Acute Renal Failure in Neonatal Intensive Care Unit (NICU)

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Case Study

- 28 week Premature infant 950g
  - Stormy antenatal course - premature rupture of membranes & chorioamnionitis
  - Poor Apgars - needed ventilation

- Week 1 develops PDA
  - Treated successfully with Indomethacin

- Also develops Sepsis
  - Rx Ampicillin / Gentamicin

- Necrotizing enterocolitis - oliguria
  - Bowel perforation - theatre

- Shocked, anuria & oedematous - fluid boluses

- Unable to adequately establish feeding
Incidence of Acute Renal Failure (ARF) in NICU

- ARF in the newborn is a very common problem:
  - 3 - 8% NICU admission - Agras PI Renal Failure 2004
  - 6 - 24% of newborns - Andreoli S. Sem in Perinatal 2004
  - Frequently multifactorial in origin

- Acute Renal Failure in PICU
  - 4.5% - Bailey D Ped Critic Care 2007

- Mortality in babies with ARF
  - 25 - 50% - Moghal N Sem in Fet & Neon Meds 2006
NICU
467 consecutive admissions/1 year
Lunn AJF et al. Arch Dis Child Fetal Neon ed 2006;91:F388-390

- ARF plasma creat >100umol/l @ 48hrs age
- Total 8.8% admissions
  - 37% <28wks
  - 8% 28-32wks
  - 4% 33-36wks
  - 2% Term infants

- Causes - multifactorial:
  - Sepsis 39%
  - Perinatal asphyxia 17%
  - Hypotension 10%

- Prophylactic Indometacin - Vent <1000g
- Death in 24%
Embryology

- Nephrogenesis continues to 34 weeks gestation
- Ischaemic/Hypoxic and toxic insults
  - Potentially interrupts nephrogenesis
  - ARF
  - Also long term complications
ARF

Traditional Classification

Haycock GB. Semin Neonatol 2003 Aug;8(4):325-34

- Failure of Renal Perfusion
  - Pre-renal

- Damage to Renal Parenchyma
  - Intrinsic renal

- Obstruction of Urinary tract
  - Post-renal “obstructive”
ARF according to urine output

- **Oligo/anuria**
  - Newborns with pre-renal failure
  - Due to hypoxia/ischaemic insults - ATN
  - Cortical necrosis

- **Normal urine output**
  - Nephrotoxic insults - aminoglycoside and contrast nephropathy
Pre-renal Failure

Decreased renal perfusion in intrinsically normal kidney

- Restoration of normal renal perfusion results in return to normal renal function

- Acute tubular necrosis (ATN) implies kidney has suffered intrinsic damage

- Evolution of pre-renal to renal failure is not sudden
  - number of compensatory mechanisms work together
Renal Hypoperfusion

- **Afferent arteriole**
  - relaxes its vascular tone & decrease vascular resistance
  - maintaining renal blood flow

- **Increased catecholamine secretion**

- **Activation of renin angiotensin system**

- **Generates Prostaglandins (PG’s)**
  - Vasodilatory PG’s including prostacyclin
  - Mediates vasodilatation of renal microvasculature
  - Maintains renal perfusion
Aspirin or NSAID's

- Inhibit PG’s and thus affects compensatory mechanism
  → precipitated renal insufficiency during hypoperfusion

- Indomethacin for PDA’s - risk of renal insufficiency
  - 56% reduction in urinary flow rate
  - 27% reduction in GFR
  - 66% reduction in free water
Aspirin or NSAID’s

- Indomethacin vs Ibuprofen
  Thomas RL. Europ J of Ped 2005;164(3):135-140

- Selective Cox-2 inhibitors no better

- Increased risk if:
  - Premature - 40% alteration in renal function
  - Infant abn renal function prior
  - Mother’s received indomethacin
  - Chorioamnionitis
Case Study

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Acute Tubular Necrosis (ATN)

- Pre-renal failure evolves if severe enough to cause vasoconstriction & ATN

**Urine analysis:**
- Unremarkable or
- Low grade proteinuria & granular casts
- Abnormal tubular function - not conserving Na and H2O

**Serum Creatinine** rises 0.5-1.0 mg/dL/day

**Radiology**
- Normal size kidneys with loss of corticomedullary differentiation

**Radionuclide renal scan**
- Poor function & delayed accumulation in renal parenchyma with no excretion of isotope
Prognosis of ATN

- Good
- Unless insult severe enough
  - Vasculature injury + microthrombi formation
  - Subsequent cortical necrosis
- Length of recovery variable
  - Days to weeks
- Diuretic phase - prevent additional injury
- Long term follow-up - late complications
- Mortality & morbidity worse in ARF in neonates with multiorgan failure

Andreoli S Curr Opin Peds 2002
Nephrotoxic Acute Renal Failure

- Endogenous agents
  - haemoglobinuria, myoglobinuria

- Drugs
  - Aminoglycosides
  - NSAID’s
  - Intravascular contrast
  - ‘Ampho-terrible’
Aminoglycosides

- Non-oliguric acute renal failure
- Urinalysis - minimal urinary abnormalities
- Toxicity related to
  - Dose & duration
  - Level of renal function prior to drug
- Aetiology - lysosomal dysfunction of prox tubule and is reversible
- After discontinuation of drug - creatinine may continue to increase for few days
  - Ongoing tubular injury due to high levels
  - Once daily dosing
Vascular Insults

- Renal Artery Thrombosis
- Renal Vein Thrombosis
Vascular Insults
Cortical necrosis

- Assoc with hypoxic/ischaemic insults
- Gross/microscopic haematuria, oliguria, hpt
- Raised Urea and Creatinine
- Thrombocytopenia
- U/S
  - normal(early)
  - then atrophy & decrease in size
- Nuclear Renal Scan
  - decreased/no perfusion with delayed/no function
- Partial or no recovery - risk of CRF later
Medical management

- Fluid management
- Electrolyte status
- Acid-base balance
- Nutrition
- Renal Replacement Therapy
Medical management
Diuretics - Mannitol

- Stimulates urine output
- Conversion of oliguric to non-oliguric ARF
  - does not alter course of ARF
- Mannitol 0.5 - 1g/kg may
  - Increase intra-tubular urine flow to limit tubular obstruction
  - Limit cell damage by prevention of swelling
  - Act as scavenger of free radicals
- Lack of response
  - Hyperosmolality and precipitates CCF
Medical management
Diuretics - Frusemide

- Also increases urine flow rate to decrease intra-tubular obstruction
- Inhibits Na/K/ATPase
  - Impact on oxygen consumption in already damaged tubules with low O2 supply
- Problems: high doses in ARF assoc with ototoxicity
- Trial of therapy: 1 - 5 mg/kg dose
  - Unresponsive to Rx - continued high doses unlikely to be beneficial
  - Do Respond - continuous infusion effective with less toxicity
Medical management

Dopamine

- ‘Renal Dose’
- Promote renal perfusion and improves urine output by promoting natriuresis
- But...studies in adults does not
  - Decrease need for dialysis
  - Improve survival

- Not effective in paeds either...but neonates?
Medical management
Hypokalaemia

- Newborns with K>6.5mmol/l in absence of ARF

- **Cardiac toxicity** - tall peaked T’s → v/tach & v/fib

- Combination of **insulin & glucose** preferred over cation resin
  - Borderline improvement of mortality
  - Reduction in incidence of IVH > grade 2

- **Albuterol** inhalation decreased K+ at 4 & 8hrs

- **Other Rx for ↑K+** - diuretics, exchange transfusion, PD and Calcium still needs RCT testing
Medical management

- Mild Hyponatremia - very common in ARF
  - Fluid overload with dilutional hyponatremia
  - Less commonly - hyponatremic dehydration

Management
- $> 120 \text{ meq/l}$ - fluid restrict or dialysis
- $< 120 \text{ meq/l}$ - correction to level of 125 meq/l

- Hypocalcaemia - ionised Ca
- Hyperphosphatemia
- Acid base disorders
Medical management

- Marked cat abolism
- Early Enteral feeding if possible
- Feeds compromised due to fluid balance issues
  - Earlier initiation of dialysis
"It's still hungry... and I've been stuffing worms into it all day."
Renal Replacement Therapy (CRRT)

- Peritoneal Dialysis (PD)

- Haemodialysis intermittently

- Haemofiltration / Continuous Veno-veno haemofiltration (CVVH) - with or without dialysis circuit
RRT
Peritoneal Dialysis

YES
- Easy to perform – practical & training
- Does not require heparinisation
- Difficult venous access
- Haemodynamically unstable babies

NO
- Slower correction of metabolic parameters
- Potential for peritonitis
- Frequent exchanges required in babies
- Recent abdominal surgery
RRT
Peritoneal Dialysis

■ Italian study: Neonates requiring RRT
  - Due to oligoanuria / fluid overload
  - 11/12 patients PD as only form of RRT
  - UF = 5 - 20ml/hr with up to 200ml/24 hr
  - Creat clearance 2-10ml/min/1.73m²

■ USA: New Catheters - Multipurpose drainage catheter (Cook)
  - Bedside placement
  - Effective dialysis with satisfactory complication free survival
**RRT PD and Ultrafiltration**

- Turkey: Complex Congenital Cardiac patients
  - Neonates & Infants < 1yr - 756 patients
  - All cases received peri-operative ultrafiltration
  - 186 patients (24.6% of total) required PD
  - Combination of modalities
    - Post-op negative fluid balance with improvement of outcome
      » Alkan T et al. ASAIO J 2006 Nov;52(6):693-7
Haemodialysis for babies

- Technologically ‘challenging’
- Trained staff
- Equipment
  A machine for haemodialysing very small infants
  - Everdell NL. Med Eng Phys 2007 May;29(4):516-24
  - Priming volumes as low as 6.8ml vs 15-40ml
  - Manual – now computer operated
Long term follow-up after ARF

- ARF may result in long term renal dysfunction
- Low birth weight babies at risk
  

- Signs of kidney injury
  - Microalbuminuria
  - Hyperfiltration (Schwartz GFR > 150 ml/min/1.73 m²) or Decreased GFR
  - Haematuria
  - Hypertension

- Survival rate 56.8% (initial hospitalisation + those died subsequently)
  - High proportion of ARF deceased 3-5 yrs after event

Acute Renal Replacement Therapy
in Developing Countries

MI McCulloch, PJ Sinclair, P Gajjar,

Departments of Paediatric Nephrology & PICU
Red Cross Children's Hospital (RXH)
Acute Renal Failure

- Increasing incidence in association with multi-organ failure in paediatric ICU's
- 1200 - 1400 admissions per year
  - Acute medical cases: 600/yr
  - Cardiac cases: 250/yr
  - Burns: 50/yr
  - Head injuries: 50/yr
  - Other: Rest
- Mortality: 10%
- Dialysis: 3.5%
## Causes of Acute Renal Failure

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>46 (22%)</td>
</tr>
<tr>
<td>Post-cardiac surgery</td>
<td>36 (17%)</td>
</tr>
<tr>
<td>Undiagnosed chronic renal disease</td>
<td>21 (10%)</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>19 (9%)</td>
</tr>
<tr>
<td>Haemolytic uraemic syndrome</td>
<td>19 (9%)</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>15 (7%)</td>
</tr>
</tbody>
</table>
## Causes of Acute Renal Failure

<table>
<thead>
<tr>
<th>Cause</th>
<th>Cases (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukaemia/ Lymphoma</td>
<td>14 (6%)</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>11 (5%)</td>
</tr>
<tr>
<td>Rapidly progressive nephritis</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Trauma/ Burns</td>
<td>8 (4%)</td>
</tr>
<tr>
<td>Toxin ingestion</td>
<td>7 (3%)</td>
</tr>
<tr>
<td>Kwashiorkor**</td>
<td>6 (3%)</td>
</tr>
</tbody>
</table>
### Equipment

<table>
<thead>
<tr>
<th>Description</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total catheters used</td>
<td>260</td>
</tr>
<tr>
<td><strong>Cook</strong></td>
<td></td>
</tr>
<tr>
<td>- 5 Fr Neonatal</td>
<td>53</td>
</tr>
<tr>
<td>- 8 Fr Pediatric</td>
<td>106</td>
</tr>
<tr>
<td>- 11 Fr Adult</td>
<td>4</td>
</tr>
<tr>
<td><strong>Kimal “peel away” Percutaneous Tenckhoff</strong></td>
<td>46</td>
</tr>
<tr>
<td><strong>Surgical inserted Tenckhoff</strong></td>
<td>51</td>
</tr>
</tbody>
</table>

- (62%)
- (18%)
- (20%)
Complications related to PD Jan 2000 - Dec 2001

- 68 patients received acute peritoneal dialysis
- 17 Catheter related problems (25%)
  - Blockage in 16 - all Cooke catheters
  - Bowel perforation in 1 case
- Infection seen especially if catheter left in longer than 5 days
## Perit Dial Int 2001
Flynn et al (Brophy & Bunchman)

<table>
<thead>
<tr>
<th></th>
<th>RXH</th>
<th>Flynn (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time period</strong></td>
<td>2 yrs</td>
<td>10 yrs</td>
</tr>
<tr>
<td><strong>Nos of patients</strong></td>
<td>68</td>
<td>63</td>
</tr>
<tr>
<td><strong>Complication Rate</strong></td>
<td>25%</td>
<td>25%</td>
</tr>
<tr>
<td><strong>Commonest problem</strong></td>
<td>Cat het er blockage</td>
<td>Cat het er malf unct ion</td>
</tr>
<tr>
<td><strong>Survival</strong></td>
<td>61%</td>
<td>51%</td>
</tr>
</tbody>
</table>
# Acute Peritoneal Dialysis

**January 1999 to January 2004**

<table>
<thead>
<tr>
<th>Age at dialysis</th>
<th>Total Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 months</td>
<td>79 (38%)</td>
</tr>
<tr>
<td>3 months - 1 year</td>
<td>45 (21%)</td>
</tr>
<tr>
<td>1 - 6 years</td>
<td>38 (18%)</td>
</tr>
<tr>
<td>6 - 12 years</td>
<td>30 (14%)</td>
</tr>
<tr>
<td>&gt; 12 years</td>
<td>20 (9%)</td>
</tr>
</tbody>
</table>

**TOTAL NUMBER OF PATIENTS**

- Total: 212
  - Male: Female: 102:110
# Acute PD

## Long term outcome

<table>
<thead>
<tr>
<th>Survival following Acute PD</th>
<th>130 (61% )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic PD required following Acute PD</td>
<td>26 (12% )</td>
</tr>
<tr>
<td>Total nos of patients requiring CVVHD (PD not possible)</td>
<td>20 (9% )</td>
</tr>
<tr>
<td>Survival following CVVHD</td>
<td>11 (55% )</td>
</tr>
</tbody>
</table>
Peritoneal Dialysis as a Form of CRRT for Infants in a Developing Country

McCulloch M, Argent A.
Red Cross Children’s Hospital
University of Cape Town
Red Cross Children’s Hospital Experience
Aug 1998 - Feb 1999

- 70 Children <13 years old dialysed
- 25 of these patients were <5kg
- 15/25 Infants (60%) survived
- Age range from 2 - 138 days
- Male:Female 2:1
Diagnosis of Infants Surviving Dialysis

**INFECTIVE CAUSES**
- Septicaemia
- Diarrhoea
- Fungal sepsis

**SURGICAL CAUSES**
- Necrotising Enterocolitis
- Cardiac Surgery - TGA’s
- Abdominal Surgery
13/15 patients received large doses of Furosemide e.g. 5mg/kg dose pre-dialysis

10/13 patients were on Dopamine infusions at time of dialysis

2 patients received Adrenaline infusions in addition

7/14 patients were on an Aminoglycoside antibiotic (amikacin/gentamicin) pre-dialysis
Weight of Infants surviving Dialysis

- <1kg
- 1-2kg: 6
- 2-3kg: 2
- 3-4kg: 5
- 4-5kg: 1

Diagram showing the distribution of infant weights surviving dialysis.
Advantages of Acute PD Catheters

- No bleeding complications
- 2/15 catheters blocked - day 3 and 4 on dialysis
- Replaced 1 catheter by “re-wiring”
Practicalities of Dialysis

**Fluid Volumes:**
- Small volumes to avoid raised intraperitoneal pressure
- Fischbach M. Perit Dial Int 1996
- 20 ml/kg/cycle
- Adapted to ventilatory requirements

**Cycle duration:**
- Short dwell times to optimize ultrafiltration
- 45 - 60 minute dwell cycles
- Continuous dialysis over 24 hours
Manual dialysis
Automated Dialysis
Home choice machine
Duration Of Dialysis

- 0-24hrs
- 24-48hrs
- 48-72hrs
- 72-96hrs
- 96-120hrs
- 120-144hrs
Added Benefit of Dialysis

- Fluid overloaded infants - “Wet lungs” with difficult ventilation
- Reduce maintenance fluid volumes to minimum e.g. 40 ml/kg/day
- Use combination of 1.5% or 4.25% dianeal to maintain blood glucose
- Use glucose concentration in dianeal to allow severe fluid restriction (not usually tolerated in these small infants)

→ Allows space for feeding/ fluids
OUTCOME

- 15/25 (60%) Infants survived to come off dialysis
- Nil required long term dialysis
- 3 Subsequently demised - not related to dialysis:
  - 1 accidental extubation
  - 1 Cerebral Palsy and developed septicaemia 1 year later
  - 1 Shock & Dehydration due to excessive colostomy losses 3 months later
COMPLICATIONS RELATED TO DIALYSIS

- 2 blocked catheters - 1 case size 5Fr catheter changed for a 8Fr catheter
- No bleeding problems related to catheter
- No infections related to peritoneal dialysis
- Hyponatremia related to dialysis not a problem
  - Na ranged from 129-138 mmol/l
CONCLUSIONS

- Peritoneal Dialysis is a safe and effective method of continuous renal replacement therapy in infants.
- Rapid insertion and safety profile makes it possible for use even in smallest infants.
- Glucose content in Dianeal allows severe fluid restriction without hypoglycaemia.
Conclusion

- Peritoneal Dialysis is a relatively easy procedure for acute dialysis even in small babies.
- It can be life saving for children.
- It is appropriate in the African setting, as it does not depend on expensive technology.
  - Even in adequately resource countries
- Survival rate is comparable to our previous audits and also to continuous haemodialysis used in other paediatric units
Take home message

- Prevention of ARF in Neonates NB
- Identify high risk infants
- Beware toxins - especially drugs
- Dialysis is possible even in smallest infant
  - Peritoneal dialysis still has a role
  - Especially in low resource countries
- Long term follow-up necessary
  - Call a friend - paeds nephrologist!