Uterus transplantation: An experimental study in primates

Liza Johannesson

Institute of Clinical sciences, Sahlgrenska Academy, University of Gothenburg
Göteborg, Sweden

ABSTRACT

Most causes of infertility are nowadays treatable, but for women that are infertile due to lack of, or severe malfunction of the uterus, there is as of today no available cure. Uterus transplantation (UTx) may provide a future possibility for treatment of these females with uterine factor infertility (UFI). It may be the only alternative for women with absolute UFI and as the last option in patients with relative UFI, not amenable to conventional surgery. During recent years, UTx has been developed and extensively studied in different classical rodent and large animal models and the remaining necessary last step before a potential clinical introduction is to include experiments on nonhuman primates. The aims of this thesis were to develop a surgical technique for autologous and allogeneic UTx in a nonhuman primate model and to evaluate the surgical feasibility of both live and deceased donor uterus transplantation in humans.

A baboon model for autologous UTx was developed wherein the ovaries and Fallopian tubes were included in the graft. Despite long durations of surgery (6 h) and ischemia (3 h), the animal survival rate (90 %) was high. However, a poor graft survival (20%) advocated the UTx procedure to be refined. A second study of auto-transplanted baboons initially included an increased perfusion with HTK-solution as the only modification. Continued poor outcome (survival rate 66 % but no well functioning grafts) led to further alterations of the surgical procedure, such as inclusion of larger vessels, modified anastomosis and extensive graft perfusion. Subsequently, the graft function improved considerably (60 %). In a third study using an allogeneic UTx baboon model, the uteri were retrieved from both live or deceased donor and transplanted using the previously described technique (live donation) or with aortal/aortal and caval/caval anastomoses (deceased donation). The recipients were either left untreated or received monotherapy of tacrolimus or induction with antithymocyte globulin followed by triple therapy (tacrolimus, mycophenolate, corticosteroids). Good survival rate (100 %) of the animals was seen. Long-term graft survival was proven with a triple immunosuppression therapy. In a human study, women undergoing modified radical hysterectomy, mimicking live donor organ retrieval, were subjected to meticulous surgical dissection of the uterine arteries and veins. Uterine vessels of 50-70 mm lengths were procured, without compromised post-operative recovery of the patients. In another study in deceased multi-organ donors, the procured vascular pedicles included either the lower aorta and vena cava or the bilateral common iliacs. Surgical feasibility of UTx with live donors, with anastomoses to the recipients' bilateral external iliacs, or deceased donors, with anastomoses to aorta and cava or external iliacs was demonstrated by the results of the two human studies.

In summary, autologous and allogeneic UTx have been demonstrated in a nonhuman primate model proving to be a donor- and recipient safe surgical procedure, regardless whether the graft is from a live or a deceased donor. Additionally, feasibility of human uterus retrieval was shown in both deceased donor and in a potential live donor setting without comprising donor safety.

It is concluded that UTx, based on solid experimental research, today stand a good chance of a successful outcome if performed in a facility with experienced expertise following a strict management protocol.

Key words: infertility, human, immunosuppression, nonhuman primates, transplantation, uterus

Göteborg, 2012, liza.johannesson@vgregion.se

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