Electrolyte Abnormalities in Neonates

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Electrolyte Abnormalities

- Sodium/Water Balance
- Hyponatremia/Hypernatremia
- Hypokalemia/Hyperkalemia
Sodium/Water Balance

- Transition from fetal physiology
  - Late term fetus
  - High $F_{xNa}$
  - Transition – to low $F_{xNa}$
    - Most species during 1st day
    - Fetal foal - before birth

- Sodium conserving mode
  - Na requirement for growth
    - Bone growth
    - ↑ body mass
      - Increase in interstitial space
  - Milk diet
    - Fresh milk is sodium poor
      - 9-15 mEq/l
Sodium/Water Balance

Sodium Overload

- Sodium containing intravenous fluids
  - 6-7 mEq Na/kg/day
  - Mare’s milk – 1.8 mEq Na/kg/day
  - 3-4 X normal Na

- Sodium overloading
  - Expansion of the extracellular fluid space
  - Sodium fractional excretion will remain low

- Difficulty dealing with volume loading
Hyponatremia
Hyponatremia

- Spurious hyponatremia
- Dilutional hyponatremia
- Depletional hyponatremia
- Redistribution hyponatremia
Spurious Hyponatremia

- Normal plasma sodium concentration
- Laboratory reports a low concentration
  - Presence of interfering substances
    - Lipids or large proteins
    - Artificially dilutes sample
    - Not with modern assay techniques
  - Mistakes in sampling
    - Venipuncture site distal to a low Na drip
    - Sample is taken from a catheter
      - Infusion of a low Na solution
      - Insufficient dead space clearing
Dilutional Hyponatremia

- Lack of balance
  - Fluid intake/urine output
- Loss of integrity of the urinary system
  - Ruptured bladder
  - Ruptured/necrotic urachus
  - Fenestrated ureters
- Renal failure
  - Low GFR
  - Na wasting
Dilutional Hyponatremia

- Failed/delayed renal transition fetal to neonatal physiology
  - Low GFR

- Water overload
  - Management mistakes
    - Dilute milk replacer
    - Excessive water enemas (retained)
    - Fluid therapy errors (Na wasting renal syndromes)
  - Syndrome of inappropriate antidiuresis (SIA)
  - Appropriate antidiuresis
    - Decreased arterial volume
Dilutional Hyponatremia

- Most common form hyponatremia in neonates
- Only occurs with intake of hyponatremic fluid
  - Fresh milk
  - Hyponatremic rehydration formulas
    - Dextrose in water or half strength saline
- Not with isotonic Na containing fluids
  - Normisol-R, Lactated Ringers, Plasmalyte
  - Less marked on milk replacer than fresh milk
Hyponatremia

Syndrome of Inappropriate Antidiuresis (SIAD)

- Synonym: SIADH
  - Syndrome of Inappropriate Antidiuretic Hormone Secretion
- Hyponatremia secondary to
  - Inappropriate reabsorption of water from urine
- Diagnosis
  - High urine osmolarity
  - Hyposmolar hyponatremia - plasma
  - Normal renal function
  - Normal adrenal function
  - Euvolemia
- Can have excessive renal sodium excretion
  - Often absent in the neonate
  - Low sodium intake
Hyponatremia

Syndrome of Inappropriate Antidiuresis (SIAD)

- Clinical syndrome
  - Sudden decrease in urine output
  - High urine specific gravity
  - Weight gain
    - 10-15% of body weight overnight
  - No edema
  - Decreasing plasma sodium concentration

- ADH increased
  - No osmotic stimulus
  - No hypovolemic stimulus
Hyponatremia

**Syndrome of Inappropriate Antidiuresis (SIAD)**

- **SIADH**
  - Inappropriate vasopressin release
    - Erratic and unpredictable release vasopressin
    - Reset of the osmostat
      - Threshold for release is lowered
      - Vasopressin release not fully suppressed at low osmolarity
      - But normal at higher osmolarity
    - Receptor abnormality (vasopressin release normal)
      - Hypersensitive receptors
      - Receptors continue to respond
        - After vasopressin levels decrease
        - Hypovasopressinemic antidiuresis
Hyponatremia

*Syndrome of Inappropriate Antidiuresis (SIAD)*

- SIAD not SIADH
  - High urine osmolarity
  - Hyposmolar hyponatremia
  - Hypovolemia
    - Appropriate vasopressin release
    - Defense of volemia
Hyponatremia

**Syndrome of Inappropriate Antidiuresis (SIAD)**

- Nonosmotic ADH release
  - Subclinical volume depletion
  - Pain
  - Stress
  - Administration of hypotonic fluids
- Abnormal adrenal function
- Abnormal renal function
Depletional Hyponatremia

- Na loss > water
- Diarrhea
  - Excessive sodium loss in feces
  - Rehydration with Na poor fluids
    - Fresh/frozen milk
    - Fresh water
- Renal sodium wasting
  - Tubular disease
  - Use of diuretics
  - Endocrine disturbances
  - Rehydration with Na poor fluids
    - Fresh/frozen milk
    - Fresh water
Redistribution Hyponatremia

- Low sodium concentration
  - Osmolarity normal
  - Isosmotic hyponatremia
    - Hyperosmotic hyponatremia
- Other osmotically active particles present
  - Redistribute fluid from intracellular space
    - Appropriate decrease Na concentration
    - Hyperglycemia (Na, Glu in mmol/L)
      - \[ Na_{\text{corrected}} = Na_{\text{measured}} + [(\text{Glu} - 5)/3.5] \]
      - 1.6 mEq/l Na decrease for 5.55 mmol/L glu increase
    - Iatrogenic addition of osmoles
      - Mannitol
    - Extreme hyperproteinemia
    - Secondary to sick cell syndrome
Hyponatremia
*Sick Cell Syndrome*

- Critically ill patients
  - Cellular insult
  - Loss of cell wall integrity
  - Solute leak
    - Fluid follows
    - Dilution of extracellular sodium
Hyponatremia
Clinical Assessment

- Classify hyponatremia
- Hypervolemic
- Euvolemic
- Hypovolemic
Hyponatremia
Clinical Assessment

- Hypervolemic hyponatremia
  - Impaired water excretion
    - Renal failure
    - Ruptured bladder
    - Decreased GFR
    - Na retention
    - ADH excess
  - Increased total body water + Na
    - Water > Na
- Edema, ascites
- Decreased arterial volume/BP
  - Stimulate ADH secretion
Hyponatremia

Clinical Assessment

- Euvolemic hyponatremia
  - Most common in hospitalized patients
  - ADH mediated water retention
    - Increased ECF
  - Iatrogenic
    - Rx hypotonic fluids in patients
    - When stimulus for increased ADH secretion
- Total body Na normal
- No edema
  - Defines euvoletic
Hyponatremia
Clinical Assessment

- Hypovolemic hyponatremia
  - Deficit water & Na
    - Na deficit > water deficit
  
- Etiology
  - Diarrhea
  - Na wasting nephropathy
  - Diuretics
Hypotonic Hyponatremia
Clinical Findings

- Asymptomatic or symptomatic
- Severe
  - < 115 mEq/l – arbitrary definition
- Acute
  - < 36-48 hr
- Progressive brain edema
  - Weakness, depressed reflexes
  - Obtunded, abnormal sensorium
  - Hypothermia
  - Cheyne-Stokes respiration
  - Seizures, Coma
  - Brainstem herniation
  - Respiratory arrest
Hypotonic Hyponatremia

Brain Edema

- Abrupt hypo-osmolarity
  - Aquaporin-4 mediated
  - Water moves into brain cells
- Compensation
  - Decreased cerebral venous pooling
  - Decreased CSF volume
    - Pediatric – less relative CSF volume
- Cell volume regulatory ions
  - Na, K, Cl
  - Released within 5 min from cells
  - Can continue for 4 hours
  - Stretched cell membranes open ion channels
  - Hormone regulated cellular ion differences
    - Predisposes females to more damage
Hypotonic Hyponatremia
Brain Edema

- Reduction of cellular osmolytes
  - Polyalcohols
    - Sorbitol
    - Inositol
  - Amino acids
  - Methylamines
- Within 2-4 days
  - Up to 50% reduction osmolytes
Hypotonic Hyponatremia
Brain Edema

- Early and late phase changes
  - Limit cellular edema
  - Limit damage

- Hypoxic ischemic encephalopathy
  - Compounds hyponatremia damage
    - Interferes with compensation
  - Cerebral edema
    - Interferes with cerebral perfusion
    - Impairs central respiratory centers
Hypotonic Hyponatremia
Chronic, severe

- Asymptomatic
  - Oligosymptomatic
  - Not treat?
- Only for days
  - Somnolent
  - Disoriented
  - Often Rx
- Causes
  - Diuretics
  - SIADH
  - Malnourishment/liver disease
  - Diarrhea
Hypotonic Hyponatremia
Chronic, severe - treated

- Risk of cerebral myelinolysis
  - Central pontine myelinulysis
  - Initial report 12 patients – weak evidence
  - Other reports extrapontine
  - May occur in 25% cases
    - Over rapid correction
    - Other risk factors
      - Hypokalemia
      - Alcoholism

- Experimental studies – Na 118 to 140 mEq/l
  - 48 hrs – OK
  - 8 hr – 90% myelinolysis
    - Rx hypertonic saline
    - Rx ADH antagonist
Hypotonic Hyponatremia
Myelinolysis - Pathogenesis

- Osmotic reloading fails
  - Rapid correction
  - Brain cell Na, K
    - Normal
    - High because of overshoot
  - Amino acid content low

- Osmotic reloading
  - Organic osmolytes take up to 5 days
    - Normal metabolic molecules
    - Parts of cellular proteins/lipids
  - External addition not speed
  - Transport depends on new gene expression
    - RNA transcription – protein production
  - Slowest where lesions occur
  - Blood brain barrier has role
Hypotonic Hyponatremia
Myelinolysis - Pathogenesis

- Blood brain barrier
  - Major target of cellular edema
  - Vascular endothelial cell
  - Astrocyte foot processes
  - Cell shrink opens cell junctions

- BBB disrupted
  - Not protect
  - Plasma constituents have access
Hypotonic Hyponatremia
Myelinolysis - Pathogenesis

- Factors associated
  - Overshoot hypernatremia
  - Increasing Na > 25 mEq/L 24-48 hr
  - Concurrent hypoxic event
  - Liver disease
- Rate of Na rise
  - Less important than magnitude
- Symptomatic hyponatremia
  - More important to treat
  - Than threat of myelinolysis
- Signs days after Na correction
- MRI lesions best seen 2 weeks after
Hypotonic Hyponatremia

Treatment

- Recognize cause
  - Don’t treat spurious, redistribution hyponatremia

- Symptomatic – euvolemia/hypervolemia, with concentrated urine
  - Hypertonic saline
  - Furosemide – limit volume expansion
  - Stop water intake

- Symptomatic – hypovolemia
  - Isotonic fluids

- Mild symptomatic – dilute urine
  - Evaporative losses only
Hyponatremia/Hypernatremia
Osmotic Shifts
Hypotonic Hyponatremia
Treatment - Correction rate

- Acute – rapid
- Chronic
  - Increase Na < 0.5 mmol/L/hr
  - Stop once serum Na = 120-126
- If seizures
  - Increase Na 1 – 1.5 mmol/L/hr for 1st 3 hr
  - Or until seizures stop
  - Give 1-2 ml/kg/hr 3% saline
    - If seizures severe up to 4-6 ml/kg/hr
  - Add furosemide
  - Stop when Na = 118 mEq/l
    - Goal 125 mEq/l
Hypotonic Hyponatremia
Estimate Effect of Infusate

For each liter given
Change in serum [Na] = \frac{(\text{Infusate Na} + \text{Infusate K}) - \text{serum Na}}{\text{Total body water} + 1}

Total body water
- early neonate = 0.75 X body wt
- pediatric = 0.6 X body wt
- adult = 0.5-0.6 X body wt
- geriatric = 0.45-0.5 X body wt
Hypotonic Hyponatremia

Treatment

- Vasopressin Antagonists
  - Better predictability
  - Better fine tuning

- Hyponatremia and ADH
  - Primarily disease of excess ADH
  - In face of continued hypotonic fluid intake

- Not use with hyponatremia because of
  - Renal disease
  - Volume contraction

- Oral products being tested
Hypotonic Hyponatremia
Vasopressin Antagonists

- Demeclocycline
  - Blocks at tubules
- Aquaretics
  - $V_{1a}$ & $V_2$
    - Conivaptan
  - $V_2$
    - Lixivaptan
    - Satavaptan
    - Tolvaptan
Hypernatremia

- Uncommon
- Deficit of water relative to Na stores
- Hypertonic hyperosmolality
- Causes of hypernatremia
  - Spurious
  - Excessive free water loss
    - Pure water loss
    - Hypotonic fluid loss
  - Hyperosmotic intake
  - Iatrogenic
Spurious hypernatremia

- Sampling errors
  - Blood samples from the intravenous catheter
    - Not large enough presample
    - Sample contamination
      - with saline
Hypernatremia

Increased free water loss

- Increased insensible loss
  - Increased respiratory rate
  - Low humidity
  - High body temperature
  - External warming
    - Radiant heat
    - Hot air heat
- Increased insensible loss with limited intake
  - Hot weather
  - Neonate unable to nurse
    - Lack opportunity
    - NE
Hypernatremia
Increased free water loss

- Water loss
  - Diabetes insipidus
    - Unusual because of neonate’s diet

- Hypotonic fluid loss
  - Furosemide
  - Osmotic diuresis
    - Glucosuria
    - Mannitol
  - Renal disease
  - Diarrhea
  - Excessive sweating
Hypernatremia
Hyperosmotic Intake

- High sodium maternal milk
  - Excessive sodium intake relative to free water

- Iatrogenic mishaps
  - Improperly mixed electrolyte solutions
    - Without the opportunity/ability to drink fresh water
  - Improperly mixed milk replacer
    - All powdered milk replacers are sodium rich
  - Use of hypernatremic intravenous fluids solutions
    - 5% sodium bicarbonate
    - Hypertonic saline
  - Use of saline in oxygen humidifiers
  - Hypertonic enemas (retained)
Hypernatremia
Normal defense against

- Concentrate urine
  - Osmolar release ADH
- Thirst
  - Only develops if can’t get to water
Hypernatremia Treatment

- Recognize cause
  - Eliminate/manage underlying problem
- If developed acutely (hours)
  - Can be corrected over hours (↓Na 1 mmol/hr)
  - Usually acute sodium loading
- If developed slowly (over days)
  - Intracellular accumulation organic osmolytes
  - Correct slowly to avoid cerebral cellular edema
  - ↓Na < 0.5 mmol/hr (target ↓Na 10 mmol/day)
Hypernatremia

Treatment

- If Na > 170
  - Don’t decrease < 150 for 48-72 hr
- Oral fluid therapy
  - As soon as possible
  - Na and K in milk
- Seizures during treatment
  - Common
  - From cerebral edema
  - Slow correction
Hypernatremia

Estimate Effect of Infusate

For each liter given
Change in serum [Na] = \[
\frac{(\text{Infusate Na} + \text{Infusate K}) - \text{serum Na}}{\text{Total body water} + 1}
\]

Total body water
- early neonate = 0.75 X body wt
- pediatric = 0.6 X body wt
- adult = 0.5-0.6 X body wt
- geriatric = 0.45-0.5 X body wt
Hypokalemia
Hypokalemia

- Hypokalemia common in neonates
- Anabolic increase in cell mass (growth)
  - Potassium major intracellular ion
- Renal K wasting
  - Diuresis
  - Renal pathology
Hypokalemia
Stress/sepsis

- Resting muscle
  - Uses 10% of available Na\(^+\):K\(^+\) ATPase activity
- Stimulated acutely by
  - Insulin
  - Epinephrine
  - Contractile activity
Hypokalemia
Stress/sepsis

- Stress/Sepsis $\rightarrow \uparrow$ epinephrine
  - $\uparrow \text{Na}^+ : \text{K}^+$ ATPase activity
  - Significant intracellular shifts of $\text{K}^+$ $\rightarrow$ hypokalemia
  - $\uparrow \text{ATPase demand}$
    - $\uparrow$ glucose utilization/requirement
    - $\uparrow$ glucose transport into the cell resulting
    - $\rightarrow$ further shift $\text{K}^+$ intracellular??
Hypokalemia
Pathogenesis

- Loss of 1% total body potassium
  - Disturbs transcellular distribution
  - Results in physiological changes

- Blood levels
  - Not correlate total body stores
  - Rapid drop more likely clinical signs

- Loss 100 mEq K
  - Blood level decreases by 0.3 mEq/l
  - If there are no confounders
Hypokalemia

Signs - man

- Muscle weakness
- Paralytic ileus
- Cardiac arrhythmias
  - Atrial tachycardia
  - Atrioventricular dissociation
  - Ventricular tachycardia/fibrillation
  - Flat or inverted T-waves
  - ST-segment depression
  - U-waves
Hypokalemia

Signs - man

- K < 2.5
  - Rhabdomyolysis with myoglobulinuria
  - Acute renal failure
- K < 2.0
  - Ascending paralysis
  - Impairment of respiratory function
- Not recognize in neonatal foals
Hypokalemia

- High levels of potassium in milk
  - Will support growth requirements
- Stressed/Septic neonates
  - Not tolerate oral feeding
- Neonates require significant K supplementation
  - Prolonged intravenous glucose
  - Parenteral nutrition
  - Limited or no milk feeding
- Glucocorticoid administration
  - Mineralocorticoid receptor stimulation
  - $\rightarrow$ urine loss of potassium
Hypokalemia

Treatment

- Neonates
  - Milk diet – not need supplement
  - Fluids only
    - If normal plasma levels – 3 mEq/kg/d
    - If hypokalemic – 6-12 mEq/kg/d or more
Hyperkalemia

- Differential diagnosis
  - Ruptured bladder
  - Urinary tract defect
  - Sick cell syndrome
  - Iatrogenic
Hyperkalemia

- Loss of integrity lower urinary tract
  - ↑K only when on a milk diet
    - Also true for ↓Na, ↓Cl
  - Receiving parenteral nutrition
    - ↑K only occur with overzealous K administration

- Sick cell syndrome
  - Suffer global cell insult
    - Perinatal hypoxic ischemic asphyxial insults
  - ↑K = 6-8 mEq/l

- Hyperglycemia – no insulin response

- Iatrogenic in the face of renal insufficiency
Hyperkalemia

Signs

- Impaired neuromuscular transmission
  - Cardiac
  - Neuromuscular paresis/paralysis
- General fatigue
- Weakness
- Paresthesia
Management of Hyperkalemia

Questions to be asked:
Is there an emergency related to hyperkalemia?
   If so, what is the plan for therapy?
Is pseudohyperkalemia present?
Did this hyperkalemia develop acutely?
   Toxicity more related to rate of increase than level
   Toxicity associated with acid-base status
What role of
   High K intake
   Decreased renal K excretion
   Transcellular K shift
Management of Hyperkalemia

- ECG changes
  - Peaked T wave
    - False + depending on lead placement
  - Decrease/absence P waves
    - False + depending on lead placement
  - Prolonged PR interval
  - Widened QRS
  - Sine wave QRS
  - Asystole
- ECG not sensitive indicator of hyperkalemia
  - K > 6.0 – 46% abnormal ECG (in man)
  - K > 6.8 – 55% abnormal ECG (in man)
- Not predictable progression
Management of Hyperkalemia

- **Pseudohyperkalemia**
  - Sample hemolysis
  - Long, tight tourniquet (man)
  - Leukocytosis (>70,000; serum)
  - Thrombocytosis (>1,000,000; serum)
  - Measure plasma vs serum
  - If serum > 0.3 higher - pseudohyperkalemia
Management of Hyperkalemia

Urgent Therapy

- Oppose direct toxic effects
  - Ca therapy
- Promote cellular uptake K
  - Insulin (glucose)
  - $\beta_2$-agonists (albuterol)
  - NaHCO$_3$ - not
- Remove from body
  - Drain uroabdomen
  - Diuretics
  - Cation exchange resins
Management of Hyperkalemia
Urgent Therapy

- Calcium
  - Ca gluconate – less irritating
  - CaCl – Ca more biologically available
  - Slow IV push
    - ECG changes within 1-3 minutes
    - Lasts 30-60 minutes
Management of Hyperkalemia

Urgent Therapy

- **Insulin**
  - Increase Na/K pump – primarily muscle/liver
    - Increase Na/H exchanger as well – may be important
  - Onset 20 min with peak 30-60 min
  - Dose related
  - Use glucose only to prevent hypoglycemia
  - Dose – 10 units as a bolus
    - Lasts 4-6 hr
  - CRI use in neonates
  - Hypoglycemia risk – monitor
Management of Hyperkalemia
Urgent Therapy

- **Adrenergic Agents**
  - $\beta_2$-receptor in the muscle and liver
  - Directly activate Na/K-ATPase
    - Increase cAMP
  - Albuterol
    - By insufflation or IV
    - K drop within 30 min, peak 90-120 min
    - Drop 0.6-1 mEq/l
  - Has no effect 40% dialysis patients (man)
  - Effect additive to insulin
Management of Hyperkalemia
Urgent Therapy

- NaHCO₃
  - Poor response
  - Requires 4 hrs for effect
  - K decreased < 0.35 mEq/l at 6 hr

- Combined therapy
  - Insulin + β₂
    - Different mechanisms
    - In theory additive 60-100%
    - But not all respond to β₂
    - Combination – less frequent hypoglycemia
  - Insulin + NaHCO₃
    - Potentiate effect?
Management of Hyperkalemia
Direct Elimination from Body

- Gastrointestinal Route
  - Sodium polystyrene sulfonate
    - Cation exchange resin
    - 1 gm removes 0.5-1 mEq/l K
    - 4-6 hr required for full effect
  - Oral, enema
    - Constipates – give with laxative
  - Minimal short term effect
  - Depends on gut perfusion
Management of Hyperkalemia
Direct Elimination from Body

- Renal
  - Na diuresis
  - Deliver Na to distal K secreting sites
  - Renal disease often attenuates effect
- Abdomen
  - Draining uroabdomen
  - Peritoneal dialysis