Monday, January 28, 2019

2:15 PM

ABSTRACT: Cardiac Xenotransplant in Infants as a Bridge to Allotransplantation: Is It Possible?

C. A. Banks, H. Hara, D. K. Cooper, D. C. Mauchley, R. J. Dabal, S. Borasino, T. Yamamoto, ***D. C. Cleveland***
University of Alabama, Birmingham

Purpose: Infants (<1 year) awaiting cardiac transplant have the highest wait list mortality of any solid organ transplant and there is no satisfactory ventricular assist device. Alternative treatment strategies are needed. To evaluate the feasibility of using genetically engineered (GE) pig cardiac xenotransplant as a bridge, preformed anti-pig antibodies were measured.

Methods: IgM/IgG antibody binding to red blood cells from wild type (WT, genetically-unmodified) and GE pigs that did not express the three main pig carbohydrate antigens (Gal/Neu5Gc/Sda, TKO) were measured in infant serum by flow cytometry. Negative control level IgM/IgG was established by binding to human blood type O RBCs. Group 1 consisted of 50 patients never exposed to any surgical procedure or blood transfusions. These patients were analyzed by age (<30 days, 30-60 days, 60-90 days, 91 days – 1 year). Group 2 consisted of 20 patients that had previous cardiac surgery, blood transfusions and exposure to biologic patches.

Results: Group 1: IgM binding above control was demonstrated in 26 of 50 samples (4/10 < 30 days, 5/10 30-60 days, 2/10 60-90 days, 15/20 90 days – 1 year). IgG binding was demonstrated to be positive in 38 of 50 samples (7/10 <30 days, 7/10 30 – 60 days, 8/10 60 – 90 days, 16/20 91 days – 1 year). In contrast, no patient demonstrated IgM binding to TKO RBCs. One infant (91 days-1 year) showed very weak IgG binding (Figure1). Group 2: There was significant increase in IgM (16/20) and IgG (17/20) binding to WT RBCs after cardiac surgery and exposure to blood transfusions and biologic patches compared to binding from patients not exposed. However, only one of 20 exposed patients demonstrated a weakly positive IgM binding to TKO RBCs and two of 20 demonstrated a weakly positive IgG binding in this group.

Conclusions: Infants have no, or minimal, anti-TKO IgM/IgG response, including patients after previous cardiac surgery, exposure to blood transfusions, and biologic patches. The absence of preformed antibodies to TKO RBCs suggests that there will be no antibody-mediated rejection. Cardiac xenotransplantation from GE pig offers promise as a potential bridge to allotransplantation.

Figure 1

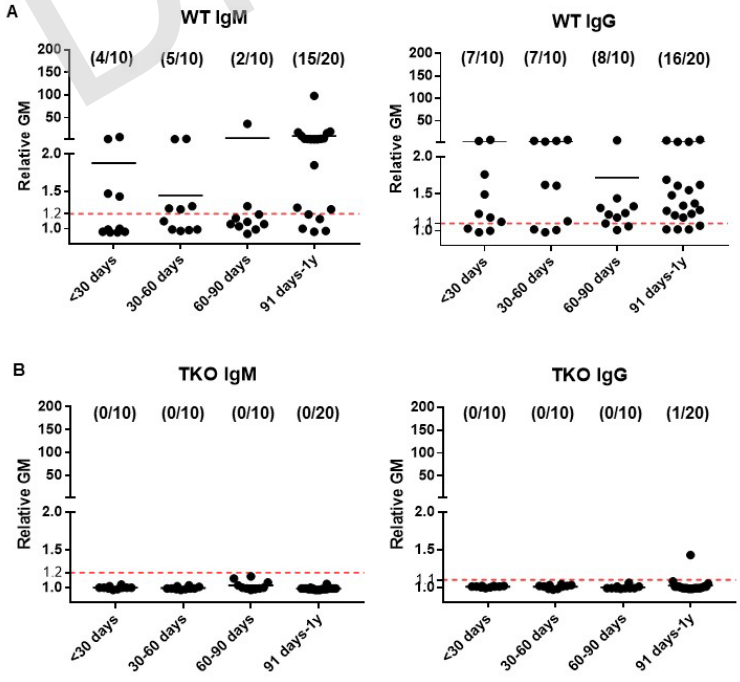

Figure Legend:
IgM (left) and IgG (right) antibody binding to wild-type (WT) (A) and TKO (Gal$^-$/Neu5Gc$^-$/Sda$^-$) (B) pig RBCs in infant sera (n=50)
Relative geometric mean (GM) values of >1.2 (for IgM) and >1.1 (for IgG) are considered to be positive (red dotted line).