Plasma Fractionation – Issues for Developing Countries

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Plasma Fractionation

- Evolved from a medical service to a global manufacturing industry
- Involves sophisticated industrial process
- High standard of hygiene & quality
- Conforms to principles of GMP
Plasma Fractionation

- 22 – 25 million plasma fractionated annually
- About 70 fractionation plants mainly in developed countries
- Recently – mergers & acquisition
- Technology – mainly cold ethanol process plus modern chromatographic purification technique
- Efficient viral inactivation process
- Extensive removal of prion during fractionation step

Burnouf T: Plasma Fractionation in the world-current status
Fractionated Products

☐ Purer, concentrated products from plasma
☐ Better and safer products
☐ Millions of lives saved or made better
☐ Contributed towards patient management – IVIG making major impact
☐ Improvement in the quality of life – especially haemophiliacs
Developed Countries

- Fractionated blood products – widely used, readily available for treatment of life-long diseases such as haemophilia & other congenital deficiencies
- Dramatic rise in the use of IVIG

Haemophilia
- Best practice – use recombinant products
- Prophylaxis – standard treatment
## CONCENTRATE USE IN DIFFERENT COUNTRIES

<table>
<thead>
<tr>
<th>Country</th>
<th>FVIII Use Index (a)</th>
<th>Economic Index (b)</th>
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<td>Pakistan</td>
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<td>-6</td>
</tr>
</tbody>
</table>

*Stonebraker et al. Haemophilia, 2003*
Virology status of haemophilia patients in Malaysia (2005)

- 94 patients (11.7% of patients) treated with factor concentrate only
- Less than 7 years old
- No HIV and HBV transmission
- 2 cases of HCV – infection was not through concentrates but from cryoprecipitate & FFP used.
Epidemiological data - Venezuela

A life time treatment with cryoprecipitate
- 40% chance of contracting HIV
- 100% risk of HCV

Giangrande P;
Haemophilia World. June 2004
BTS in Developing Countries

- Rely on family replacement donors
- Only 39 countries out of 178 have 100% voluntary donors
- 20 countries do not screen for HIV 100%
- 24 countries don’t screen for HBC 100%
- 37 countries don’t screen for HCV 100%
- A number of countries do not screen at all
- Of the estimated 81 million units of blood 39% comes from developing countries – contributing to a global shortfall of 40 million units annually
Global Population and Blood Supply
Global Data Base on Blood Safety 2001-2002

% Donations: 61 million

% Population:
- High: 61%
- Medium: 36%
- Low: 11%

HDI
- High: 19%
- Medium: 70%
- Low: 3%

BTS

World Health Organization

Health Technology and Pharmaceuticals

Essential Health Technologies
Countries WITHOUT 100% Blood Screening
Global Data Base on Blood Safety 2001-2002

- **HIV**: 152 (100% testing: 152), 21 (Less than 100% testing)
- **HBV**: 145 (100% testing: 145), 28 (Less than 100% testing)
- **HCV**: 106 (100% testing: 48), 68 (Less than 100% testing)
- **Syphilis**: 137 (100% testing: 137), 34 (Less than 100% testing)
BTS in Developing Countries

- Blood is still collected in bottles in the peripheral hospitals in some developing countries.
- Blood grouping & crossmatching done on plates.
- Reagents for TTI screening are bought when there is funding available.
- Reagents for TTI have very short expiry – not uncommon that expired reagents are used.
- Equipment was donated – obsolete after some years, no spare parts, results are adjusted.
- Practices vary from capital city and the peripheries.
Developing Countries

- Making blood available is a major challenge
- Quality of life of transfusion-dependant patient is compromised
- Haemophilia – inadequate treatment; fresh frozen plasma/cryoprecipitate used
- Risk of TTI is high – prevalence of HIV/HBV/HCV in population is high, reagents issues, technology, algorithm....
- Commercial fractionated products are costly – not affordable to all
The current safety of plasma derived products depend on

- Reduction of viral load in source plasma
- Inactivation or elimination of infectious agents that may have escaped screening
- Production process in accordance with principles of GMP
Reduction of viral load in source plasma

- Responsibility of collection centres
- Donor criteria and selection
- Quality system in place
- Appropriate screening tests and algorithm
- Inventory hold of donated units
# Prevalence of TTI markers among blood donors in western Pacific Countries 2001/2

<table>
<thead>
<tr>
<th>Countries</th>
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<td></td>
<td>0.02 (2008)</td>
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<td>ND</td>
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<tr>
<td>Vietnam</td>
<td>1.8</td>
<td>1.7</td>
<td>0.8</td>
</tr>
</tbody>
</table>
New Threats

- New emerging viruses/infective agents
  - GBV
  - TTV
  - Sen V – hepatitis
  - West Nile Virus – no report on transmission through fractionated products
  - Dengue
  - Prion
  - H1N1

Transfusion Transmission but no evidence of pathogenicity
Relationship between Economic Development & the Status of the BTS

- The more developed the economy the better organised the health delivery system.
- The more organised the health system, the better the BTS in terms of organisation, structure, system & operation.
- The more organised the BTS, the better the supply of blood in terms of quantity, quality & safety.
Developing country - Options

- Setting up local fractionation plant
- Regional joint venture
- Contract Fractionation
- Buy Commercial product
- Pathogen inactivation of FFP/
  Cryoprecipitate
Setting a Plasma Fractionation Plant

- Fundamental infrastructure requirement
  - Well organised, centralisation BTS
  - Sufficient & consistent plasma available
  - Efficient & functioning QMS/GMP programme
  - Skilled personnel
  - Large capital funding
  - Regulation & Control
Local Fractionation

Advantages:

- One regulatory body
- Less potential losses due to cold chain failure
- Reduce delay to return finish products
- Reduce cost of freight & warehouse
- Availability in time of emergencies
Regional Fractionation Plant

- Joint venture – a few countries
- Common problems – resources, intellectual capacity, capital cost
- Plasma volume
- Cost effective
- Many national regulatory bodies involved
Contract Fractionation

- Practiced in many countries in Asia
- Surplus of plasma but not enough for setting up a local fractionation facility
- Responsible for procurement of safe, quality plasma
- Integral part of the national blood programme
- Cost effectiveness is achieved
- Two regulatory bodies involved
Responsibility & Accountability

- Both the plasma supplier & fractionators must agree & establish responsibility & accountability
- BTS is obliged to ensure donor criteria & selection, testing & processing of plasma in accordance with international standard
- Fractionators - to ensure safe, quality products, GMP, maximum yield
- Fractionators – need to understand local process & procedures
**Contract Fractionation - Advantages**

- Huge capital cost - not required
- Do not need to depend on one fractionator
- National supply available during global shortage
- The source of plasma is known
- Excess plasma is not wasted
- Improves collection
- Improves quality

- Contract Fractionation WFH 2004
Contract fractionation

- Government commitment – different from other activities in other healthcare establishment they are used to
- Long term contract
- Resources – to establish quality system
- 2 different cultures:
  - govt vs commercial entities,
  - service vs business,
  - red tapes vs outcome,
Purchasing commercial products

- Must have a system of acquiring only safe & quality products
- Regulatory Agency to allow only safe products are imported through well established principles of evaluation
  - selection appropriate plasma raw material
  - screening TTI
  - elimination of virus during processing
  - GMP in production facility
Regulation

- Safeguard public from unsafe products
- System for licensing, regulation and control of plasma products within the national regulatory authority – not strong in plasma derivatives or independent enough
- Developing countries may not have the resources to establish complex regulatory decision-making framework for assessing & choosing products
- Focus on starting plasma
Inadequate volume

Safety – high prevalence of TTI, known reactive donor repeatedly donate blood, testing techniques, testing algorithm, unsafe process & procedure e.g. donor management, quarantine & storage etc.

Quality : Donor management, transport & storage, FFP processing etc.
Challenges in the Developing World

- Getting enough supply
- Getting safer donors & safer blood supply
- Getting adequate resources – people, equipment, reagent etc.
- Achieve better outcome with available resources
- Exploiting potential resources – available in the country but not in the BTS
Major Challenge for Fractionation & Biotechnology Business

- High quality safe factor concentrate
- Affordable for patients in developing countries
Lessons learnt

- It is easier to buy products but it is costly
- Excess plasma will go to waste
- Dependent on commercial products has its disadvantages - depend on world market
- Fractionation programme expedite the quality improvement process
- Getting safe plasma of good quality – needs a lot of hard work
- National agenda – expedite coordination of BTS, improves collection
- Improvement in Regulatory criteria for plasma products – emphasis on plasma master file
- Fractionation programme as part of the Blood Programme in developing countries - safer
Option for Developing Countries

- Strengthen National Blood Programme
- Regulate imported commercial products
- Fractionation – contract/ local plant/joint venture
- Cryoprecipitate/FFP – minimise risk by:
  * donor selection
  * appropriate screening for TTI
  * quarantine until donor returns
- Centralised haemophilia treatment centres
THANKYOU