Neonatal Renal Function and Failure

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Session Summary

Homeostasis of the newborn is dependent upon a functioning renal system. The immature renal system of the newborn responds slowly and erratically to physiologic changes and demands that are placed on it. Knowledge of renal physiology and embryological development is essential in caring for these newborns, as renal disease, specifically renal failure, is common in ill neonates.

Acute renal failure (ARF) in the neonatal period has been recognized with increasing frequency and may occur in as many as 8% of infants in neonatal intensive care units. This lecture presents a practical overview of ARF in the newborn, reviewing practical considerations regarding diagnosis, recognition, and management of the infant with acute renal failure.

Session Objectives

Upon completion of this presentation, the participant will be able to:

- differentiate between pre-renal, intrinsic, and post-renal causes of renal injury in the newborn;
- discuss the differences in neonatal vs. adult renal function;
- indicate the practical laboratory/radiology tests used to evaluate renal injury;
- discuss the evaluation and management of the newborn with renal injury.

References


### Session Outline

See handout on the following pages.
Neonatal Renal Function & Injury

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- At end of this lecture participants will be able to:
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  - discuss the evaluation and management of the newborn with renal injury.

Function of Kidney
- Non-excretory functions
  - Produces renin
  - Produces erythropoietin
  - Metabolizes vitamin D
  - Degrades insulin
  - Produces prostaglandins

- Excretory functions
  - Maintain plasma osmolality
  - Maintain electrolyte balance
  - Maintain water balance
  - Excretes nitrogenous end products

Nephron
- Functional unit of kidney
- Nephrogenesis
  - Begins @ 7-8 weeks EGA
  - Completed by 34 wks EGA
- Three major functions
  - Filtration
  - Reabsorption
  - Secretion

Renin Angiotensin Aldosterone System (RAAS)
- Stimulation leads to:
  - Systemic vasoconstriction
  - Sodium retention
  - Expansion of ECF
- Renin
  - Juxtaglomerular cells
  - Walls of afferent arteriole
Renin Angiotensin Aldosterone System

- GFR is reflective of renal function
  - Plasma creatinine is best clinical measure of GFR

Medications and Renal Function

- Lasix
  - Loop diuretic
  - Blocks reabsorption of Cl-
  - Increases RBF
  - Impairs Ca++ & Mg++ reabsorption
  - Onset of action & duration differs in neonates

- Thiazides
  - Acts on distal tubule
  - Augment K+ wasting
  - Stimulate Ca++ resorption
- K+ sparing
  - competitive inhibition of aldosterone
  - Potassium retained

- Theophylline
  - Mild diuretic effect
  - Inhibits Na+ reabsorption

- Dopamine
  - Dilation of renal arteries
  - Inhibits Angiotension II
  - Inhibits ADH release

- Indocin (PGE inhibitor)
  - Inhibits cyclooxygenase pathway
  - Decreases GFR
  - Increases ADH secretion
    - SIADH
    - ↑ reabsorption of H2O & decreased UOP
**Acute Renal Injury**

- Loss of water & electrolyte homeostasis
- Secondary to abrupt decrease in GFR
- Associated with a decrease in UOP
  - progressive rise in BUN & Cr
  - Levels above 130 mcmol/l (1.5mg/dl) considered indicative of renal impairment in the newborn

**Risk Factors for ARI Development**

- Multifactorial
  - Sepsis (39%)
  - Perinatal asphyxia (17%)
  - Hypotension not associated with sepsis (10%)
  - “Just being premature” (32%)

**Incidence of Acute Renal Injury**

- Incidence varies between 8 – 24%
- Lunn (2006) – 467 admissions to NICU
  - 8.8% fulfilled diagnosis of ARF
    - 37% of infants less than 28 weeks (23 of 63)
    - 8% of infants between 28-32 weeks (10 of 123)
    - 4% of infants between 33-36 weeks (4 of 93)
    - 2% of term infants (4 of 188)

**Risk Factors for ARI Development**

- Cataldi et al (2005) - Case-control study of 172 preterm infants (<38 weeks gestation)
  - 71 had ARF
  - 101 control cases matched for sex, gestational age, weight
  - 78% cases of ARF <1500 grams
  - Most presented by day 4
  - ARF usually transient
  - Increased usage of cephalosporins, ibuprofen, furosemide in case vs control
  - Higher percentage of cases had medullary hyperechogenicity (25% vs 5%)
  - Increased severity of RDS seen in case vs control

**Acute Renal Failure**

- Three categories
  - Prerenal ARF (80%)
  - Intrinsic ARF (11%)
  - Postrenal ARF (3%)

**Prerenal ARF**

- State of relative hypoperfusion
- Predisposing conditions
  - Hypotension
  - Hypovolemia
  - Hypoxemia
Prerenal ARF

- Dehydration
- RDS
- CHF
- Asphyxia
- Septic shock
- Hemorrhagic conditions
- Cardiac surgery

- Uncorrected prerenal ARF can progress to frank renal damage leading to intrinsic ARF!

Intrinsic ARF

- Loss of renal function due to structural damage
- Associated conditions
  - Acute tubular necrosis
    - Hypoxemia
    - Perinatal asphyxia
    - Prolonged hypoperfusion
    - Direct nephrotoxic injury

- Associated conditions
  - Infection/inflammatory
  - Vascular conditions
    - Aortic & renal artery thrombosis
    - Renal vein thrombosis
    - DIC
  - Congenital renal abnormalities

Postrenal ARF

- Secondary to obstruction of urine flow
  - Generally considered reversible
- Associated conditions
  - Bilateral ureteropelvic junction obstruction (UPJ)
  - Posterior urethral valves
  - Neurogenic bladder

Differential Diagnosis (Review of History)

- Family history
- Oligohydramnios
- Increased maternal alpha-fetoprotein
- Hearing disorders
- Maternal drugs
- Vesico-ureteral reflux
- IDM
- Hypertrophied placenta
- Umbilical cord anomalies
- Void
- Spontaneous pneumo-thorax
Differential Diagnosis
(Review of Physical)

- Thorough physical examination
  - Renal masses are most common abdominal masses in the NB
  - Hydrops or ascites
  - Isolated ear anomalies

Differential Diagnosis
(Laboratory Studies)

- Creatinine
  - Best clinical measure of GFR
  - Five days to reflect neonatal values
  - Levels above 130 mcmol/l (1.5mg/dl) considered indicative of renal impairment in the newborn
    - Levels influenced by gestation and postnatal age
    - Gestation –and-age based reference charts should be used in interpretation of creatinine values in the VLBW
    - ↑ 0.3-0.5 mg/day abnormal

Differential Diagnosis
(Laboratory Studies)

- Urinalysis: reflects structure of tubules
  - Protein
  - Blood
  - Pyuria
  - Microscopic exam
    - Epithelial cells
    - Casts

Differential Diagnosis
(Laboratory Studies)

- Urine indices: reflect functional ability of the renal tubules
  - Calculate FeNa (fractionated excretion of sodium)
  - FeNa (%) = \( \frac{U\text{ Na}}{P\text{ Na}} \times \frac{U\text{ Cr}}{P\text{ Cr}} \times 100 \)

Mean Plasma Creatinine (µM/l) (10th, 90th Percentiles) with Postnatal Age During First 6 Weeks

<table>
<thead>
<tr>
<th>Age</th>
<th>22-24 weeks (n=33)</th>
<th>25-26 weeks (n=50)</th>
<th>27-28 weeks (n=72)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>192 (158, 212)</td>
<td>172 (139, 194)</td>
<td>164 (137, 187)</td>
<td>0.2</td>
</tr>
<tr>
<td>24 h</td>
<td>110.6 (90, 124)</td>
<td>103.8 (84, 122)</td>
<td>98.1 (80, 120)</td>
<td>0.06</td>
</tr>
<tr>
<td>48 h</td>
<td>118.3 (99, 140)</td>
<td>112.2 (83, 143)</td>
<td>100 (82, 122)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 3</td>
<td>117.7 (97, 143)</td>
<td>111.3 (79, 143)</td>
<td>108.8 (80, 126)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 7</td>
<td>112.8 (84, 151)</td>
<td>112.1 (83, 133)</td>
<td>88 (69, 108)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 2</td>
<td>110 (89, 113)</td>
<td>94 (82, 113)</td>
<td>74 (57, 94)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 3</td>
<td>92 (61, 115)</td>
<td>74 (49, 95)</td>
<td>63 (40, 77)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 5</td>
<td>70 (48, 97)</td>
<td>52 (41, 72)</td>
<td>48 (32, 67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 6</td>
<td>59 (44, 79)</td>
<td>52 (38, 62)</td>
<td>46 (30, 57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak Cr</td>
<td>132.5 (106, 162)</td>
<td>126.7 (89, 151)</td>
<td>109.7 (87, 134)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>


Fractionated Excretion of Na

- FeNa values
  - in utero: 15%
  - 28 wk EGA: 5-6%
  - 33 wk EGA: 3-5%
  - 40 wk EGA: 1-3%

B6: NEONATAL RENAL FUNCTION & FAILURE
Differential Diagnosis (Work-up)

- Bladder catheterization
- Renal ultrasound
- VCUG

Differential Diagnosis (Fluid Challenge)

- 10 ml to 20 ml/kg NS IV over 1-2 hours
- Lasix 1-2 mg/kg should oliguria persist
- Response is defined as UOP > 2 ml/kg/hr

Management

- Postrenal
  - Drain bladder with indwelling catheter
  - Consult urology
- Prerenal
  - Volume resuscitation
  - Treat specific causes
- Intrinsic: supportive care

Management

- Maintenance of state of euvolemia
  - IWL plus urinary losses
  - Full term: 30 ml/kg + ml/ml UOP
  - Premature: up to 70 ml/kg + ml/ml UOP

Management of Intrinsic Renal Disease

- Maintenance of electrolyte balance
  - Overhydration
    - Edema, CHF, ↑BP
  - Hyponatremia
    - Excess free water due to fluid overload
    - Manage by fluid restriction
    - Serum sodium concentration less than 125 mEq/L associated with seizures & lethargy

Management of Intrinsic Renal Disease

- Diuretics
  - Do not alter course of ARF
  - Conversion of oliguric to nonoliguric state
- Dopamine Administration
  - Does “renal” dose dopamine have a role?
Hypertension

- Secondary to renal damage or fluid overload
- Hydralazine (0.2-0.5 mg/kg IV)
- Severe elevation → renal thrombosis

Hypertension

- Term infants: 100/70; Preterm 90/60
- After ARF the most common cause of neonatal hypertension is:
  - Renovascular disease - congenital or acquired (UAC)
  - Coarctation of the aorta
  - Polycystic kidney disease

Management of Intrinsic Renal Disease

- Hyperkalemia
- IV calcium, NaHoco3, insulin & glucose infusion are only temporizing
- Kayexelate → must be used cautiously
  - Complications include hypernatremia, constipation
  - Associated with intestinal necrosis

Metabolic Acidosis

- Common in intrinsic failure
- Treat for pH <7.2 or CO2 <14
- Chronic failure may require HCO3 supplements (bicitra)
- If treating acidosis monitor ionized calcium

Hyperphosphatemia & Hypocalcemia

- Use formula containing low phosphorus (PM 60/40)
- Oral phosphate binder to prevent phosphorus uptake (Calcium carbonate)
- Hypocalcemia usually refractory

Nutrition

- Goal → prevent excessive tissue breakdown
- Provide 100 cal/kg with fat & CHO
- 1-2 gm/kg/d protein
Dialysis

- Indicated in protracted course when conservative treatment fails
  - Peritoneal dialysis
    - Safe, effective, technically easy
  - CAVH (continuous arteriovenous hemofiltration)
    - Need adequate BP, vascular access, systemic heparinization

Prognosis

- Oliguria in ARF can last up to three weeks
- Outcome variable
  - 50% mortality
  - survive without compromise
  - Intermediate group
  - Permanent failure

What Do You Think?

- Baby B is a FT delivered by C/S for severe fetal distress associated with placenta abruption. Apgars were 2 & 4. Vigorous resuscitation, including intubation, ventilation and volume expansion for hypotension. At 24 hours of age, she is severely oliguric, edematous, & urine is grossly bloody
  - Post renal disease
  - Prerenal renal disease
  - Intrinsic renal disease