5. Severity of heart failure according to the New York Heart Association classification was similar in both groups at day 5 and at discharge. The evaluation of severity of heart failure using the New York Heart Association classification (NYHA) was likewise similar in both groups at day 5 and at discharge. Fifty-six (64%) of patients in the captopril group and 55 (66%) in the losartan group were classified as NYHA class I; 29 (33%) and 18 (20%), respectively, in NYHA class II; 3 (3%) and 4 (5%), respectively, as NYHA class III; and no patient in any arm as NYHA class IV.

Peak CPK (23.96 ± 17.18 μkat/l) in the captopril group occurred 19.15 ± 7.58 h after the onset of chest pain; in the losartan group, peak CPK (23.42 ± 16.36 μkat/l) occurred 18.20 ± 5.81 h after the onset of chest pain (P = NS) (μkat/l × 60 = international units).

The mean doses of captopril were 25.30 ± 7.89 mg, 31.28 ± 14.26 mg, and 43.17 ± 19.46 mg at days 1, 5, and 15, respectively, while the corresponding mean doses of losartan were 24.86 ± 1.33 mg, 27.84 ± 7.98 mg, and 30.25 ± 10.15 mg.

Patients in the captopril group were admitted an average of 7.30 ± 6.06 h after the onset of pain compared with 8.48 ± 5.25 h in the losartan group (NS). The patients were discharged after 15.12 ± 2.98 days in the captopril group and after 14.25 ± 3.74 days in the losartan group (NS). One (1%) patient in the captopril group and one (1%) in the losartan group were not discharged but transferred to cardiosurgery for acute coronary artery bypass grafting after day 15. Both operations were successful, and patients were discharged 2 weeks after acute coronary artery bypass grafting. There was no need for acute percutaneous transluminal coronary angioplasty other than as the primary revascularization procedure; elective angiography with possible percutaneous transluminal coronary angioplasty was recommended after day 15.

Of the 176 patients who completed the study, 152 patients (76 in each group) had three echocardiographic readings of suitable quality. The mean age of these 76 patients was 66.23 ± 11.60 years in the captopril group and 65.16 ± 10.99 years in the losartan group (NS). There were 54 (71%) males and 22 (29%)

Table 2
Baseline characteristics of patients who completed the study according to the protocol[a]

	Captopril ($N = 88$)	Losartan ($N = 88$)	P
Age (years)	65.2 ± 12.1	65.0 ± 11.1	NS
Gender (no.)			
Female (%)	30 (34)	24 (27)	NS
Male (%)	58 (66)	64 (73)	NS
Clinical history (%)			
Myocardial infarction	23 (26)	26 (30)	NS
Angina pectoris	28 (32)	29 (33)	NS
Hypertension	40 (45)	35 (40)	NS
Heart failure	10 (11)	8 (9)	NS
Diabetes mellitus	21 (24)	21 (24)	NS
Medication before hospital admission (%)			
Calcium-channel blockers	20 (23)	21 (24)	NS
β blockers	16 (18)	12 (14)	NS
Nitrates	20 (23)	20 (23)	NS
ACE inhibitors	9 (10)	9 (10)	NS
Diuretics	11 (13)	11 (13)	NS
Other	32 (36)	35 (40)	NS

[a]All three echocardiographic examinations performed. ACE = angiotensin-converting enzyme.

Table 3
Echocardiographic parameters at baseline, after 5 days and after 15 days, and statistical differences between echocardiographic parameters[a]

	Echocardiographic parameters			Statistical analysis		
	Baseline	Day 5	Day 15	Baseline vs. day 5	Day 5 vs. day 15	Baseline vs. day 15
Captopril (N = 76)						
EDV (ml)	117 ± 32	120 ± 40	122 ± 36	NS	NS	NS
ESV (ml)	76 ± 29	76 ± 34	76 ± 34	NS	NS	NS
EF (%)	36 ± 10	38 ± 10	39 ± 10	< 0.02	NS	< 0.001
WMI	1.61 ± 0.45	1.66 ± 0.46	1.61 ± 0.43	NS	NS	NS
Losartan (N = 76)						
EDV (ml)	107 ± 38	109 ± 37	108 ± 38	NS	NS	NS
ESV (ml)	68 ± 33	67 ± 33	61 ± 29	NS	< 0.001	< 0.001
EF (%)	39 ± 11	40 ± 11	43 ± 11	NS	< 0.001	< 0.001
WMI	1.68 ± 0.47	1.58 ± 0.48	1.48 ± 0.40	< 0.02	< 0.001	< 0.001

[a]One sample analysis. EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; and WMI, wall-motion index.

females in the captopril group, and 47 (62%) males and 29 (38%) females in the losartan group (NS).

The first echocardiographic reading was performed immediately before the first dose of study drug; the second at day 4.63 ± 1.10 in the captopril group and day 4.58 ± 0.93 in the losartan group; and the third at day 14.08 ± 2.94 in the captopril group and at day 13.49 ± 3.51 in the losartan group (all NS).

Results of the echocardiographic examinations are shown in Table 3 and Figs. 1–4.

There were no statistical differences between the groups in any of the four parameters at baseline for between-group comparisons. EDV and ESV were statistically significantly higher in the captopril group ($P < 0.05$), ejection fraction tended to be higher in the losartan group (NS), and wall-motion index was statistically significantly lower in the losartan group ($P < 0.05$) at the end of the study.

5. Discussion

Acute MI leads to complex alterations in neurohumoral systems [17–19]. Particular attention has recently been directed to the renin–angiotensin system, because blockade of ATII formation by ACE inhibition attenuates progressive ventricular dilatation, which frequently complicates acute MI [20]. Infarct expansion has been important for our understanding of the changes in ventricular architecture occurring as a consequence of acute MI. During the first hours after myocyte necrosis, edema and inflammation are

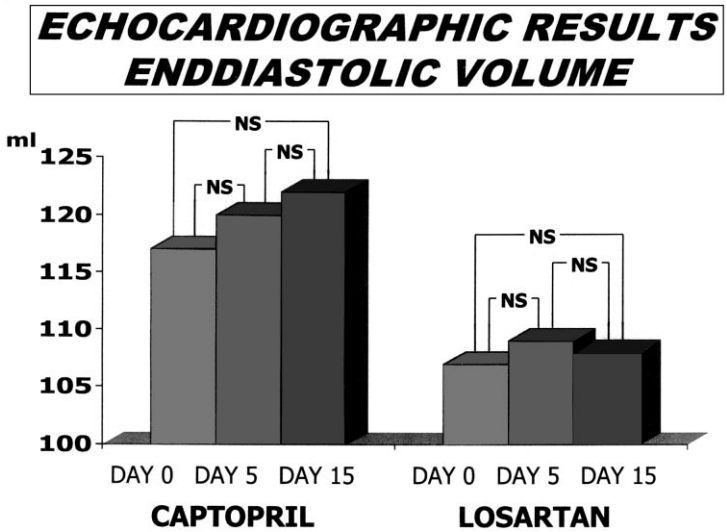

Fig. 1. Between groups: the change in end-diastolic volume from baseline to Day 15 on losartan was significantly ($P < 0.05$) less than the change on captopril. Within groups: NS, non-significant.

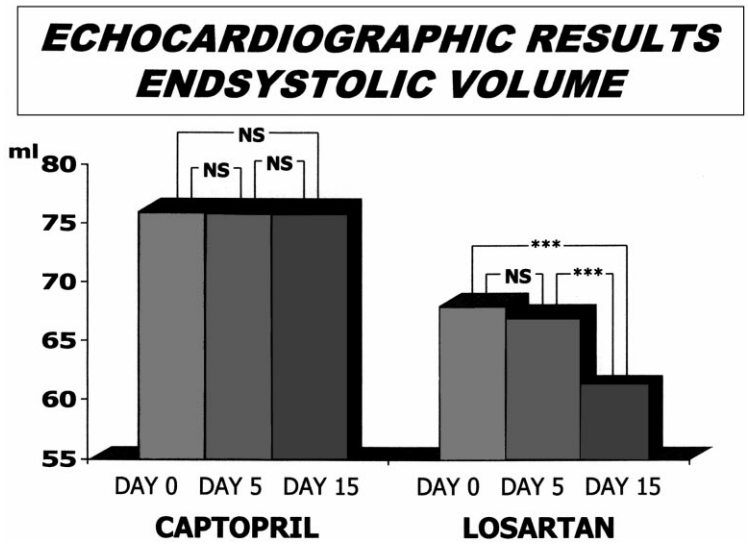

Fig. 2. Between groups: the changes in end-systolic volume from baseline to Day 15 on losartan was significantly ($P < 0.05$) less than the change on captopril. Within groups: $^{*}P < 0.05$; $^{***}P < 0.001$; and NS, non-significant.

localized to the infarcted region. This is followed by a long-term phase of fibroblast proliferation, collagen deposition, and subsequent change in its composition, leading to scar formation. Before and during the period of resorption of necrotic tissue, but before extensive deposition of collagen occurs with an increase in the tensile strength, the infarcted region can thin and elongate. Histological examination has revealed that this thinning of the infarcted region is a consequence of slippage between muscle bundles, resulting in a reduction in the number of myocytes across the infarcted region [20,21]. During the course of healing, connective tissue cells enter the myocyte fibers, providing resistance to further stretching [22]. Patients with infarct expansion are more likely to experience complications such as the development of heart failure, aneurysm formation, and myocardial rupture [23–25]. This process can be partly blocked by ACE inhibition.

It has been suggested that the use of losartan in the early phase of MI would be at least as safe and effective as the use of an ACE inhibitor [26]. ACE inhibitors reduce blood pressure, improve left ventricular hypertrophy, reduce morbidity and mortality in patients with heart failure, and prevent progression to overt cardiac failure in patients with depressed ventricular function or MI [27–29]. ACE inhibitors are widely used in the treatment of hypertension, congestive heart failure, and after MI.

Losartan reduces blood pressure and pulmonary

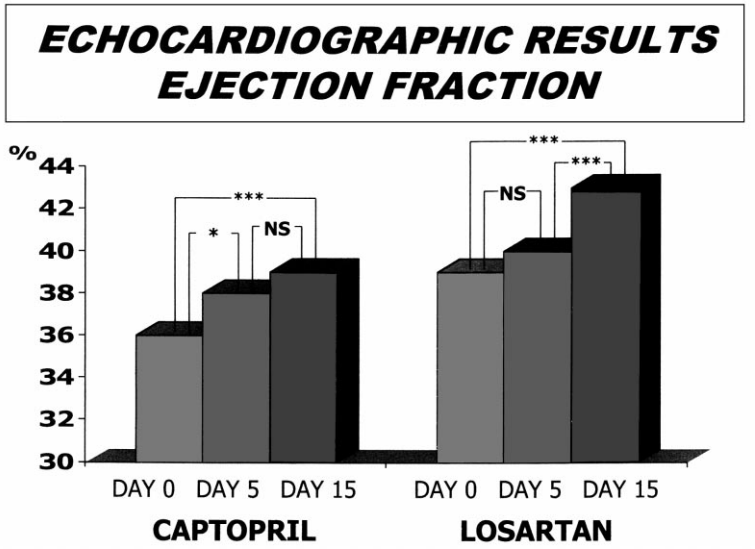

Fig. 3. Between group differences were not significant. Within groups: changes in ejection fraction. $^{*}P < 0.05$; $^{***}P < 0.001$; and NS, non-significant.

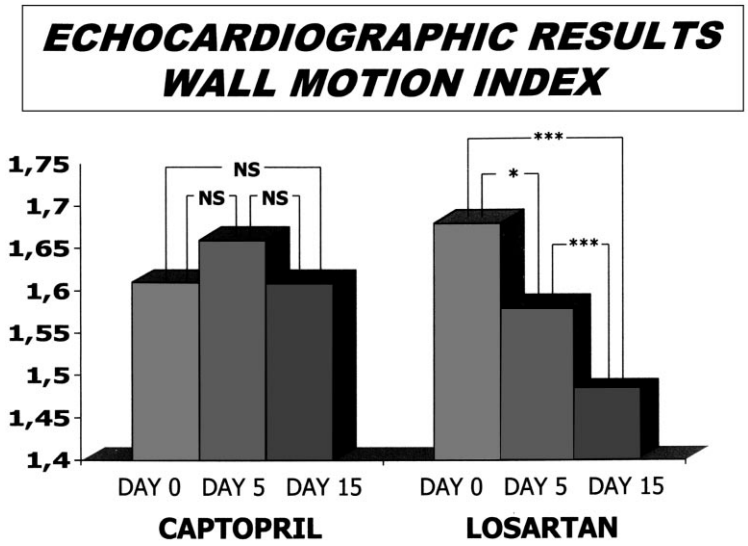

Fig. 4. Between groups: changes in wall-motion index. $^{*}P < 0.05$; $^{***}P < 0.001$; and NS, non-significant. Within groups: the improvement in wall-motion index was significantly greater ($P < 0.05$) on losartan compared to captopril.

wedge pressure, and increases cardiac output [12,30]. It also increases plasma renin activity and exercise tolerance [12] but decreases serum aldosterone and plasma norepinephrine [12]. Losartan and other ATII antagonists have been tested in several hypertension trials and have shown an effect comparable to ACE inhibitors but with fewer adverse events (cough is less frequent) [31,32]. Losartan is already registered and widely used for the treatment of hypertension in many countries and for the treatment of heart failure in some countries.

Several trials have demonstrated comparable effects of losartan and ACE inhibitors on hemodynamic parameters in patients with heart failure. Cumulative data from the US and International Exercise Trials and from the Evaluation of Losartan in the Elderly Trial (ELITE) have led to a hypothesis that losartan may have more favorable effects on mortality in patients with heart failure than an ACE inhibitor [14]. In addition, the trials have demonstrated fewer adverse events with losartan compared with ACE inhibitors [14]. These results have led to larger clinical trials in which mortality in heart failure is the main endpoint. The two largest are ELITE II and the Valsartan Heart Failure Trial (VAL-HEFT).

There are, however, only experimental data on the effect of ATII antagonists in acute MI [33,34]. It was, therefore, considered necessary to try to obtain clinical data on the effect of these drugs. The present study was thus initiated in January 1996 with approval from the Czech Ministry of Health and Ethics Committee.

5.1. Safety and tolerability

Hypotension after the first dose was quite rare in both groups and led to withdrawal in two patients in the captopril group and one patient using losartan. Hypotension after the first dose of ACE inhibitor in patients with confirmed MI has been observed, especially when the ACE inhibitor was given intravenously [35]. Hypotension was also more frequently observed after captopril than after placebo in the Captopril and Thrombolysis Study (CATS); however, it was only rarely the reason for discontinuation of treatment. Both the Cooperative North Scandinavian Survival Study (CONSENSUS) II and CATS reported hypotension more frequently than we have observed. This could be due to a very high intravenous dose of enalapril in the CONSENSUS II study and to a shorter interval between thrombolysis and captopril in CATS. In CATS, streptokinase could have caused hypotension [36]. This was unlikely in our study, because the mean time between acute intervention and first dose of study drug was approximately 10 h.

Cough is often reported as an adverse event after ACE inhibitors [8,18]. This may be the result of an accumulation of bradykinin [37]. As losartan does not influence the degradation of bradykinin, cough following losartan is reported with the same frequency as after placebo [14,31]. A higher incidence of cough in both groups could result from the main disease (i.e. MI with consequent pulmonary congestion). Cough was significantly more frequent in the captopril group than in the losartan group.

5.2. Left ventricular volumes and function

Earlier studies have demonstrated that left ventricular volumes increase after MI and that this increase can be attenuated by ACE inhibitors. Nevertheless,

both Pfeffer [38] and Kingma [4] reported an increase in end-diastolic volume and only small changes in end-systolic volume in patients treated with ACE inhibitors. One may, therefore, speculate that ACE-inhibitor therapy decreases the process of dilatation but does not completely prevent it. This was indeed observed in our study in which end-diastolic volume tended to increase and end-systolic volume remained unchanged in patients treated with captopril. The increase in end-diastolic volume resulted in an increase in the ejection fraction.

No changes in the wall-motion index confirmed that the increase in ejection fraction was not caused by improved left ventricular function but by improved filling.

In contrast, end-diastolic volume remained unchanged and end-systolic volume decreased in patients treated with losartan; these changes led to a statistically significant increase in ejection fraction. This positive effect was confirmed by a statistically significant decrease in the wall-motion index. Because end-systolic volume is supposed to be one of the most important prognostic factors in patients after MI [39], its decrease should be considered beneficial. The pathophysiological mechanism is not clear yet, but one possible mechanism might be activation of non-ACE pathways in the production of ATII and inadequate blockade by ACE inhibitors. Another possible mechanism is activation of the ATII type 2 receptor, which may have anti-proliferative and vasodilatative properties [37]. Increased vascularization after losartan has also been described [40]. In addition, the role of kinins is not completely explained. Attenuated degradation of kinins, well established with ACE-inhibitor therapy, does not occur with ATII-antagonist therapy.

5.3. Clinical endpoints

No differences were observed in clinical outcome between the two groups of patients. The incidences of death, reinfarction, heart failure (reported as the New York Heart Association class classification at day 5 and at discharge), and signs of lung congestion on chest X-ray at day 5 were similar in both groups.

5.4. Limitations of the study

Before any recommendations for clinical practice can be derived from this study, several limitations should be taken into account.

First, the study was not double blind; it was computer randomized, however, and echocardiographic evaluations were done from a videotape by two independent echocardiographers who had no knowledge of patient outcome and medication.

Second, the use of echocardiography for quantitative measurements of left ventricular volumes and function resulted in the loss of one-sixth of the patients for evaluation.

Third, the dose of both drugs was relatively small and the effects of captopril, which is the reference group, have been observed with the higher dose level. This dosing regimen is likely to reflect real-life practice, in which lower doses, especially of ACE inhibitors, are often used. A similar dose of captopril caused a significant increase in plasma renin activity and a decrease in ACE activity in CATS [4]; results from the Assessment of Treatment with Lisinopril Survival (ATLAS) study seem to indicate that higher doses should be used, however [41,42].

Finally, the number of patients included in the study is too small and the duration of observation too short to positively detect the effect of treatment on mortality and morbidity.

5.5. Implications for clinical practice and future research

The beneficial effect of early use of oral ACE inhibitors after MI is already confirmed [9,10]. This study was designed as a pilot study to compare a widely used treatment (the ACE inhibitor captopril) with a new promising drug (the ATII antagonist losartan). The study provides important data on the safety and tolerability of losartan in patients after MI and reveals a potential beneficial effect on left ventricular remodeling and function post-MI. These results need to be confirmed by a larger study. Such a study has already been designed (OPTIMAAL — the Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan) and will compare the two drugs on overall, all-cause mortality. The combination of another ATII antagonist, valsartan, and an ACE inhibitor will be evaluated in the VALIANT (Valsartan in Acute Myocardial Infarction) study. The results of these studies will not be available before the year 2000. Nevertheless, on the basis of the above studies, we recommend losartan in the treatment of patients with signs and symptoms of heart failure after MI when an ACE inhibitor is not tolerated.

Acknowledgements

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