Medicine and Health Sciences
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Transplantation in the HIV Era:

Should HIV positive donor organs be transplanted in HIV negative recipients?

UNIVERSITEIT STELLENBOSCH UNIVERSITY

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No conflict to declare

- This presentation reflects my personal view and should not be construed to represent any third party's view or policy.

Introduction

- High success rate of solid organ transplantation – even for HIV patients
  - Improved modern immunosupression
- Primary limitation is available donor organs
  - +/- 500 donors for > 100 000 on waiting lists in the USA
- Need to increase the donor pool
- Organs rejected due to safety
- Disease free organs not guaranteed
  - CMV
  - Hep C
  - HIV: reported cases in the literature

Introduction

- Using HIV-infected donors is beneficial for HIV-infected recipients
  - However, potential increased risk of infections in recipients
  - So far good 5 year survival*
  - Caution: limited data yet available
- HIV Organ Policy Equity (HOPE) Act of the USA legalizes HIV-infected organ donation transplantation research#

*Muller et al. NEJM 2010, #Malani P. JAMA 2016

Concerns regarding the HIV+ donor

- HIV superinfection
- Protease inhibitor use
- Latent opportunistic infection
- Acute rejection

Richterman A & Blumberg E. Curr Inf Dis Rep 2015

Concerns regarding the HIV+ donor

- HIV superinfection
  - Important if HIV infections are heterogenous (different clades etc)
  - No detectable viral load as requirement
  - Sirolimus act as a reservoir modifying agent in HIV
  - Measure HIV DNA and RNA in donor's urine to determine viral load and predict risk of superinfection*
- Protease inhibitor use
- Latent opportunistic infection
- Acute rejection

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*Canaud G et al. J Am Soc Nephrol 2014

Concerns regarding the HIV+ donor

- HIV superinfection
- Protease inhibitor use
  - Potential significant medicine interactions with anti-rejection medicines
  - Donor controlled viral load – lead to need for protease inhibitor containing regimen in recipient
- Latent opportunistic infection
- Acute rejection

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Concerns regarding the HIV+ donor

- HIV superinfection
- Protease inhibitor use
- Latent opportunistic infection
  - History of opportunistic infections in donor may necessitate prophylaxis in recipient
- Acute rejection

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Concerns regarding the HIV+ donor

- HIV superinfection
- Protease inhibitor use
- Latent opportunistic infection
- Acute rejection in HIV-infected recipients
  - Immune dysregulation
  - Suboptimal dosing of antirejection medicines
  - Reinfection of organ (example kidney)

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Organ allocation

- Scarce resources
- Need a fair system of distribution
- Different resource allocation systems – each with disadvantages as well

United Network for Organ Sharing

- Organ allocation – 3 principles
  - sickest-first (current medical condition)
  - first-come, first-served (waiting time)
  - prognosis (antigen, antibody, and blood type matching between recipient and donor)
- Advantage – Flexibility
- Disadvantage – prognosis often less important

Persad G et al. Lancet 2009

Ethical arguments

- No for HIV+ to donate to HIV- patients
- Yes for HIV+ to donate to HIV- patients

No for HIV+ to donate to HIV- patients

- Dealing with a particular vulnerable group of patients
- Create an additional burden of disease
- Unknown what other complications may occur
- May need life long HAART
- May have additional organ damage due to HIV infection eg end stage renal disease due to HIV
- Need for more data regarding HIV+ recipients' long term survival after transplant
  - Quality adjusted life years (QALY)
  - Disability adjusted life years (DALY)

Yes for HIV+ to donate to HIV- patients

- Autonomy
- Beneficense/Non-maleficence
- Justice

Richterman A & Blumberg E. Curr Inf Dis Rep 2015

Wispelwey BP et al. J Med Ethics 2015

Yes for HIV+ to donate to HIV- patients

- Autonomy
  - Informed patient decision-making: process intensive
  - Not much different from the CMV risk for recipients of CMV+ donors
- Beneficence/non-maleficence
- Justice

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- Autonomy
  - Informed patient decision-making: process intensive
  - Not much different from the CMV risk for recipients of CMV+ donors
- Beneficence/non-maleficence
  - Must assist in allowing more potential recipients access to organs
  - Improved quality of life
  - Anyway receiving immunosupression, added ART may not be that problematic
- Justice

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  - Informed patient decision-making: process intensive
  - Not much different from the CMV risk for recipients of CMV+ donors
- Beneficence/non-maleficence
  - Improved quality of life
  - Anyway receiving immunosupression, added ART may not be that problematic
- Justice
  - Improved chance of transplantation

Need research: HIV+ donor to HIV- recipient

- Must determine the risk-benefit ratio
- Two approaches to apply to risk-benefit assessment
  - Component analysis
  - Net risks test

Risk-Benefit Assessment: Component Analysis

- Requires state of clinical equipoise
  - Genuine uncertainty
- Posed risks acceptable in the context of the expected benefits
- Applied to this scenario
  - Risks of HIV infection versus life saving transplantation
    - Normal life expectancy on HAART for HIV-infected patients
  - Strict guidelines to be developed – similar to HOPE guidelines

Risk-Benefit Assessment: Net Risks Test

Intervention	Risk/Burden-Benefit Assessment
Organ transplantation	Known risks
HIV-infected donor's organ	Burden: Potential HIV-recipient infection
Net overall risk/burden	*Moderate to severe

*Must minimize risk/burden – again need strict guidelines

Proposed guidelines for HIV+donor to HIV-recipient

- Standardised screening for HIV in solid tumour organ donors – Both HIV-Abs & Nucleic acid amplification testing (NAT)
- Risk of HIV infection in donated organ unknown – Donor should be on HAART with no detectable viral load
  - Need research into latent infection in organs to be transplanted eg kidneys, liver
- Donor should be on first line HAART with not potential for HIV resistance
- Donor should not have any opportunistic infections (need to investigate cause of death carefully)
- Informed consent – lengthy process
  - Vulnerable population
  - Potential need for lifelong HAART
  - Precedent all ready exists with regards to potential fatal CMV infection in organ transplantation

Propose HOPE Criteria: National Institute of Allergy and Infectious Diseases (NIAID) (HIV+ recipients)

	New HIV infection diagnosis	History of HIV infection	Living donor
CD4 count (cells/mm3)	≥200	≥200	≥500 for 6 months prior to organ procurement
HIV VL (copies/mL)	No requirement	≤50	≤50
Antiretroviral resistance	≤1 antiretroviral class	≤1 antiretroviral class	≤1 antiretroviral class
Opportunistic infection	None active	None active	None active No history of: Chronic cryptosporidiosis CNS lymphoma Progressive multifocal leukoencephalopathy

Adapted: Odim J. ICAAC 2014, Washington

Conclusion

- Based on respect for autonomy and from a beneficence/non-maleficence perspective
  - Allow HIV+ organ donation to HIV- recipient subject to
    - Need more research regarding outcome of HIV+ recipients
    - Need intensive standardized screening of organs for HIV infection
    - Strict criteria as mentioned namely donor on HAART with no detectable viral load and complicated opportunistic infections

Thank you for the invitation