Postoperative Care in ITU

Dr Elizabeth Sizer
Kings College Hospital
Liver Transplantation For ALF

- Only therapeutic intervention of proven benefit in pts with advanced ALF
- Outcome improved since first cases, but still worse than for CLD
- High early post-op mortality accounts for survival difference
- Most deaths are now as a consequence of MOF and sepsis
- Early neurological deaths less common?
Predictors of survival post transplant : ALF
33 survivors vs 11 non-survivors

• **Pre-op data** : unhelpful
  – On admission: Age, sex, Apache III (67 vs 68), pH (7.34 vs 7.27), creatinine (290 vs 253), INR (8.5 vs 8.6), cerebral oedema (12 vs 9%)
  – Pre Tp: Apache III (81 vs 82), pH (7.35 vs 7.34), creatinine (332 vs 264), Bilirubin (106 vs 94), cerebral oedema (48 vs 45%)

• **Operative data**
  – Listing to Tp (24 vs 24 hrs), donor age (46 vs 42), cold ischaemic time (8.5 vs 11 hrs), whole graft (30 vs 6), steatotic graft (4 vs 3), reduced graft (3 vs 5)*

• **Post-operative data**
  – Day 1 AST (896 vs 2119)**, INR (1.7 vs 2.1)**
  – Day 2 AST (350 vs 991)*, INR (1.44 vs 2.1)**
KCH Data 1994-2004 Super-Urgent listing

- 359 listed, 275 transplanted (77%)
- Aetiologies changing (less POD, more seroneg and other)
- 90 day patient survival:

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>1994-99</th>
<th>2000-2004</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Survivors</td>
</tr>
<tr>
<td>Drug</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Seroneg</td>
<td>38</td>
<td>22</td>
</tr>
<tr>
<td>Other</td>
<td>34</td>
<td>19</td>
</tr>
<tr>
<td>POD</td>
<td>46</td>
<td>32</td>
</tr>
<tr>
<td>Viral</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>All</td>
<td>136</td>
<td>85</td>
</tr>
</tbody>
</table>
Univariate Comparison 90day Survivors/ Non-Survivors

- Age >45yrs
- Non-Caucasian
- POD
- Donor BMI> 24

Multivariate Analysis of Predictors of 90day survival

- Age >45yrs, Non-Caucasian, Donor BMI> 24
What makes a difference?

• Retrospective data
  – Aetiology of ALF
  – Ethnicity
  – Quality of graft/match
  – Renal Function
  – Sepsis

• Little evidence base for post transplant ITU care

• General Principles…
  – Attention to detail
  – Individual patient based care, continual assessment
  – Continue principles of pre-transplant care
Early Post Operative Care

• Continuation of principles of pre-op management, attention to detail
• Depends on patient factors and graft factors
• Whole versus auxiliary grafts
• Specific Problems
  – Cerebral Oedema, ICP, RJ sats, temp, Na+, Vent, Sedation, Drugs
  – Renal failure and fluid management
  – Sepsis
Patient Factors

• Aetiology of ALF
• Risk of Cerebral Oedema
• Preop Condition/ Severity of MOF
• Intraop events
• Type and quality of graft
• Complications
• Time
Graft Factors

• Optimal vs Marginal Graft
  – Early experience (worse outcome with marginal, size reduced or ABO incompatible grafts)
  – Risk-Benefit balance whilst waiting for optimal graft

• Whole vs Auxilliary
  – Theoretical attraction, allows potential regeneration. Technically demanding, patient selection important, residual ‘toxic’ liver

• Early Graft Function
  – Pivotal to good outcome, extrahepatic organ dysfunction perpetuated by early graft dysfunction. Rapid resolution with good graft function.

• Monitors of Graft Function
  – Difficult (Clinical experience & Gut feeling)
  – Standard monitoring, Lactate, pH, INR, bleeding, Glucose, Pressor requirement, ICP, AST and decrement, Doppler USS
  – ICG clearance
What are the problems?

- Multiple!
  - Sepsis
  - Cardiovascular failure
  - Renal failure
  - Immunosuppression
  - Coagulopathy/Thrombocytopenia
  - Encephalopathy
  - Insulin resistance
  - Glucose, Sodium, Potassium, Magnesium, Phosphate
  - Energy requirements
  - Metabolic acidosis
  - Diagnosis and assessment
  - Speed of deterioration and management planning
Practicalities…
‘How long to manage as a Fulminant?’

• RRT
  – Early vs late
  – Standard vs HVHF (SIRS & Shock & ICP etc.)

• Duration of
  – Sedation,
  – Cooling
  – Standards of care, monitoring
Renal Failure & Renal Replacement. Why & How to do it?

- Prognostic factor?
- Common 45%, Multifactorial aetiology
- Facilitates fluid balance, feeding, metabolic control, allows other modalities of therapy.
- Extrapolation from Sepsis? CVS modulation etc
- Continuous mode: CVS & CNS stability
- The faster the better? Standard dose vs HVHF & VHVHF
- Buffer choice (Bicarb vs Lactate)
- Anticoagulation
Abdominal Compartment Syndrome

- Relatively common
- Problematic both pre and post transplant
- Incidence (pressure >25mmHg) ? 31%
- Major effects organ function (renal, respiratory, cardiovascular, liver & gut)
- Multifactorial Aetiology
- Measure routinely (bladder, gastric)
- Laparostomy, Skin only closure
Encephalopathy/ Resolution

• With good graft function risk of cerebral oedema & ICH reduced dramatically by 48hrs. Return of autoregulation, diminished hyperaemia
• Plan to start rewarming at 36hrs
• Risk/Benefit …Sepsis
• Maintain tight metabolic control and wean gradually
• Recrudescence of ICH with sepsis
• Removal Of ICP monitor?/ RJ line
• Management of intracranial hypertension as for pre-transplant (Cool, Sedation, NaCl, Indomethacin etc)
• Clinical parameters guide management
Sepsis

- Major cause of early mortality
- ‘High’ risk prophylaxis (Abx & Antifungal)
- Viral infection important (CMV, HSV)
- Low Index of suspicion, culture everything
- Sepsis vs SIRS
- Vicious cycle of sepsis and graft dysfunction
- Multiresistance
- APC
Lung Injury

- Hypoxaemia common, diverse aetiologies:
  - ACS, reperfusion syndrome, primary and secondary lung injury, effusions, sepsis, RV dysfunction
  - May see rapid resolution in first few hours post transplant
- ALI/ARDS associated with MOF, high mortality
- Manage along conventional lines, monitoring etc
- Discuss proning with surgical team!
- ?HFOV in post transplant patients (100% mortality, oscillatory PV flow)
Housekeeping

- Metabolic Control (Glucose, Na, Mg)
- Invasive Monitoring
- Line Care
- Fluid Balance
- Feeding
- Immunosuppression, Drugs, Prophylaxis
- Respiratory wean, Tracheostomy
Standard dose 35 ml/kg: hyperlactataemia and vasopressor dependency awaiting OLT increase dose
Historical controls: Longer period to OLT in HVHF 44% vs 20% were transplanted

50% survival with ARF and ALF
Renal support and Liver failure

_Davenport et al Crit Care Med 1993 21(3) 328-38_

- 32 patients with ALF and ARF - Rx with HD or CAVH or CAVHD

- Differences were seen with a significant fall in:-
  - Cardiac index 15 ± 2% in HD group vs 3 ± 3% in the CAVH or CAVHD group
  - Mean arterial pressure fell in the HD group 82 ± 2 to 66 ± 2 mmHg with no change with the continuous modes of renal support
  - ICP rose with HD

- Continuous modes result in superior CVS and CNS Stability.
Cerebral oedema and renal failure

- Patients with FHF have specific problems
  - low MAP, encephalopathy, development of cerebral oedema
- Aetiology of cerebral dysfunction unclear
  - vasogenic and cytotoxic mechanisms, cerebral hypoxia, fitting
  - monitor with reverse JV line, CFM, ICP bolt
- Allows control of osmolarity following treatment with mannitol (first line therapy for increased ICP)
- Fluid balance and serum Na is optimised
Cerebral oedema and renal failure
Davenport et al Nephron Dial Transplant 1990 5 (3) 192-8

- Control of ICP and CPP are better achieved with continuous modes of therapy
  - 6 pts had intermittent Rx and 4 CAVH
  - intermittent Rx resulted in
    - increases in ICP from $9 \pm 1.4$ to $13 \pm 1.8$ mmHg
    - a fall in MAP from $92 \pm 2.7$ to $81 \pm 3.2$
    - fall in osmolarity $314 \pm 4$ to $309 \pm 4$ mOsm
  - no changes were seen in these parameters with CAVH
Cerebral oedema and renal failure


• Intermittent HF (6) vs CAVH (4) in FHF with ARF
• ICP 8.9 ± 1.4 to 14.8 ± 2.1 with IHF (p<0.05)
• ICP 19.4±4.8 to 11.2 ± 2.3 with CAVH
• ICP > 25 mmHg for 5 minutes or more on 11 occasions with IHF
• No such surges seen in CAVH group
Renal Support

• Renal replacement therapy in ALF
  – Continuous filtration rather than intermittent dialysis
  • Improved metabolic, cardiovascular stability in ALF
  – Additional benefits from high filtration rates?
    • Improved survival >35 ml/kg/hr
    • Improved haemodynamic stability?
    • Mediator clearance?
Metabolic Support

– Normalisation of electrolytes
– Glucose
  • Van der Berge et al NEJM 2001;345:1359-67
  • Tight control 4-6mMol/l
– Sodium
  • Murphy et al Hepatology 2004;39(2):464-70
  • Continuous infusion 30% NaCl
  • Target 145-150 mMol/l
Hypernatraemia

Murphy et al Hepatology 2004;39(2):464-70

– Prospective RCT of moderate hypernatraemia
– 30 ALF patients; Grade III or IV
– All with ICP monitoring
  • Feasibility / safety of use
  • Effects on ICP, onset of ICH
– Randomised to
  • SMT
  • SMT and 30% saline by infusion; target 145-155 mMol/l
Hypernatraemia
Murphy et al Hepatology 2004;39(2):464-70

Increase in serum sodium in treatment group (p<0.01)

Reduction in ICP in treatment group (p<0.005)

Reduced risk of intracranial hypertension (p<0.05)

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP &gt;25 mmHg</td>
<td>3 (20%)</td>
<td>7 (47%)</td>
</tr>
<tr>
<td>Time of ICH (hrs)</td>
<td>30 (12-96)</td>
<td>12 (1-42)</td>
</tr>
<tr>
<td>Early deaths</td>
<td>3 (20%)</td>
<td>6 (40%)</td>
</tr>
<tr>
<td>Cerebral MOF</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>ICU deaths</td>
<td>8 (53%)</td>
<td>7 (47%)</td>
</tr>
</tbody>
</table>
Summary

• **Prompt diagnosis**

• **Comprehensive supportive care**
  – Optimise circulating volume
    • Appropriate vasopressors/ionotropes
  – Low threshold for antimicrobial therapy
  – Metabolic stability
    • Glycaemic control / moderate hypernatraemia
  – Continuous hemofiltration
    • Appropriate dose
  – Nutritional support
    • Enteral, Protein 0.7-1 g/kg/day

• **Early transplantation of ‘Non-survivors’**