Effects of Intracoronary Thrombolysis Therapy on Left Ventricular Function after Acute Myocardial Infarction

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To treat the acute phase of myocardial infarction, nitroglycerin and urokinase were injected directly into the infarct-related coronary artery.

Left ventricular ejection fraction and regional ejection changes were significantly preserved in the chronic phase, compared with conventional therapy in patients with obstruction at the same site.

Comparing left ventricular function in the acute and chronic phases, left ventricular ejection fraction, regional ejection changes and left ventricular end-diastolic pressure were significantly improved in the chronic phase in patients with reperfusion within 6 hours.

On the other hand, in patients who had no reperfusion in either the acute or chronic phase, left ventricular ejection fraction deteriorated in the chronic phase. Even in patients with reperfusion in the acute phase, reocclusion later meant a worse left ventricular ejection fraction in the chronic phase.

These results suggest that intracoronary thrombolysis with urokinase within 6 hours gives a good chance of recovery from myocardial damage in patients with myocardial infarction.

For a long time, the direct cause of acute myocardial infarction has been discussed. There is no doubt that spasm and thrombosis play an important role, superimposed on arteriosclerosis of the coronary artery.

We have performed coronary cine-angiography during the earliest stage of acute myocardial infarction and injected both nitroglycerin (NTG) and urokinase (UK) directly into the infarct-related occluded coronary artery, for intracoronary thrombolysis.

Left ventricular function was measured both before this percutaneous transluminal coronary recanalization (PTCR) and 4 weeks after. The efficacy of this therapy against acute myocardial infarction was studied from several viewpoints.

SUBJECTS AND METHODS

The study group consisted of 159 patients who were admitted to the CCU at Hiroshima City Hospital within 24 hours of a severe attack, and in whom acute coronary angiography was performed with permission of the patient and his family.

The diagnosis of acute myocardial infarction was based on electrocardiographic changes compatible with acute myocardial ischemia and clinical findings, while the patients had severe chest pain at rest that lasted for more than 20 minutes, not alleviated by sublingual NTG.

All patients had an electrode catheter placed into the right ventricle to prevent bradyarrhythmias during the procedure.

After left heart catheterization and left ventricular angiography, selective coronary angio-
Fig. 1. Mortality rate: Comparison of PTCR therapy and conventional therapy in acute phase of myocardial infarction.

Fig. 2. Mortality rate—pump failure—: Comparison of PTCR therapy and conventional therapy in acute phase of myocardial infarction.

Firstly heparin sodium, 5000 units, was injected intravenously.

A catheter was left in the appropriate coronary ostium and 0.5 mg of NTG dissolved in 5% glucose 5 ml was infused into the occluded coronary artery. After 2½ minutes coronary angiography was performed to exclude coronary spasm.

Urokinase (UK) (Uronase®, Mochida Pharmaceutical Co. Ltd.,) in a 240,000 international units bolus dose dissolved in 25 ml was infused for 10 minutes into the occluded coronary artery. This was repeated three times if no changes in the angiographic appearance were found.

RESULTS

Cardiac catheterization and coronary cineangiography were performed within 24 hours in 159 patients with acute myocardial infarction.

One hundred and ten patients had total occlusion of an infarct-related coronary artery.

In 13 patients, intracoronary infusion of NTG resulted in perfusion of the distal coronary artery.

Fifty-nine patients showed reperfusion with intracoronary UK.
Mortality
Mortality after acute myocardial infarction was 11.9% in 159 patients after intracoronary NTG-UK treatment. On the other hand, it was 21.5% in 298 patients over the 3 years before this trial in the same CCU (Fig. 1).
It is suggested that the significant decrease of pump failure after intracoronary thrombolysis causes the decrease in mortality (Fig. 2). But patients with severe coronary stenosis had a poor prognosis despite this treatment (Figs. 3 & 4).

Comparison of left ventricular function after PTCR treatment and conventional treatment
A group: successful PTCR treatment n=50
B group: unsuccessful PTCR treatment n=19
C group: incomplete obstruction at acute phase n=24

Fig.7. Elapsed hours to maximum value of S-GOT S-CPK and S-LDH at acute myocardial infarction.

A group: successful PTCR treatment n=17
B group: unsuccessful PTCR treatment n=7
C group: conventional treatment n=11

Fig.8. Elapsed hours to maximum value of S-GOT and S-CPK at same obstructed site (6) of anterior wall infarction.
Fig. 9. LVEDP at acute phase and chronic phase of myocardial infarction.

Fig. 10. LVEF in successful PTCR treatment at acute phase of anterior wall infarction.
Fig. 11. Comparison of regional wall motion at acute phase and at chronic phase of anterior wall infarction in cases with successful PTCR treatment within 6 hours.

Fig. 12. LVEF in cases with certificated recanalization of infarct-related coronary artery at chronic phase after successful PTCR treatment at acute phase.

The efficacy of left ventricular function in the chronic phase was studied, comparing intracoronary thrombolysis therapy with the former one. Patients who had reperfusion of the left anterior descending branch (6) had a significantly preserved left ventricular ejection fraction (LVEF) compared with conventionally treated infarctions of the same site (Fig. 5). Regional
Fig. 13. LVEF in completely obstructed cases of infarct-related coronary artery at chronic phase after successful PTCA treatment at acute phase.

Fig. 15. LVEF in completely obstructed cases of infarct-related coronary artery at chronic phase after unsuccessful PTCA treatment at acute phase.

Fig. 14. LVEF in cases with recanalization of infarct-related coronary at chronic phase after unsuccessful PTCA treatment at acute phase.

Ejection changes showed a similar tendency in patients with intracoronary thrombolysis (Fig. 6).

It was suggested that if the patients had reperfusion within 6 hours, left ventricular function would be better in the chronic phase compared with in conventionally treated patients.

On the other hand, serum enzymes such as GOT, CPK and LDH were serially measured every three hours after acute myocardial infarction.

The time from onset until the maximal value of serum enzyme was significantly shorter in patients with successful PTCA treatment (Fig. 7).

For an exact assessment, elapsed hours to peak level of GOT and CPK were studied in patients with anterior wall infarction of the same site, LAD(-6). A similar tendency was clearly demonstrated (Fig. 8).

These results seem to indicate interruption of the progression of the infarct.

Comparison of left ventricular function in the acute and chronic phases after intracoronary thrombolysis

Left ventricular function was monitored after the onset of reperfusion. The patients were divided into two groups: those who had reperfusion within 6 hours and after 6 hours.

Left ventricular end-diastolic pressure (LVEDP) was significantly better in the chronic phase compared with the acute phase in these patients with successful PTCA treatment within 6 hours (Fig. 9).

LVEF was also measured in the acute phase before therapy and in the chronic phase in those patients with anterior wall infarction. LVEF was also significantly better in the chronic phase compared with the acute phase in patients with successful PTCA treatment within 6 hours.
(Fig. 10). When regional wall motion was examined, regional ejection changes showed good results at Seg. 2 and 3 in the same patients (Fig. 11).

**DISCUSSION**

For percutaneous transluminal coronary recanalization, streptokinase has been injected into the infarct-related coronary artery.

There have been few reports on urokinase as a treatment for acute myocardial infarction.

In 30 of 41 patients (Mathy\(^1\)), 18 of 26 patients (Reduto\(^2\)), 41 of 47 patients (Ganz\(^3\)), and 22 of 29 patients (Rentrop\(^4\)) with total occlusion, an intracoronary infusion of streptokinase resulted in reperfusion of the distal coronary artery.

We can affirm the usefulness and safety of urokinase (Uronase\(^5\)) for direct coronary infusion in the earliest period of evolving myocardial infarction.

To evaluate early reperfusion in acute myocardial infarction we tried to compare the results
of the former treatment with this one.

The mortality fell in patients who underwent intracoronary thrombolysis.

According to a multicenter report by Merx and coworkers, 129 of 204 patients recanalized after an intracoronary infusion of streptokinase and mortality was only 5.4%.

These patients in whom the obstructing was proximal to the first diagonal branch of the left anterior descending branch and who were reperfused within six hours, had significantly better ejection fraction and regional ejection changes in the chronic phase than those who underwent conventional therapy.

We believe that early recanalization is an important factor in the treatment of acute myocardial infarction.

Comparing left ventricular ejection fraction and regional wall motion in the acute and chronic phases, early reperfusion within six hours results in a good chance of recovery.

In those patients with complete obstruction for more than six hours, recovery of left ventricular function can not be expected (Fig. 12).
But in patients with complete obstruction of the infarct-related coronary artery in the chronic phase, the LVEF clearly fell despite successful PTCR treatment in the acute phase (Fig. 13). If they had proven recanalization in the chronic phase after unsuccessful PTCR treatment, their LVEF did not show any improvement (Fig. 14). In completely obstructed cases in the chronic phase after unsuccessful PTCR treatment, the LVEF showed a change for the worse in the chronic phase (Fig. 15). These findings demonstrate the importance of recanalization in the chronic stage.

As reocclusion can often be found in patients with severe stenosis after PTCR treatment, we try to perform percutaneous transluminal coronary angioplasty and give a continuous intracoronary infusion of UK to multiple thrombi after successful PTCR treatment (Figs. 16 & 17).

Rentrop showed that ejection fraction increases slightly immediately after recanalization of a completely obstructed coronary vessel, while local wall motion usually improves. Reduto reported that, in patients with reperfusion of the infarct-related coronary artery, left ventricular ejection fraction increases from admission until discharge. In contrast, left ventricular ejection fraction does not change in patients with severe proximal stenosis alone nor in patients with total occlusion who do not achieve reperfusion following streptokinase administration. On the other hand, Reduto mentioned that the hemodynamic index of left ventricular performance and ejection fraction, determined by gated cardiac blood pool imaging, does not change immediately after reperfusion.

Rentrop, Cowley, Markis, Lee and Ganz reported the effects of intracoronary application of streptokinase in acute myocardial infarction.

De Feyter and Smalling also concluded that recanalization has a beneficial effect on left ventricular function in patients with myocardial infarction. Schuler reported that successful intracoronary fibrinolysis may reduce the size of the thallium-201 perfusion defect.

Urokinase and streptokinase are the most effective thrombolytic agents for percutaneous transluminal coronary recanalization in the earliest stage of myocardial infarction.

But reperfusion is only a first step to the salvage of the ischemic myocardium and improvement of left ventricular performance.

Several experiments suggest the possibility of a newer treatment after reperfusion in acute myocardial infarction. Nayler proved that Coenzyme Q10 protected the myocardium against the deleterious effects of ischemia and reperfusion.

Kaltenbach and Nayler reported the efficacy of calcium channel blocking agents and Stockman mentioned the usefulness of nitroglycerin.

REFERENCES


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