ACUTE MYOCARDIAL INFARCTION: SELECTIVE OR ISA-TYPE β -ADRENOCEPTOR BLOCKING DRUG?

J. HEIKKILÄ & M.S. NIEMINEN

Cardiovascular Laboratory, University Central Hospital, Helsinki, Finland

β -adrenoceptor antagonists are widely used in the treatment of a number of cardiovascular diseases, however, it is recognized that the use of these drugs may be associated with the occurrence of specific side effects. One of the most important of these side effects is the development of overt heart failure as a result of β -adrenoceptor blockade in patients who are critically dependent on sympathetic drive to maintain adequate cardiac output.

The present study was carried out to compare the effects of metoprolol, a β_1 -selective antagonist, with those of pindolol, an antagonist possessing marked intrinsic sympathomimetic activity (ISA), on myocardial function and central haemodynamics. A full report of this data will be published elsewhere (Heikkilä *et al.*, 1982).

The mechanical performance of the ischaemic and noninfarcted myocardial segments was directly documented from 8 standardized segments around the left ventricle, using a multidirectional echocardiographic method (Heikkilä & Nieminen, 1978). The effect of 0.2 mg pindolol intravenously on haemodynamic, electrocardiographic and echocardiographic signs of ischaemia was studied in 22 patients with acute myocardial infarction. In 36 other subjects (healthy, severe angina pectoris, acute myocardial infarction: 6 matched patients in each group) the relative cardiac safety provided by the intrinsic sympathomimetic activity (ISA) property of pindolol was compared with β_1 -selective metoprolol. Intravenous doses of pindolol were 0.2 and 0.8 mg and of metoprolol, 2 and 8 mg; the effects were recorded 15–20 min after each dose.

Pindolol was haemodynamically safe in patients with uncomplicated acute infarction or even in those with moderate heart failure. Left ventricular filling pressure and stroke volume by Swan-Ganz thermodilution did not change, nor did any ventricular dilation take place. The ST segments improved by 30% ($P < 0.0005$) in 15 min. The systolic wall motion amplitudes of the ischaemic myocardial segments improved by 26% of the normal ($P < 0.0005$). The performance of the uninvolved myocardial seg-

ments was not depressed. Consequently, the total left ventricular regional performance, characterized by summed amplitudes of the eight standardized segments (echoventriculographic contraction index), was clearly improved by pindolol (18%, $P < 0.0005$). Chest pain was relieved.

Pindolol and metoprolol produced rather similar reductions in rate-pressure product ($P < 0.001$ each), heart rate ($P < 0.001$) and systolic blood pressure ($P < 0.05$ to 0.001). The ejection fraction decreased ($P < 0.05$) and the left ventricular diameter increased ($P < 0.001$) after metoprolol but not after pindolol. Pindolol did not reduce the wall motions of healthy myocardial segments, while metoprolol did ($P < 0.01$). In ischaemic hearts the echoventriculographic contraction index improved after pindolol ($P < 0.005$), but remained unchanged after metoprolol.

Conclusions

1. In acute myocardial infarction a small intravenous dose of pindolol was haemodynamically safe, and relieved the clinical, electrocardiographic and myocardial mechanical signs of ongoing ischaemia.
2. While pindolol and metoprolol produce similar reductions in rate-pressure product, in the case of ischaemic left ventricular dysfunction the ISA-type drug provides a safety factor not afforded by β_1 -selectivity.

Reference

- HEIKKILÄ, J. & NIEMINEN, M.S. (1978). Rapid monitoring of regional myocardial ischaemia with echocardiography and ST segment shifts in man. Modification of 'infarct size' and hemodynamics by dopamine and beta blockade. *Acta med. Scand.* [Suppl] **623**, 71–95.
- HEIKKILÄ, J. & NIEMINEN, M.S. (1982). Cardiac safety of acute beta blockade: Intrinsic sympathetic activity is superior to beta₁-selectivity. *Clin. Pharmac. Ther.* (in press).