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Plasma free triiodothyronine (fT3) levels in baboons undergoing pig organ transplantation; relevance to early recovery of organ function

Hayato Iwase[#], Burcin Ekser[#], Vikas Satyananda, Mohamed Ezzelarab, and David K.C. Cooper

Thomas E. Starzl Transplantation Institute, University of Pittsburgh, Pittsburgh, PA, USA

[#] These authors contributed equally to this work.

It has been well-documented that the level of plasma free triiodothyronine (fT3) falls rapidly following brain death (1, 2, reviewed in 3) or during certain surgical procedures, e.g., heart surgery carried out on cardiopulmonary bypass (4-8). The level in patients following cardiopulmonary bypass usually recovers within 48 hours.

We have measured plasma fT3 in healthy baboons (n=19) and healthy monkeys (n=5), in two groups of baboons undergoing transplantation (Tx) with pig organs (heterotopic heart Tx [n=9] or orthotopic liver Tx [n=10]), and in one group of monkeys undergoing heterotopic heart alloTx (n=5).

The levels in healthy baboons ranged from 1.9-3.6pg/mL (mean 2.7pg/mL) and in healthy monkeys from 2.3-2.9pg/mL (mean 2.6pg/mL).

Following heterotopic pig heart xenoTx in baboons, there was a rapid fall from a mean pre-Tx level of 2.3pg/mL to 0.9pg/mL at 4 hours (a reduction of 62% from pre-Tx) and 0.7pg/mL at 24 hours (a reduction of 69% from pre-Tx). Four days after the surgical procedure, the level had recovered to the low normal range (approximately 2.0pg/mL), where it remained for the 28 days of follow-up.

Following orthotopic pig liver xenoTx in baboons, there was a rapid fall from a mean pre-Tx level of 3.0pg/mL to 0.4pg/mL at 4 hours (a reduction of 90% from pre-Tx) and to 1.0pg/mL at 24 hours (a reduction of 66% from pre-Tx). Thereafter, the level remained in the subnormal range (approximately 1.0pg/mL, or 33% of pre-Tx) for the next 4-7 days, at which time the baboons were euthanized.

Following heterotopic heart alloTx in monkeys, the level fell from a mean pre-Tx level of 2.6pg/mL to 1.1pg/mL at 24 hours (a reduction of 60% from pre-Tx), recovering to 2.6 on day 4 where it remained for the 14 days of follow-up.

Address correspondence to: David K C Cooper MD, PhD, FRCS Thomas E. Starzl Transplantation Institute Starzl Biomedical Science Tower, W1543 University of Pittsburgh Medical Center 200 Lothrop Street, Pittsburgh, PA 15261, USA Telephone: 412-383-6961; Fax: 412-624-1172 cooperdk@upmc.edu.

The cause of the rapid fall in plasma fT3 (resulting in a euthyroid sick syndrome) in brain-dead potential organ donors and after major surgical procedures is associated with a generalized inhibition of mitochondrial function, which results in the loss of energy stores and diminished organ function, particularly of the heart (9; reviewed in 3).

In the present study in the monkeys with cardiac allografts, recovery of fT3 to normal levels was more rapid and better sustained than in baboons with pig cardiac xenografts. Following xenotransplantation, the persisting low fT3, particularly in the liver recipients, may be associated with an ongoing inflammatory state (Ezzelarab M et al, manuscript submitted). We have documented high levels of C-reactive protein for several weeks after pig organ and artery patch transplantation in baboons (Iwase H et al, manuscript submitted).

Deterioration of organ function after brain death or after open heart surgery can be reversed by hormonal replacement therapy in which T3 plays a critical role (2, 3, 6-8, 10, 11). This results in rapid replenishment of myocardial energy stores and improvement in cardiac output (2, 3, 6-8, 10, 11).

There have been reports of a high early mortality after pig orthotopic heart Tx in baboons, particularly within the first 48 hours (12; Mohiuddin M, personal communication). If the baboon survives for 48 hours, then there is recovery of the myocardial function and longer-term survival is likely (12). We suggest that the early high morbidity and mortality may be associated with a reduced level of plasma fT3, and that consideration should be given to T3 replacement therapy.

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