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Targeting the NO-cGMP-PKG Signalling Pathway Protects the Heart Against Ischemia/Reperfusion Injury

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In cardiac surgery the ischemic time is an important factor. The duration of ischemia and consequent reperfusion is one of the most important points determining the outcome of the surgical procedure. Therefore possibilities are sought to reduce the adverse effects of ischemia/reperfusion injury and thereby to optimize the outcome of surgical interventions. Recently the impact of the NO-cGMP-PKG pathway on cardiac protection has been demonstrated by researchers. In the present work the effect of activating this pathway has been examined in the context of ischemia/reperfusion injury.

Three studies have been performed using the model of heterotopic heart transplantation in Lewis rats. The main target parameters were left ventricular function and apoptosis. The NO-cGMP-PKG was targeted by three different agents: 1) vardenafil as an inhibitor of the PDE-5 reduced the degradation of cGMP. 2) cinaciguat as an activator of sGC increased the production of cGMP. And 3) l-arginine as a NO-donor activated sGC.

In each of these experiments a significant improvement of left ventricular function and a significant reduction of myocardial apoptosis was found.

From these results it can be concluded that targeting the NO-cGMP-PKG pathway has a major impact in reducing the adverse effects of ischemia/reperfusion injury. I believe that also in routine cardiac surgery with the consequent use of extracorporeal circulation the activation of the NO-cGMP-PKG pathway has a great potential to reduce ischemia/reperfusion injury.