Atenolol, regional myocardial blood flow and S-T segment in canine ischaemic myocardium

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The effects of atenolol on regional myocardial blood flow (measured by tracer microspheres) and the S-T segment were compared in normal and ischaemic regions on a reproducible model of temporary coronary occlusion in the dog.

The control coronary occlusion did not modify heart rate but induced in the ischaemic area an increase in S-T segment and a decrease in endo- (−71%) and epicardial (−49%) blood flows, resulting in a diminished endo/epi ratio (0.55 ± 0.05 as compared with 1.02 ± 0.05 in the non-ischaemic region).

Atenolol (1 mg/kg, i.v.) decreased heart rate (−28%), lowered S-T segment elevation (−60%) and further reduced endo- and epicardial blood flows without inducing redistribution (endo/epi ratio: 0.61 ± 0.09 in the ischaemic area). In the non-ischaemic area, atenolol also decreased endo- and epicardial blood flows (−40%) without affecting endo/epi ratio (1.08 ± 0.07). Bilateral stellectomy induced similar effects to atenolol administration.

After bilateral stellectomy, atenolol (1 mg/kg, i.v.) induced no additional effects. Finally, under electrosystolic pacing, atenolol (1 mg/kg, i.v.) no longer lowered S-T segment elevation and did not further modify regional blood flows and endo/epi ratio.

It is concluded that atenolol (1) reduces regional myocardial blood flows and S-T segment elevations, these two phenomena being correlated with the decrease in heart rate, (2) does not induce endo-epicardial blood flow redistribution neither in ischaemic nor in non-ischaemic regions.

An indolizine with an amiodarone-like haemodynamic profile

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L 9394 or 2-ethyl-3-(4-γ-di-n-butylaminopropoxy-benzoyl)-indolizine hydrochloride (each 10 mg/kg, 5% aqueous solution) produces amiodarone-like haemodynamic effects when injected i.v. (2 min) into the atropinized (1 mg/kg i.v.) and anaesthetized (sodium pentobarbitone, 30 mg/kg i.v.) mongrel dog. Maximal changes in all measured haemodynamic parameters occurred at the end of the injection-time, except for heart rate for which the maximal change was noted after 5 minutes. The average changes were as follows in 11 treated dogs compared to 18 control dogs receiving saline. Heart rate decreased consistently by 31%. Mean blood pressure fell by 48%, diastolic pressure being more reduced than systolic pressure. Myocardial oxygen consumption computed according to the index of Robinson (1967) diminished sharply by 58%. Cardiac output increased by 74%, stroke volume by 160%. L 9394 also enhanced coronary arterial blood flow (as measured electromagnetically in 10 open chest dogs) by 123% on the average. All these changes were very highly significant ($P < 0.001$). Heart rate decrease lasted for at least 3 h without any change, but the other parameters wore off within different times; 1 h in the case of blood pressure and cardiac output, 20 min in the case of coronary blood flow, while myocardial oxygen consumption was still reduced by 30% ($P < 0.05$) after 1 h and stroke volume was still increased by 30% ($P < 0.05$) at the same time. L 9394 is furthermore endowed with non-competitive adrenoceptor-blocking properties since adrenaline and noradranaline-induced hypertension as well as adrenaline- and isoprenaline-induced tachycardia were markedly antagonized but never blocked.

The overall haemodynamic properties of L 9394 are qualitatively similar to those of amiodarone (Charlier, Deltour, Baudine & Chaillet, 1968), which is a very effective medication for the long term treatment of angina pectoris (Charlier, 1971). Furthermore drug-induced bradycardia has been shown to be a highly desirable property for an antianginal drug (Gomoll & Braunwald, 1973; Charlier, 1974), because heart rate is a major determinant of myocardial oxygen consumption (Braunwald, 1971). It is therefore considered that L 9394 is worthy of a clinical trial in patients with angina.

References

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