Coronary microcirculatory vasoconstriction induced by low-flow ischemia in mouse hearts is reversed by an A2A adenosine receptor agonist

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Coronary microcirculatory vasoconstriction was observed during ischemia in patients with severe coronary stenosis. This event can be mimicked experimentally by lowering the coronary perfusion pressure (CPP) and is attenuated by adenosine. To determine if the selective A2A agonist, regadenoson, could modify this response, coronary vascular resistance (CVR) was monitored for 70 min in isolated mouse hearts (Langendorff configuration) using two protocols.

Protocol 1: CPP was lowered from 65 to 30 mmHg at 20 min, maintained for 20 min and restored to 65 mmHg for the remaining 30 min. In untreated hearts (n=12), lowering CPP increased CVR up to 191%±9 above baseline (p<0.001). Regadenoson 3 nM (n=6) reduced this increase (131%±15 above baseline), and abolished it at 10 and 30 nM (n=6; p<0.001). Protocol 2: CPP was lowered to 30 mmHg at 20 min and maintained for 50 min. In untreated hearts (n=9), the lowering of CPP set off a rise in CVR with maximum at 70 min (240%±21 above baseline). Addition of regadenoson 10 nM to the perfusate either at 10 (n=6) or 30 (n=6) min after lowering CPP resulted in a rapid vasodilation bringing CVR to baseline values within 10 min.

The isolated heart reacts to lowering of CPP with a severe vasoconstriction prevented by pre-treatment with an A2A agonist. Further, activation of A2A adenosine receptors during the vasoconstriction can blunt and reverse this reaction and hence improve myocardial perfusion.