

# Cord Blood Transplantation

## An update

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## Cord Blood Transplantation

- Biologic waste
- First CBT - Fanconi Anemia: 1988
- Up till now: > 6000 CBT
- More than 40 CBB: Both public & private
- > than 400,000 units stored in CBB
- Children & Adults are being benefited
- Benign & malignant conditions treated

# Why Umbilical Cord Blood for Transplantation

Basically a quest for more safe stem cell donors

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1 / 3 patients: **matched related donors**

1 / 3 patients: **matched unrelated donors (MUD)**

Search time 3 – 4 months

34 % unavailable or refuse

Ethnic minorities under represented.

Inferior outcome

1 / 3 patients: **no related or unrelated donor**

## CORD BLOOD: ADVANTAGES

- Large donor pool & Easy procurement
- No risk to donors
- High self renewal & proliferation
- Less alloreactive: less GvHD
- Less transmission of infections
- HLA mismatch / Multi units permissible
- Feasible for gene therapy
- rapidly available & Stored frozen for years

## CORD BLOOD: LIMITATIONS

- Haematopoietic **recovery delayed**
- Quantity variable – **cell dose ?**
- ? **Less GvL – More Relapse**
- ? **Engraftment in adults**
- **No DLI** if there is a relapse
- Contamination with Maternal Cells

## Hemopoietic Recovery

- Median time to neutrophil recovery: 25 – 30 days
- Shorter for children than adults
- No difference for related or unrelated in children

### Important determinants of engraftment:

#### Cell dose:

Total nucleated cell (TNC):  $> 3.7 \times 10^7$

CD34:  $1.7 \times 10^5$

HLA match: 6 / 6 - 1 -3 / 6 Ag mismatch

Primary disease: Malignant vs Benign

## Graft vs Host disease

- Lower compared to Matched or mud BMT
- May be higher after double UCBT
- HLA match or CD3 dose not correlated in children
- cGvH is more responsive

	Children	Adults
<u>aGvH ( grade II – IV):</u>	3 – 20 %	30 – 70 %
cGvH (extensive):	6 – 14 %	20 – 50 %

## DOUBLE CBT: MYELOABLATIVE THERAPY

- Strategy to overcome the cell dose barrier
- Consistent engraftment observed
- Higher GvH and lower relapse observed

one study with various malignant disorders

Cyclophos: 120 mg/kg

Fludara: 75 mg/m<sup>2</sup>

TBI: 1300 cGy

Engraftment: 91 %

aGvH: 57 %

TRM: 18 %

OS & DFS: 57 & 55 %

## DOUBLE CBT: REDUCED INTENSITY Transplant

- ? Optimal conditioning regimen
- Median time to neutrophil recovery: 9 – 20 days
- Engraftment is sustained
- Sustained donor chimerism seen in 85 – 95 %

Study on 95 high risk patients: median age 50 years

Fludara: 40 mg / m<sup>2</sup> x 5

Cyclo: 50 mg / kg / d x 1

TBI: 200 cGy

TRM 18 %

a/c GvH: 25 / 25 %

OS 50 %

Low Relapse

# CBT IN BENIGN DISORDERS

Has been used successfully in Thalassaemia

High rates of engraftment and survival

Late graft rejection is observed

High cell dose and HLA match CBT suggested

CBT in AAA has not been precisely reported

## CBT in Ac Leukemia: Eurocord study

541 patients with Acute Leukemia

262 Standard BM – More GvH

180 TCD – BM – More relapse

99 HLA mismatched CBT – Early deaths

Probability of survival was same in 3 groups

----- Rocha et al, Blood – 2001

In children, ALL / AML outcomes similar ( DFS at 2y: 35 – 50)

In adults: data is emerging

One study: CBT equivalent to MUD - inferior to HLA match BMT

Another study: Equivalent to MUD

## Summarising

- CB is an important source of Stem Cells
- Simultaneous search for MUD-BM and CB
- Standard alternative in children
- May be considered in adults if no HLA matched donor is available as 1-2 antigen mismatch double CBT are encouraging.

## Results

- Engraftment:
  - ANC . 500 at 28 days average
- GvH: II – IV 37 + / - 7 %
- Survival at 2 years: 49 + / - 8 %
  - same for 5 / 6 & 6 / 6 Ag match
  - same for benign & malignant disorders
- Infection was main cause of TRM

Davey et al, BJH, 2004

# Transplantation: Historical Background

1939: Aplastic Anaemia

1960: 1st BMT (Allogenic) - NHL

1984: 1st PBSCT (Autologus) - CML

1985 -1995: Increasing success of PBSCT

Mobilization, CD<sub>34</sub> antigen, Leukapheresis

1989: 1st CBT - Fanconi`s Anaemia

1995: NST (Mini Transplants)

2000: SC in Regenerative Medicine

# Haematopoietic Stem Cell Transplantation

- Bone Marrow (Allo - BMT)
- Peripheral Blood (Allo - PBSCT)
- Cord Blood (CBT)

Eurocord

Netcord

BMDW

Asia - India

## Cord Blood & Cord Blood Banks

- For centuries CB has been a Biologic Waste
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- Being increasingly used for Transplantation
- Optimum dose of SC for Transplantation ?

## London Cord Blood Bank

- 44 patients with heterogenous disorders
- Follow ups 14 months (3 – 44)
- Median volume 79 ml (40 – 240)
- Median TNC count:  $11.9 \times 10^9 / l$  (10.0 – 24.8)
- Median NC infused:  $4 \times 10^7$  ( 1.1 – 16)
- Average Wt: 29 Kg

