DAPAGLIFLOZIN IMPROVES HAEMODYNAMIC RECOVERY AFTER CARDIOPLEGIC ARREST IN ISOLATED WORKING MOUSE HEART

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Cardioplegic arrest in cardiac surgery is associated with temporary or long-term myocardial contractile dysfunction. Beyond the glucose-lowering effects, sodium glucose cotransport 2 inhibitors (SGLT2-i) have shown dramatically beneficial cardiovascular effects in the last years. However, whether SGLT2 inhibitors protect the heart after cardioplegic arrest and global cold ischaemia is unknown.
Adult male C57BL/6J mice were anaesthetised, the hearts were excised and then mounted in a perfused isolated working heart system. Cold ischaemia (4°C) for 100 min was induced by St. Thomas cardioplegia. The cardioplegic solution was applied every 20 min, followed by 30 min reperfusion. Cardiac hemodynamic variables were continuously recorded. Isolated hearts were randomised to cardiac arrest with/without applying Dapagliflozin (control n=5, SGLT2-i n=4, respectively; 0.1 µg/ml per gram bodyweight) directly to the perfusion buffer prior to cardiac arrest.
Cold ischaemia and reperfusion resulted in a significant reduction in aortic flow (63%±6%, $p<0.05$) in addition to systolic and diastolic parameters such as dP/dt_{max} (75%±8%, $p<0.05$) and dP/dt_{min} (76%±9%, $p<0.05$) compared to baseline. In contrast, a significantly higher rate of systolic (dP/dt_{max} 88%±2%, $p<0.05$) and diastolic (dP/dt_{min} 104%±10%, $p<0.01$) recovery was measured in the SGLT2-i group compared to the control group. Similar improvement in aortic flow recovery was shown (73%±3%, $p<0.05$) compared to control.
Our study emphasises the novel, proof-of-concept character of SGLT2 inhibitor administration before cardiac arrest, which subsequently improves hemodynamic recovery. These results pave the way for a new area of using SGLT2 inhibitors in elective cardiac surgery.