# APPLICATION OF DONOR HEART AND RECIPIENT WITH MOLECULAR HYDROGEN ALLEVIATES GRAFT DYSFUNCTION AND OVERALL CONDITION AFTER SIMULATED TRANSPLANTATION OF THE PIG HEART

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Heart transplantation has become a routine method of end-stage heart failure treatment but restoring the graft full function often requires repeated electrical defibrillation shocks until the heart resumes the full physiological function. This critical transient period of ventricular fibrillation is largely due to the increased formation of oxygen free radicals during cumulative actions of anesthesia, cardiac ischemia reperfusion, extracorporeal circulation (ECC), and defibrillation after cold asystole storage. It has recently been shown that molecular hydrogen ($H_2$ gas) selectively reduces $^{\bullet}OH$ radicals and modifies several inflammatory pathways. Benefits of $H_2$ in treating oxidative stress related dysfunctions are here assessed.
*Two main pig groups were established: a group with simulated heart transplantation, and a similar group but supplemented with hydrogen-rich air (4% of hydrogen, >40% of oxygen) in anesthesia administered during the whole experiment.* Markers of inflammation, tissue damage, and oxidative stress were determined. Protein expression of total and phosphorylated connexin 43, protein kinase C epsilon type, and activity of matrix metalloproteinases 2 and 9 were measured. Furthermore, the histochemistry of hypoxic/ischemic injury sensitive enzymes were analyzed and electron microscopy of cardiac tissue was evaluated.
In addition to the donor's heart, the recipient's entire body is affected by long-term anesthesia, hyperoxia, circulatory dyshomeostasis caused by ECC. A substantial body of our experimental evidence suggests that hydrogen can significantly alleviate transplantation-related ischemia-reperfusion injury and may have a protective effect against hyperoxia and ROS formation during anesthesia as well as against heart damage induced by repeated electric shocks during cardiac defibrillation. The present study should encourage well-designed clinical trials aimed to test the efficacy of this strategy.

**Keywords**: heart transplantation, inflammation, inhalation, molecular hydrogen, oxidative stress

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