

Osmolality, Osmolrity, Anions, and Unexplained Gaps

Mart in Potash
Pathology Resident R1

Clinical Scenario

- 49 year old man presents to the emergency room
- History is limited
 - Patient is belligerent
 - Threatening ER staff
 - Reeks of alcohol

Initial Laboratory Results

- Electrolytes
- Na 140
- K 3.5
- Cl 101
- CO2 23.7
- BUN 13
- Creatinine 0.7
- Glucose 105

What to make of these lab values

- Sodium—
 - Can tell about the patients hydration status
 - Concentration of sodium dependant on water
- Potassium—
 - Can be affected by several factors
 - Nutrition
 - Intracellular/extracellular shifts due to acid production
- CO2 (Bicarbonate)
 - Acid/base status of the patient
- Glucose
 - Especially important in diagnosing/monitoring diabetes
- Play important roles in diagnosing serum osmolality and anion gap

Goals of this talk

- Understand osmolality/osmolality
 - Understand the concept of osmolality gap
- How do these help a clinician assess patients
 - How the lab impacts patient care

Definitions

- Osmole—
 - Unit that defines the number of moles of a chemical compound that contribute to a solution's osmotic pressure
- Osmolarity—
 - Measure of the osmoles of solute per liter of solution
- Osmolality—
 - Measure of the concentration of solute per kilogram of solvent

Published Literature

- Some articles talk about osmolality
- Some articles talk about osmolarity
- Who's talking about what and do they know what they are talking about?
 - You are likely wondering the exact same thing right now

Osmole

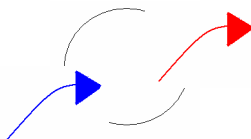
- Number of moles of chemical compound that contribute to a solution's osmotic pressure
- Amount of a substance that yields a specific number of particles that would depress the freezing point of the solvent by 1.86K

Osmolality

- Non-SI unit of measurement
 - Defines the number of moles of a chemical compound that contribute to solutions osmotic pressure
- $\text{Osmolality} = \Phi * nC$
 - Φ —osmotic coefficient
 - n —number of particles into which a molecule dissociates
 - C —molar concentration of the solution

Osmotic Pressures

- **Hydrostatic pressure**
 - Requires division by a semipermeable membrane
 - Directs net movement of water out of a compartment
 - In biology: from circulation to cell
- **Oncotic pressure**
 - Osmotic pressure exerted by proteins in blood plasma that pull water into the circulatory system
 - Colloid osmotic pressure



Serum Osmol in Practice

- Assume that the osmolarity and osmolality are essentially equal
 - 1L=1kg
 - Human serum is a dilute aqueous solution
 - Specific gravity of around 1.01
- Major osmotic particles in plasma
 - Sodium
 - Chloride
 - Bicarbonate
 - Urea (blood urea nitrogen)
 - glucose

Measurement-Osmolality

- Direct measurement by freezing point depression
 - Amount of a substance that yields a specific number of particles that would depress the freezing point of the solvent by 1.86K
 - Osmolality is preferred over Osmolarity because weight is independent of temperature and volume is not
 - remember—
 - Osmolality=osmoles/kilogram of solvent
 - Osmolarity=osmoles/liter of solution

Calculation-Osmolarity

- $\text{Osmolarity} = (2 \times \text{Sodium [mEq/L]}) + (\text{glucose [mg/dL]} / 18) + (\text{BUN [mg/dL]} / 2.8)$
 - $(2 \times \text{Na}) + (\text{GLU} / 20) + (\text{BUN} / 3) + (2)$
- Important to note
 - Numerous equations have been used to estimate osmolarity

Osmol Gap

- Normally—a gap between calculated and measured osmolarity exists
 - gap (measured osmol – calculated osmol)
 - 5-15 mmol/L
 - University of Iowa—10
 - Due to different units without conversion—comparing osmolarity and osmolality
 - Simplicity of the equation—it is just an estimate
- Can become increased in the presence of low molecular weight substances → greater than 25
 - Ethanol
 - Ethylene glycol
 - Methanol
 - Isopropyl alcohol

Plasma Osmolality

- When is the test ordered?
 - Symptoms
 - Intoxication
 - Ataxia
 - Hallucinations
 - Slurred speech
 - coma
 - Thirst
 - Confusion
 - Nausea
 - Headache
 - Lethargy
 - Seizures

Common Clinical Scenarios

- Increased Measured Osmolality
 - Ketoacidosis****
 - Diabetic
 - Alcoholic
 - Lactic Acidosis
 - Renal failure
 - Salicylate ingestion

Challenge Scenarios

Na	140	Na	135
K	3.5	K	3.5
Cl	105	Cl	110
BUN	12	BUN	12
CO2	22	CO2	25
Glu	105	Glu	500
Measured	340	Measured	305

Challenge Scenarios

Na	140	Na	138
K	3.5	K	3.5
Cl	110	Cl	108
BUN	15	BUN	15
CO2	25	CO2	23
Glu	100	Glu	80
Measured	350	Measured	305

Challenge Scenarios

- What is the calculated Osmol?
 - Case 1—290
 - Case 2—299
 - Case 3—290
 - Case 4—285
- Is there a gap?
 - Case 1—yes
 - Case 2—no
 - Case 3—yes
 - Case 4—yes

Next Step—Can the gap be explained

- Unexplained Osmol Gap
 - A gap (measured osmol – calculated osmol) that CANNOT be entirely explained by available laboratory and clinical data

Common Clinical Scenarios

- Increased Osmol Gap
 - Measured elevated out of proportion to Calculated
 - Creates gap
 - Ethanol
 - Easiest one to rule out—we routinely test for ethanol level
 - GAP*4.6=Expected ETOH blood level
 - IMPORTANT—ethanol CAN be associated with an elevated UNEXPLAINED GAP
 - Usually at high doses
 - Can "watch" these patients when the ethanol level is above 200
 - » UNEXPLAINED GAP closes as the ethanol level gets closer to 100
 - Ethylene glycol
 - Methanol
 - Isopropyl alcohol

Increased Osmol Gap

- Activated Charcoal
 - Gut decontamination—propylene glycol
- Acetone****
 - Produced during ketoacidosis
- Mannitol
 - Given for increased intracranial pressure

Challenge Scenarios

Na	140	Na	135
K	3.5	K	3.5
Cl	105	Cl	110
BUN	12	BUN	12
CO2	22	CO2	25
Glu	105	Glu	500
Measured	340	Measured	305

- Measured ETOH is 89
- NO OSMOL GAP

Challenge Scenarios

Na	140	Na	138
K	3.5	K	3.5
Cl	110	Cl	108
BUN	15	BUN	15
CO2	25	CO2	23
Glu	100	Glu	80
Measured	350	Measured	305

- Measured ETOH 215

- Measured ETOH 0
- Pt was in a motor vehicle accident—seen at outside ER

IS GAP EXPLAINED?

- CASE 1
 - No
- CASE 3
 - Yes
 - ETOH of that level can explain the gap
- CASE 4
 - Yes
 - Patient likely received mannitol for increased intracranial pressure after motor vehicle accident



Ethylene Glycol

- HOCH₂CH₂OH
- In pure form
 - Odorless
 - Colorless
 - Sweet flavor
- Lowers freezing point
 - Used in automobiles, computers, and as a deicer for windshields

Ethylene Glycol

- Neurological symptoms
 - Intoxication
 - Dizziness
 - Headaches
 - Slurred speech
 - Confusion
- Accumulation of toxic metabolites
 - Tachycardia
 - Hypertension
 - Hyperventilation
- Kidney damage
 - Renal failure

Treatment

- Initial stabilization
 - Gastric decontamination
- Further management
 - Competitive enzyme inhibition
 - Ethanol
 - Fomepizole
 - Hemodialysis

Methanol

- Wood Alcohol



Methanol

- CH_3OH
- Colorless
- Flammable
- Sweet tasting
- Denaturant additive for ethanol for industrial use

Methanol

- Neurologic symptoms
 - CNS depressant
 - Headache
 - Nausea
 - Dizziness
- Toxic breakdown → formaldehyde and formic acid
 - Via alcohol dehydrogenase
 - Causes blindness

Treatment

- Important to begin treatment as soon as possible
 - Competitive enzyme inhibition
 - Ethanol
 - Fomepizole

Isopropyl Alcohol

- Rubbing alcohol



Isopropyl Alcohol

- $\text{C}_3\text{H}_7\text{OH}$
- Many uses
 - Disinfectant
 - Common solvent
 - Good electronic cleaning agent

Isopropyl Alcohol

- Clinical Triad
 - CNS Depression
 - Fruity Breath
 - Ketosis without metabolic acidosis
- Broken down into acetone
 - Acetone is not an acid—thus patients do not develop metabolic acidosis
- More toxic than equivalent volume of ethanol
 - However-does not produce anion gap
 - WILL produce osmol gap
 - Can see distinct crystals in urine
 - Specific finding, not sensitive

Isopropyl Alcohol

- Similar risks as ETOH
 - CNS depression
 - Liver and kidney toxicity
 - Coma and brain damage

Treatment

- Treatment based on clinical picture
 - Isopropanol levels do not correlate well with clinical status
- “Watch and Wait”
 - Depending on the severity
 - May have to use dialysis if the level is too high
 - Hemodialysis is more effective than peritoneal dialysis
- If caught early—can try decontamination
 - Activated charcoal
- Supportive care
 - Support respiratory function
 - BiPAP
 - Cardiovascular monitoring and support
 - IV Fluids for hypotension

Summary

- Understand osmolality/osmolarity
 - Understand the concept of osmol gap
 - gap (measured osmol – calculated osmol)
 - Measured=freezing point depression
 - Calculated(+/-)= $2 \times \text{Na} + \text{BUN}/3 + \text{GLU}/20$
- How do these help a clinician assess patients
 - Determine if there is an unexplained osmol gap
 - Triage use of volatile screen to clinically indicated cases
 - UNEXPLAINED OSMOL GAP