Bridging the Gap

A Case from Brigham and Women's Hospital

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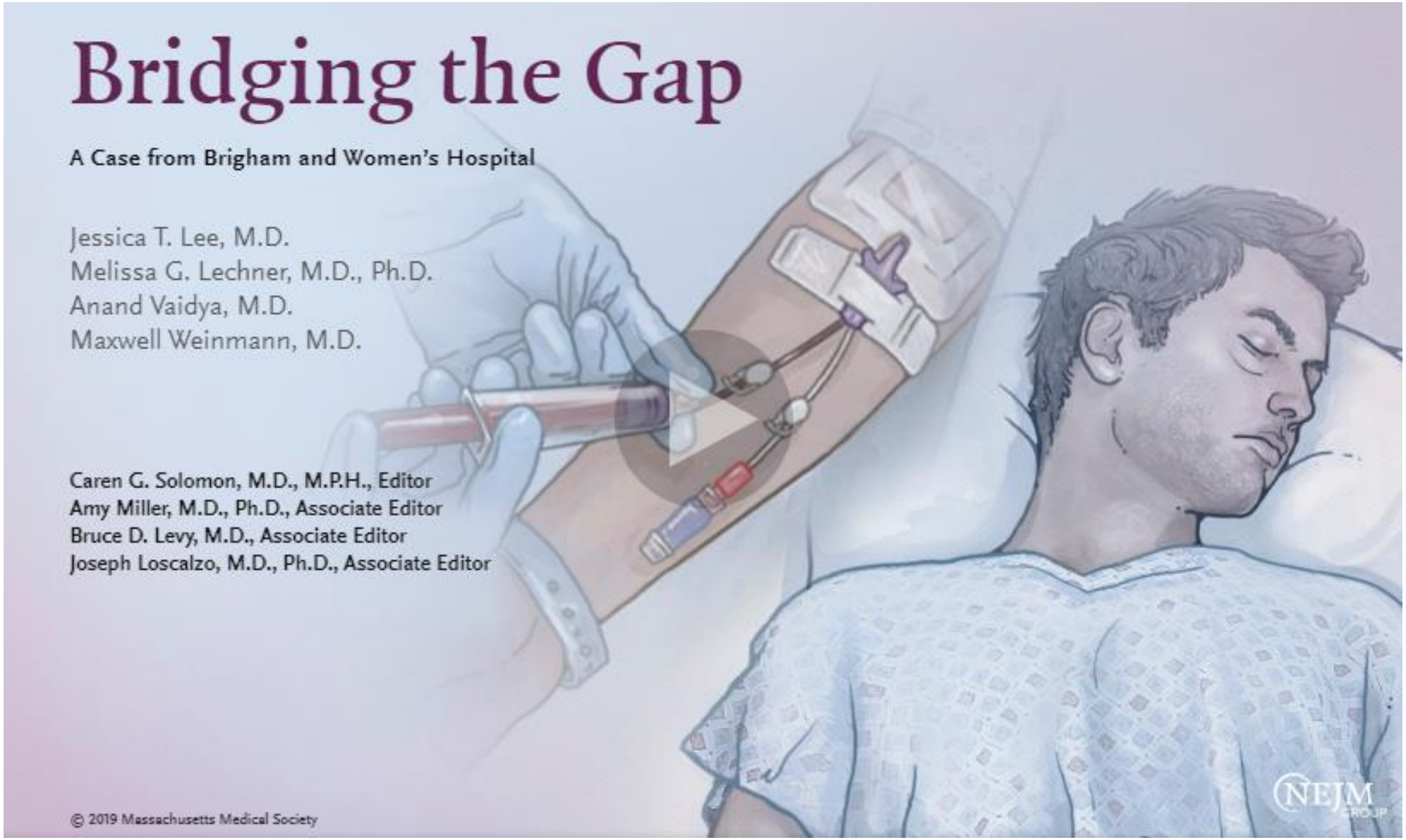

Case Presentation

A 21-year-old man was found unresponsive in a park, with a 1-gallon container of green liquid, approximately half of it gone, nearby. The label was not legible, but the liquid was presumed to be antifreeze. The man was brought to the emergency department by ambulance.

Physical Examination

- Rate regular but tachycardic
- Normal S_1 and S_2 sounds
- No murmurs, rubs, or gallops

Abdomen

No appreciable hepatosplenomegaly

Arms and legs

- No edema in the legs or ankles
- Strong dorsalis pedis pulses
- No swelling or erythema
- No abnormalities of nail beds, cyanosis, or clubbing

Skin

No rashes, no macular or nodular lesions on hands and feet

Nervous system

- Is somnolent but can be aroused by loud voice and by touch
- Slurs speech but is able to state name and year
- Has no facial asymmetry or focal cranial nerve deficits
- Moves arms and legs spontaneously

Vital signs

- Temperature, 36.2°C
- Heart rate, 110 beats per minute
- Blood pressure, 90/50 mm Hg
- Respiratory rate, 16 breaths per minute
- Oxygen saturation, 88% while breathing ambient air

General appearance

- Somnolent, but agitated when aroused by touch
- Well-nourished

Head, eyes, ears, nose, and throat

- Pupils equal in diameter at 4 mm, round, and reactive to light
- No conjunctival hemorrhages; retinal examination not performed
- Mucous membranes moist, with no oral lesions or ulcers; good dentition
- Neck supple, with no nuchal rigidity
- No cervical lymphadenopathy

Lungs

Clear to auscultation — no wheezing, rales, or rhonchi

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Heart

Laboratory Results

Laboratory results were obtained. Arterial blood gas and serum osmolality were assessed, given the likelihood that the patient had ingested ethylene glycol.

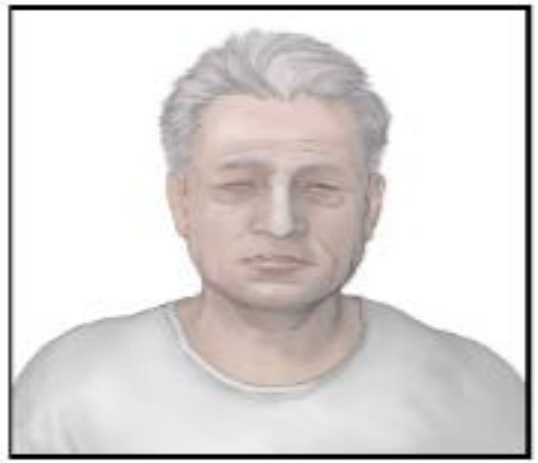
Variable	Result	Normal Range	Flag
Blood			
White-cell count (per mm^3)	8000	4000–10,000	
Hematocrit (%)	45.9	36.0–48.0	
Hemoglobin (g/dl)	16.0	11.5–16.4	
Platelet count (per mm^3)	189,000	150,000–450,000	
Sodium (mmol/liter)	141	136–142	
Potassium (mmol/liter)	4.3	3.5–5.0	
Chloride (mmol/liter)	106	98–108	

Bicarbonate (mmol/liter)	21	23–31	Low
Urea nitrogen (mg/dl)	14	9–25	
Creatinine (mg/dl)	1.1	0.7–1.3	
Glucose (mg/dl)	101	54–118	
Alanine aminotransferase (U/liter)	27	10–50	
Aspartate aminotransferase (U/liter)	22	10–50	
Alkaline phosphatase (U/liter)	42	40–130	
Total protein (g/dl)	6.5	6.0–8.0	

Albumin (g/dl)	4.0	3.5–5.2	
Total bilirubin (mg/dl)	0.8	<1.0	
Serum osmolality (mOsm/kg)	309	275–295	High
Lactate (mmol/liter)	1.2	0–2.0	High
pH	7.32	7.35–7.45	Low
Pco_2 (mm Hg)*	38	35–45	
Po_2 (mm Hg)*	367 on Fio_2 of 1.0	80–100 while breathing ambient air	

Identifying Acid–Base Disorders

This practice element presents the circumstances of three patients with acid–base disorders and provides the information needed to determine the nature of the disorder.



Identifying Acid–Base Disorders

Overview | **Patient 1** | Patient 2 | Patient 3

A 65-year-old man with a history of heroin use and untreated obstructive sleep apnea is found unresponsive in a park with a needle nearby.

Arterial Blood Gas

Variable	Result	Normal Range
pH	7.20	7.35–7.45
Pco_2 (mm Hg)*	82	35–45
Po_2 (mm Hg)*	69, while breathing 2–4 liters of oxygen by nasal canula	80–100

Laboratory Results

Variable	Result	Normal Range
Sodium (mmol/liter)	141	136–142
Chloride (mmol/liter)	101	98–108
Bicarbonate (mmol/liter)	31	23–31
Anion gap	10	10–12

* Pco_2 denotes the partial pressure of carbon dioxide, and Po_2 the partial

1. Does the patient have an acidemia or an alkalemia?

✓ (●) Acidemia

✗ ( ) Alkalemia

Since the pH is less than 7.4, the patient has an **acidemia**.

2. Is the primary problem metabolic or respiratory?

( ) Metabolic

( ) Respiratory

ENTER

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2. Is the primary problem metabolic or respiratory?

✗ ○ Metabolic

✓ ◉ Respiratory

Since the bicarbonate (HCO_3^-) level is elevated, the patient has a **respiratory acidosis**.

The bicarbonate level in the blood gas can be calculated with the Henderson–Hasselbach equation to ensure that the calculated and measured values are within approximately 10% of each other. Since the serum and the arterial blood gas are not always obtained at the same time, and since the bicarbonate level in each is assessed with a different platform, it is important to ensure that the levels of bicarbonate in each are similar.

$$HCO_3^- = 0.03 \times Pco_2 \times 10^{(pH - 6.1)}$$

Here, the values for both the calculated and measured bicarbonate levels are 31.

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La réponse métabolique est elle adéquate

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Here's the values for both the calculation and metabolic compensation levels are 31.

3. Is the metabolic compensation appropriate?

Acute respiratory acidosis

(82 − 40) ÷ 10 + 24 = **28**

Enter the patient's Pco_2 to calculate the HCO_3^- level that would be expected if compensation is appropriate.

Chronic respiratory acidosis

(82 − 40) ÷ 10 × 4.5 + 24 = **43**

Enter the patient's Pco_2 to calculate the HCO_3^- level that would be expected if compensation is appropriate.

○ Yes

○ No

ENTER

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✗ ○ Yes

✓ ◉ No

In acute respiratory acidosis, the expected bicarbonate compensation would be 28 mmol per liter.

In chronic respiratory acidosis, the expected bicarbonate compensation would be 43 mmol per liter.

Since the patient's bicarbonate levels are 31 mmol per liter, the metabolic compensation is not appropriate.

Comments

Given the clinical context, this patient probably had a **chronic respiratory acidosis** (most likely due to his history of sleep apnea), followed by the development of an **acute respiratory acidosis** (probably induced by respiratory depression resulting from opioid use). He now has an incomplete metabolic compensation.

The causes of respiratory acidosis include obstructive airway disorders, restrictive ventilatory defects, central respiratory depression (as may be seen in opioid intoxication), neuromuscular disorders, and thoracic-cage abnormalities.

Identifying Acid–Base Disorders

A 46-year-old woman is found unresponsive in a park, with an empty bottle of vodka nearby.

Arterial Blood Gas		
Variable	**Result**	**Normal Range**
pH	7.20	7.35–7.45
Pco_2 (mm Hg)*	22	35–45
Po_2 (mm Hg)*	98, while breathing ambient air	80–100

Laboratory Results		
Variable	**Result**	**Normal Range**
Sodium (mmol/liter)	132	136–142
Chloride (mmol/liter)	95	98–108
Bicarbonate (mmol/liter)	9	23–31
Anion gap	28	10–12

* Pco_2 denotes the partial pressure of carbon dioxide, and Po_2 the partial pressure of oxygen.

✓ ◉ Acidemia

✗ ○ Alkalemia

Since the pH is less than 7.4, the patient has an **acidemia**.

2. Is the primary problem metabolic or respiratory?

✓ ◉ Metabolic

✗ ○ Respiratory

Since the bicarbonate (HCO_3^-) level is low, the patient has a **metabolic acidosis**.

The bicarbonate level in the blood gas can be calculated with the Henderson–Hasselbach equation to ensure that the calculated and measured values are within approximately 10% of each other. Since the serum and the arterial blood gas are not always obtained at the same time, and since the bicarbonate level in each is assessed with a different platform, it is important to ensure that the levels of bicarbonate in each are similar.

$$HCO_3^- = 0.03 \times Pco_2 \times 10^{(pH - 6.1)}$$

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Étape suivante ?...

Identifying Acid–Base Disorders

Overview | Patient 1 | **Patient 2** | Patient 3

Comments

This patient, who was found after the probable recent ingestion of alcohol, has an anion-gap metabolic acidosis. The most likely cause of the acid–base disorder is lactic acidosis. There is evidence of appropriate respiratory compensation.

Some common causes of a high anion-gap metabolic acidosis include lactic acidosis, diabetic ketoacidosis, uremia, and toxic ingestions (e.g., ethylene glycol, methanol, acetaminophen, aspirin, and salicylates).

…taboic acidosis.

the respiratory compensation appropriate?

ambient air

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Est-ce que la réponse respiratoire est adaptée

Question 1 (A–E)

Evaluate the acid–base disorder for the patient in this case.

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Variable	**Result**	**Normal Range**
Sodium (mmol/liter)	141	136–142
Chloride (mmol/liter)	106	98–108
Bicarbonate (mmol/liter)	21	23–31
Anion gap	14	10–12

* Pco_2 denotes the partial pressure of carbon dioxide, and Po_2 the partial pressure of oxygen.

A. Does the patient have an acidemia or an alkalemia?

✓ ◉ Acidemia

✗ ○ Alkalemia

Since the pH is less than 7.4, the patient has an **acidemia**.

B. Is the primary problem metabolic or respiratory?

✓ ◉ Metabolic

✗ ○ Respiratory

The bicarbonate (HCO_3^-) level is low; therefore, the primary problem is a **metabolic acidosis**.

The bicarbonate level in the blood gas can be calculated with the Henderson–Hasselbach equation to ensure that the calculated and measured values are within approximately 10% of each other. Since the serum and the arterial blood gas are not always obtained at the same time, and since the bicarbonate level in each is assessed with a different platform, it is important to ensure that the levels of bicarbonate in each are similar.

$$HCO_3^- = 0.03 \times Pco_2 \times 10^{(pH - 6.1)}$$

Here, the calculated bicarbonate level is 19 and the measured bicarbonate level is 21, which suggests concordance.

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$$HCO_3^- = 0.03 \times Pco_2 \times 10^{(pH - 6.1)}$$

Here, the calculated bicarbonate level is 19 and the measured bicarbonate level is 21, which suggests concordance.

C. Is the anion gap normal?

( ) Yes

( ) No

SUBMIT

Question 1 (A–E)

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✗ ○ Yes

✓ ◉ No

The range for a normal anion gap is usually considered to be 10 to 12, but values of 9 to 14 may be considered normal in some laboratories. On the basis of the reference range for the anion gap in this laboratory (10 to 12), the patient has a slightly elevated anion-gap metabolic acidosis.

D. Is the respiratory compensation appropriate?

Pco_2

$1.5 \times$ 21 $+ 8 \pm 2 =$ **38 to 42**

Enter the patient's HCO_3^- level to calculate the Pco_2 that would be expected if compensation is appropriate.

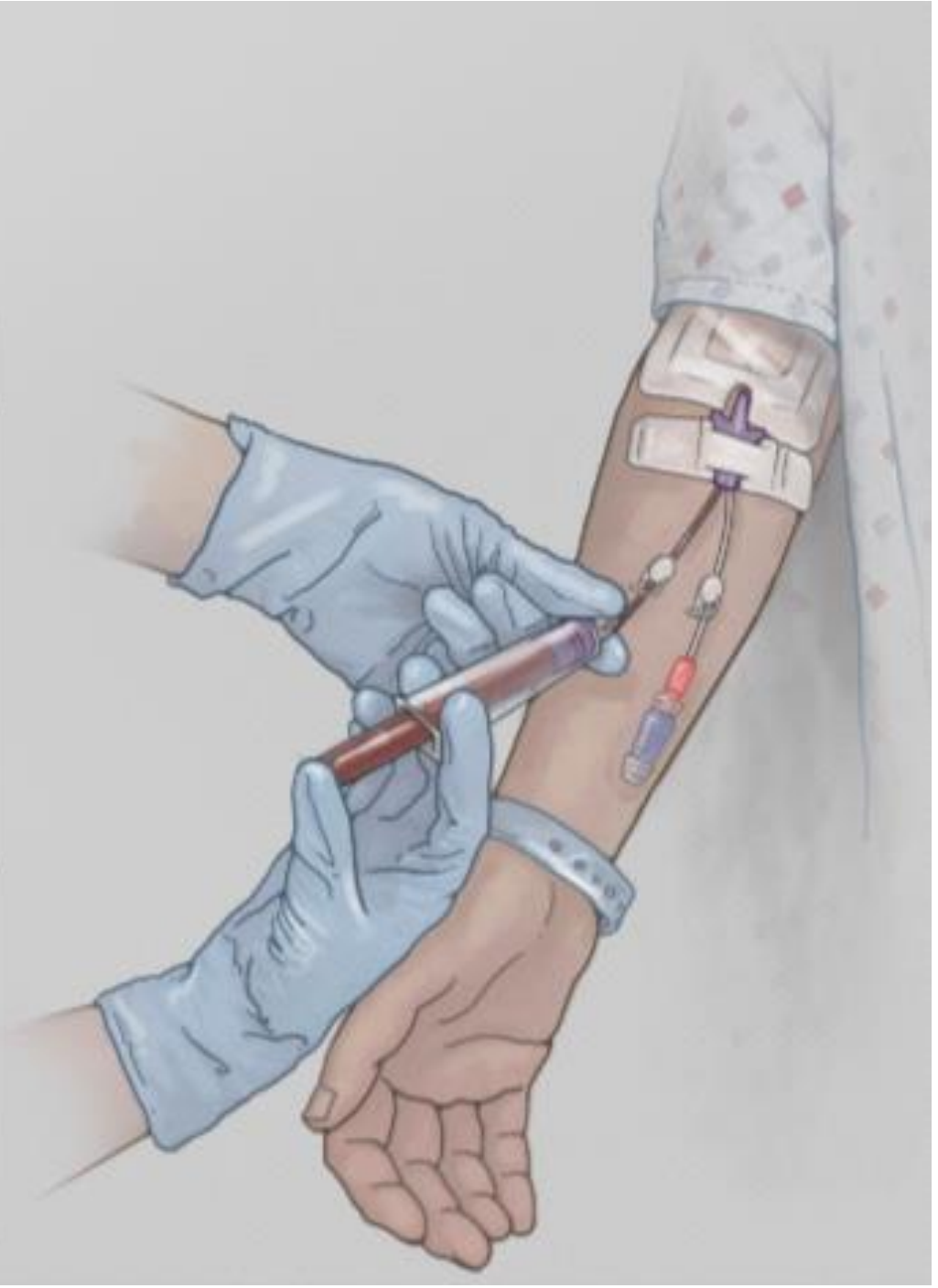
✓ ◉ Yes

✗ ○ No

Toxicology Results

Given the patient's elevated osmolal gap and slightly elevated anion gap, a diagnosis of ethylene glycol poisoning was made. Toxicologic screens for amphetamines and cannabinoids were positive, but test results for the ethylene glycol level were pending. The available results are shown below.

Variable	Result	Normal Range	Flag
Serum			
Acetaminophen (µg/ml)	Negative	10–20	
Salicylates (mg/dl)	Negative	<0.4	
Ethanol	Negative	Negative	
Tricyclics	Negative	Negative	
Ethylene glycol	Positive	Negative	
Urine			
Amphetamines	Negative	Negative	Positive



Barbiturates	Negative	Negative
Benzodiazepines	Negative	Negative
Cocaine	Negative	Negative
Methadone	Negative	Negative
Opiates	Negative	Negative
Oxycodone	Negative	Negative

Intoxication à l'ethylène glycol ?

- Les glycols sont des composés portant plusieurs fonctions alcool.

- L'éthylène glycol (EG) est utilisé comme :

➢ antigel (liquide de refroidissement pour automobiles, circuits de réfrigération ou chauffage central)

➢ comme adjuvant de préparations exposées au gel (lave-vitre ou produits phytosanitaires)

➢ comme solvant industriel et intermédiaire de synthèse chimique (polyesters et éthers de glycols).

Intoxication à l'ethylène glycol ?

- Il s'agit d'un liquide visqueux incolore et de saveur sucrée.
- L'intoxication par l'EG est rare mais grave.
- Il s'agit le plus souvent d'une ingestion accidentelle d'EG, suite au déconditionnement du produit commercial de son emballage d'origine.
- Il peut s'agir aussi d'une tentative de suicide.

Physiopathologie

L'EG est métabolisé dans le foie par l'alcool déshydrogénase (ADH) en glycolaldéhyde puis en acide glycolique

D'autres métabolites peuvent également apparaître à la suite de différentes réactions d'oxydation : l'acide glyoxylique, l'acide oxalique, l'acide formique et la glycine.

L'acide glycolique est le principal responsable de l'acidose métabolique et sa concentration est corrélée au trou anionique,

- L’acide oxalique précipite dans les tubules rénaux sous forme de cristaux d’oxalate de calcium provoquant une insuffisance rénale en deux à trois jours et une hypocalcémie par déplétion

- Le traitement antidotique vise donc à inhiber le plus rapidement possible le métabolisme de l’EG en ses dérivés toxiques

Tableau clinique

- Six à douze heures après l'ingestion, apparaissent au premier plan des troubles digestifs et neurologiques : nausées, vomissements, ébriété, somnolence puis coma et convulsions.

- Il existe initialement une polyurie osmotique à l'origine de déshydratation intracellulaire.

- Les examens biologiques mettent en évidence une acidose métabolique à trou anionique élevé non expliqué par les lactates.

- Vu précocement, le patient peut être asymptomatique. Douze heures après, apparaissent des symptômes cardiorespiratoires avec une tachycardie, une polypnée, un œdème pulmonaire lésionnel ou cardiogénique et un état de choc pour les formes sévères où le décès fait suite à la défaillance multiviscérale.

Tableau clinique

- Biologiquement, mis à part l'acidose, on peut retrouver une hyperglycémie, une hyperleucocytose et une hypocalcémie, responsables de myoclonies, de crises de tétanie et de convulsions.

- Après la 24e heure et en l'absence de traitement, alors que les premiers signes régressent, apparaît une insuffisance rénale aiguë tubulaire avec oligurie, douleurs lombaires, protéinurie et leucocyturie.

- Comme toute nécrose tubulaire aiguë, la guérison est de règle en quelques semaines ; elle peut cependant évoluer vers l'insuffisance rénale chronique.

- Le pronostic à l'admission est lié au retard du traitement spécifique, à la profondeur de l'acidose métabolique, à la présence d'un coma, de convulsions

What Would You Do?

Which one of the following strategies represents a preferred definitive treatment for this patient?
Select a strategy to see whether it is an appropriate choice for treatment and to learn about the probable outcome.

You will be able to return to the list of choices to review the probable consequences of each.

- Perform gastric lavage
- Administer fomepizole
- Administer sodium bicarbonate
- Administer ethanol
- Initiate hemodialysis

What Would You Do?

Make another choice

✕ Gastric lavage is an inappropriate treatment choice.

Outcome of This Strategy

Gastric lavage is performed, and there is a return of bilious fluid. Acidosis becomes more severe, hypotension develops, and emergency dialysis is required.

Comments

Gastric lavage and agents such as activated charcoal and syrup of ipecac are typically ineffective in patients who have ingested ethylene glycol, because it is rapidly absorbed by the stomach.

What Would You Do?

Make another choice

✕ The initiation of hemodialysis is an inappropriate treatment choice.

Outcome of This Strategy

On consultation, a nephrologist strongly advised against hemodialysis, stating that it would not be useful in this patient.

Comments

Hemodialysis is typically reserved for patients who have toxic levels of alcohol, severe acid–base derangements, or indications of end-organ toxicity. Hemodialysis is unlikely to be helpful in the case patient, whose acidosis is mild.

What Would You Do?

Make another choice

✓ **The administration of fomepizole is an appropriate treatment choice.**

Outcome of This Strategy

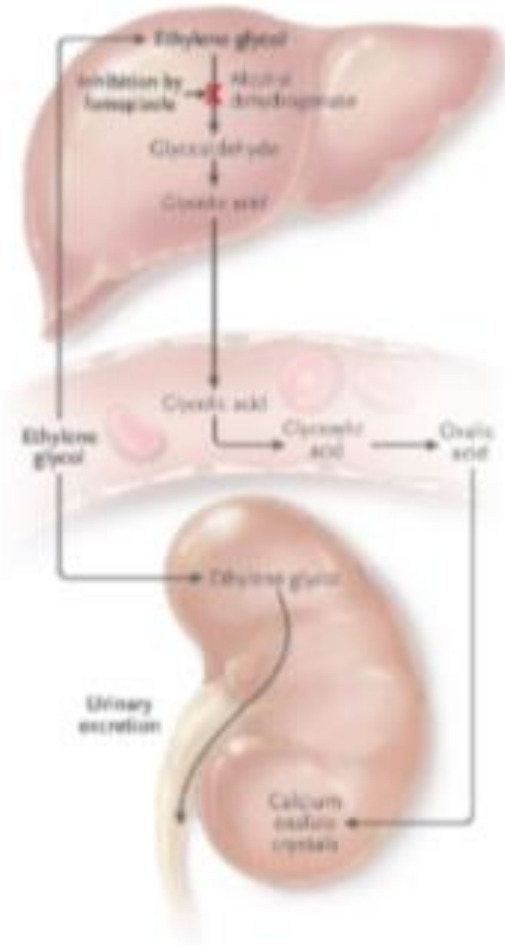
Fomepizole is administered at a rate of 10 mg per kilogram of body weight every 12 hours until the patient's ethylene glycol level falls below 20 mg per deciliter. An increasingly large anion gap develops during the first 12 hours after the initiation of treatment, but thereafter the electrolyte levels and the anion gap normalize.

Comments

Fomepizole inhibits alcohol dehydrogenase (see figure), the enzyme responsible for converting ethylene glycol to its toxic metabolites: glycolic acid, glyoxylic acid, and oxalic acid. A patient's anion gap correlates with the level of toxic acid metabolites. In the case patient, the anion gap is close to normal, which indicates that there is an opportunity to intervene before these metabolites accumulate.

A loading dose of 15 mg per kilogram of body weight is administered intravenously, up to a maximum dose of 1500 mg, followed by 10 mg per kilogram every 12 hours for 48 hours, after which the dose is increased to 15 mg per kilogram every 12 hours to compensate for increased metabolism of fomepizole. The treatment is continued until the patient has an ethylene glycol level that is below 20 mg per deciliter and is asymptomatic, with a normal pH.

Patients who receive fomepizole should also receive cofactor therapy with thiamine, pyroxidine, and folate. Those who receive hemodialysis require more frequent dosing. The dosing and administration of fomepizole is the same for children and adults.



What Would You Do?

Make another choice

✓ **The administration of sodium bicarbonate is an appropriate treatment choice if it is used in combination with fomepizole.**

Outcome of This Strategy

An infusion of sodium bicarbonate (approximately 150 mmol in 1 liter of 5% dextrose) is administered at a rate of 200 ml per hour in addition to fomepizole. An anion gap develops and increases in the initial 12 hours after the infusion, after which the patient's electrolyte level and anion gap normalize.

Comments

The toxic metabolites of ethylene glycol (glycolic acid, glyoxylic acid, and oxalic acid) are more likely to permeate end organs if the metabolites are protonated. Sodium bicarbonate can mitigate the effects of ethylene glycol toxicity by preventing systemic acidemia. If administered with fomepizole, sodium bicarbonate is a reasonable therapeutic option, but it should not be used in lieu of fomepizole.

What Would You Do?

Make another choice

✓ The administration of ethanol is generally not preferred.

Outcome of This Strategy

Ethanol is administered. The patient becomes progressively obtunded and is intubated after an aspiration event.

Comments

Ethanol is a competitive inhibitor of alcohol dehydrogenase and can prevent the metabolism of ethylene glycol to toxic metabolites, since the enzyme has greater affinity for ethanol. However, it is difficult to determine the correct dose of ethanol, and the incorrect dose can cause behavioral problems in addition to sedation, respiratory depression, and hypotension. In addition, the affinity of fomepizole for alcohol dehydrogenase is 8000 times as high as that of ethanol. Therefore, ethanol might be a reasonable choice only if fomepizole is not available.

What Would You Do?

Make another choice

✕ The initiation of hemodialysis is an inappropriate treatment choice.

Outcome of This Strategy

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Comments

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- ✓ Administer fomepizole
- ✓ Administer sodium bicarbonate
- ✓ Administer ethanol
- ✗ Initiate hemodialysis

Patient Outcome

Given the absence of both acute kidney injury and severe acidemia, hemodialysis was not performed. The patient was thought to have early manifestations of ethylene glycol toxicity and received treatment with fomepizole and a sodium bicarbonate drip. Thiamine, pyridoxine, and folate were also administered.

The patient's anion gap and osmolal gap resolved. The assessment of the ethylene glycol level was returned at 1998 mg per liter, and 24 hours later the level had decreased to 1573 mg per liter.

Within 48 hours after this patient's initial presentation, his electrolyte levels and acid–base status had normalized. His neurocognitive status also returned to normal.

The patient acknowledged his alcohol dependence and said he had thought that antifreeze could be consumed as a substitute for alcohol. He was referred to psychiatry for counseling and treatment of substance abuse.

TAKE HOME MESSAGE

- ANALYSE FINE DU GDS A LA RECHERCHE DE TROUBLES COMPLEXES

- PENSER A L'INTOXICATION AUX ALCOOL TOXIQUE FACE A UNE ACIDOSE METABOLIQUE NON EXPLIQUEE (LACTATE ELEVEE, IR, ACD)