Organ perfusion prior to transplantation

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Introduction

• Organ perfusion with blood products prior to transplantation is an emerging technology

• Poses new questions:
  – Compatibility
  – Traceability and fating
  – Multiple ‘recipients’ of blood products
  – Regulatory requirements
Outline

• Demand for novel perfusion technology
• Novel technologies in organ perfusion
• Usage by organ
• Implications of using blood products
• Approach at Guy’s Hospital
Novel perfusion technology

• Static cold storage has been the mainstay of organ preservation for 60 years
• Cheap, easy to deliver and effective
• Novel preservation techniques now being implemented
  – What are they?
  – What is the demand for these?
Organ preservation / perfusion

- Machine perfusion
  - Normothermic 37°C
    - In situ
    - Ex ‘vivo’
  - Hypothermic 4°C
    - Oxygenated
    - Non-oxygenated

- Static cold storage

Blood-based perfusate

Non-blood based perfusate
Why the need?
Deceased donor type over time

Donors after brain death (DBD)  Donors after circulatory death (DCD)

Number


61  73  87  127  169  200  288  335  373  436

716  697  664  637  634  609  611  624  637  652
Deceased donor age over type

Number of donors

Age (yrs)

- 70 or over
- 60 to 69
- 50 to 59
- 18 to 49
- 0 to 17

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Demand for novel organ preservation techniques

• Increasing demand for organs
• Increasing DCD donors
  – Pre-existing ischaemic damage
• Donor quality:
  – Rising age
  – Co-morbidities
• Emerging evidence of organ intolerance to prolonged static cold storage
Organ preservation / perfusion

Organ preservation

Machine perfusion

Normothermic
37°C

In situ

Ex ‘vivo’

Blood-based perfusate

Static cold storage

Hypothermic
4°C

Oxygenated

Non-oxygenated

Non-blood based perfusate
Normothermic Regional Perfusion (NRP)

- Restorage of regional circulation of oxygenated blood in the donor after death
- Major artery and vein cannulated
- Ballon or cross-clamp to thoracic aorta
- Closed circuit of circulating warm oxygenated DONOR blood
Normothermic Regional Perfusion (NRP)

• May improves organ quality (especially liver)
• May expand DCD donor pool
• Organ viability assessment (liver?)
• If allogeneic blood needed: donor-typed
  – Exposure to multiple recipients
• Tracing - captured on HTA-A form under DIN
Organ preservation / perfusion

- Organ preservation
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  - Static cold storage

- Blood-based perfusate
- Non-blood based perfusate
Ex-situ organ perfusion

• Clinical uses:
  – Heart
  – Lung
  – Liver
  – Kidney

• Allows better organ viability assessment

• May resuscitate organ and improve quality
Ex-situ organ perfusion

• This may occur at (any combination of):
  – Donor hospital
  – During transportation
  – Recipient hospital
Kidney EVNP

• Led by Chris Callaghan at Guy’s
• Ex ‘vivo’ normothermic perfusion (EVNP) uses clinical CPB technology to perfuse a kidney with oxygenated pRBCs at body temperature
• Pioneered by the Leicester / Cambridge group
• Possible indications for EVNP:
  – Attempt to reduce rates of DGF
  – Viability testing pre-transplant
Kidney EVNP at Guy’s

Venous reservoir

Primer:
- Heparin
- Ringer’s lactate
- Dexamethasone
- Mannitol
- NaHCO$_3^-$

Flow probe

Pressure transducer

3-way tap

ABG

Temp

36° C

Membrane oxygenator

Centrifugal pump

Ringer’s lactate

Prostacyclin

Dextrose

Insulin

Blood loss from cradle

ABG

Pressure transducer

3-way tap

ABG

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Dextose
Paired kidney comparison

Creatinine Level

EVNP patient
56yo female
CIT 13hr40

Paired control
59yo male
CIT 8Hr01

Sep 2016
Donor with AKI

**Donor**: 17 yo male DBD with severe AKI creatinine 250 umol/L

**Recipient**: 28yo male failing allograft on HD (1 session)
Considerations of using pRBCs on EVNP

- Residual transfused erythrocytes, leukocytes and plasma remain within the organ – compatibility issues?
- Risk of transfusion reaction or transfusion-transmitted infection
- Traceability
  - Law demands evidence of final fate (retained for 30 years)
  - Small (<1/100) chance of changing recipient after EVNP performed
  - EVNP prior to planned recipient arrival in hospital?
- Cross-match to donor, planned recipient, or...?
Approach at Guy’s

- Multiple, complex discussions between EVNP and Transfusion teams
  - Understanding of technology and novel issues
  - No written guidance available elsewhere
  - Evolving clinical use of EVNP has changed the ways that pRBCs were used, requiring revised guidance

- Potential risks balanced against known benefits of transplant and possible benefits of EVNP

- Existing practice with residual donor blood in organ (and transfusions pre-mortem)
Approach at Guy’s

• Consent issues
  – Risks discussed, leaflet given
  – Need for irradiated blood identified

• Additional patient ID band generated and checked

• Band on EVNP machine

• Usual prescription chart with planned recipient addressograph
Approach at Guy’s

- O Rh neg pRBCs from theatre fridge
  - Residual pRBCs
    - Compatible with potential donors / recipients
  - Plasma in pRBCs
    - Too low to cause rejection of kidney
    - Too low to cause haemolysis in recipient
  - Rh
    - Avoid sensitisation if females

- ‘Bedside’ check before giving pRBCs on EVNP
Approach at Guy’s

• Blood bank informed at time of use
• ID band and prescription chart scanned to EPR, and left in paper notes
• ‘EVNP’ in traceability book
• Traceability tag returned to Lab with recipient’s details
• EVNP team trained by Transfusion practitioners
Approach at Guy’s

- Defined pathways for organ re-allocation
  - Recipient at Guy’s
  - Recipient elsewhere
  - Organ discarded
  - Organ sent for research and discarded
Summary

- Emergence of perfusion technologies prior to transplantation
- Pose questions regarding compatibility, unit traceability and fating
- Detailed protocol for use of blood products
- Collaborative effort between transplantation and haematology
- Approaches needed at a local and national level
  - Will vary depending on perfusion technology and local issues
Acknowledgements

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- EVNP lead at Guy’s
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- Vanessa Fulkes and team
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