

CHAPTER

66

Metabolic Abnormalities in Critically Ill Patients

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Introduction

Critically ill patients have a unique set of problems, ranging from metabolic, endocrine, nutritional, respiratory and hemodynamic complications. Addressing these problems is like playing a game of chess, checkmating each disturbed parameter and restoring them to normalcy. Unfortunately these abnormalities are interlinked. To focus unilaterally on a abnormality in a critically ill patient is unfair. However it would be worthwhile to discuss at present the common metabolic problems in critically ill patients.

The common metabolic abnormalities one faces while treating critically ill patients are :

- a. Glycemic Control.
- b. Acid-Base Abnormalities.
- c. Electrolyte imbalance.

Glycemic Control

Glycemic control is a challenge in critically ill patients. Until 2001, it was thought that maintenance of blood sugar values upto 220 mg/dl would benefit critically ill patients, since hyperglycemia due to stress occurs and higher values were also required to support the energy needs of glucose-dependent organs. However current opinion based on evidences supports a different view point.

Hyperglycemia commonly occurs in situations of stress such as trauma, burns, major surgery, sepsis, and in patients receiving dextrose infusions, particularly as part of parenteral nutrition. It is associated with complications such as fluid and electrolyte disturbances and increased risk of infections. Studies have shown that impairment of host defences occurs with a decrease in polymorphonuclear leukocyte mobilization, chemotaxis and phagocytic activity related to hyperglycemia.

Stress induced hyperglycemia also induces increased sympathomimetic activity, with increased release of counterregulatory hormones and proinflammatory cytokines. Counterregulatory hormones enhance glycogenolysis and gluconeogenesis to increase glucose production. Growth hormone inhibits peripheral uptake of glucose and stimulates gluconeogenesis. Proinflammatory cytokines also contribute to hyperglycemia by stimulating gluconeogenesis and glycogenolysis. Release of counter regulatory hormones namely glucagon and cortisol are also stimulated by proinflammatory cytokines. Proinflammatory cytokines also contribute to the development of insulin resistance by inhibiting insulin release. These mechanisms interfere in maintaining euglycemic state in critically ill patients. The problem gets more compounded if the patient is a diabetic.

Evidence through several studies between 2001 till date have shown that tight glycemic control decrease morbidity and mortality in critically ill patients. Current evidence points towards maintaining blood sugar between 80 -120 mg/dl.

In patients receiving nutritional support, strict glycemic control is essential. Hyperglycemia in these group of patients can lead to higher rates of infection, already prone to infectious complications in view of the central venous catheters or existing premorbid conditions requiring parenteral nutritional support.

In these group of patients prevention of hyperglycemia should be the first step. The first step is to eliminate all other dextrose sources and start with low dextrose load and advance slowly. A starting dextrose infusion rate of 2 mg/kg/min should be advanced to 4 mg/kg/min or less. Supplemental insulin administration using a sliding scale for 1-2 days, then the average of 24 – hour insulin required is calculated. 70% of that is added in the parenteral nutrition bag (not less than 10 units), while HGT monitoring is continued at regular intervals. However use of sliding scale may not be very effective in these group of patients. To maintain tight glycemic control ideally one should use continuous insulin infusion with dose titration to achieve the goal of 80 – 120 mg/dl.

Acid-Base Abnormalities

The maintenance of normal acid –base equilibrium in the blood is essential for the normal body function. Acid-base abnormalities are a common problem in intensive care settings. Commonly encountered is metabolic acidosis, lactic acidosis and to a certain extent metabolic alkalosis. Studies have shown that metabolic acidosis adversely affect the outcome in critically ill patients irrespective of the etiology. Experimental evidence also suggests that acidosis itself can influence hemodynamics and innate immunity. Studies also suggest that different acids are associated with different responses. In comparison with chloride, acidosis due to lactate or other anions was associated with much higher

mortality in hospital. It has been a widely accepted fact that lactic acidosis is associated with a high mortality when compared to metabolic acidosis due to other causes. It is therefore imperative to measure serum lactate levels in critically ill patients to prognosticate the outcomes.

The diagnosis of metabolic acidosis rests on a clinical perception of the presence of the problem. It should be suspected in patients with uncontrolled diabetes mellitus, renal failure both acute or chronic, toxic ingestion with acids, drugs like aspirin, alcohol and in patients with dehydration from any cause. Metabolic acidosis can also occur following hypoxia, hypoperfusion, shock or cardiac arrest. In general determination of type of metabolic acidosis can be made by calculating the anion gap. **2 group of metabolic acidosis occur, one with a normal anion gap and the other with a high anion gap.**

The group with normal anion metabolic acidosis is characterized by loss of bicarbonates. To compensate for this loss and to maintain electrical neutrality, replacement of chloride ions occur causing hypochloremic metabolic acidosis.

Common causes of normal anion gap metabolic acidosis seen in critically ill patients are:

- Acute gastro-enteritis.
- Renal tubular acidosis.
- Compensation for respiratory alkalosis.
- Intestinal or pancreatic fistula, and
- Fluid infusion having a high chloride content.

The second type is characterized by addition of a fixed acid eg, lactic acid leading to high anion gap metabolic acidosis. Studies have pointed to that fact that acidosis resulting from lactate were associated with a higher mortality rate.

Common causes of high anion gap metabolic acidosis include

- Lactic acidosis
- Ketoacidosis (Diabetics and Alcoholics).

- Renal failure, and
- Poisonings. (salicylates, acids, ethylene and methyl alcohol).

Lactic acidosis deserves a special mention as it is associated with high mortality rates if undiagnosed or untreated.

Common causes of lactic acidosis in critically ill patients,

- Shock of any etiology.
- Severe anemia (Hb < 5 gms).
- Hypoxia particularly when associated with a low cardiac output.
- Hepatic failure.
- Severe respiratory or metabolic alkalosis.
- Thiamine deficiency.
- Drugs e.g., epinephrine or nitroprusside.

Correction of metabolic acidosis is very important. Treatment should be directed towards rectifying the etiology of metabolic acidosis while administering sodium bicarbonate to restore the pH. The amount of sodium bicarbonate given is calculated using one of the 2 underlying formulae;

- NaHCO_3 to be given = body wt (kg) x 0.3 x base deficit.
- NaHCO_3 to be given = 0.5 x body wt (kg) x (desired HCO_3^- - serum HCO_3^-)

The usual practice is to give half the dose immediately, balance over the next 4-6 hours. However the best guideline for correction is to maintain an arterial pH above 7.3.

Metabolic Alkalosis

Metabolic alkalosis is also commonly encountered in critically ill patients. Focus on metabolic acidosis invariably causes the clinician to overlook metabolic alkalosis.

Commonly encountered situations causing metabolic alkalosis are vomiting, ryles tube aspiration, diuretics and hypokalemia. It is worth noting that metabolic alkalosis can cause shift in

oxygen dissociation curve to the left, which can cause a further fall in PaO_2 , which might lead to adverse effects in critically ill patients. In almost all ICU patients, metabolic alkalosis is chloride responsive, and the chloride should be replaced with normal saline. Management is also directed towards correction of the etiological factor. Associated hypokalemia should also be corrected. Concurrent Mg^+ deficiency will impair K^+ correction. Hence correction of Mg^+ deficiency must be dealt with, which will allow easier correction of K^+ deficiency.

The volume of normal saline to be infused should depend on the precipitating etiology, clinical condition of the patient and the degree of electrolyte disturbance. Recommended formula for correction of chloride deficit is,

Chloride deficit = $0.27 \times \text{wt}(\text{kg}) \times (100 - \text{present chloride in mEq/L})$

Volume of saline to be administered (L) = Cl deficit/154*

*(the Cl present in 1 Litre of Normal Saline = 154 mEq).

Electrolyte Abnormalities

Electrolyte abnormalities are a common occurrence in critically ill patients. Though a myriad of electrolyte abnormalities occur, we will restrict to mentioning about common abnormalities viz sodium and potassium.

Sodium Abnormalities

Disorders of plasma sodium concentration i.e. hyponatremia and hypernatremia are the most common clinically observed problems in critically ill patients. The approach to management needs a delicate balance between correction of the imbalance and risk of treatment of the etiology.

Hypernatremia

Hypernatremia is a common clinical problem in approximately 15% of patients admitted in intensive care unit. The maintenance of normal

serum sodium concentration (135 to 145 mEq/L) is dependent on the balance between water intake and water excretion. Hypernatremia occurs when concentration of serum sodium is > 145 mEq/L. It may present as;

Etiology

Hypervolemic Hypernatremia

- Diet
- Hypertonic saline
- Excessive NaHCO_3 administration
- Cushing's syndrome, Conn's syndrome

Isovolemic Hypernatremia

- Fluid loss through sweat / lung
- Diabetes Insipidus. (Central and Nephrogenic)

Hypovolemic Hypernatremia

- Diabetes insipidus in setting of impaired thirst or unavailability of water.
- Increased Renal Water Loss, e.g. Diuretics, Osmotic Diuresis, Salt – Wasting Nephropathy,
- Increased Non Renal Water Loss, e.g. GI Losses like vomiting, Diarrhea, Biliary drainage, Fistula, Fluid loss.
- Cutaneous losses, e.g. Insensible water loss, Burns injury, Perspiration.
- Respiratory losses.

Treatment of Hypernatremia

Once diagnosis of Hypernatremia is made prompt treatment is necessary. During correction of hypernatremia caution should be exercised in following a set guideline, rather than rapid correction. If hypernatremia is corrected rapidly than likelihood of cerebral edema can develop. Monitoring of serum sodium should be done, with careful assessment of ongoing fluid loss. Correction of hypernatremia therefore depends on the following guidelines.

Hypovolemic Hypernatremia

Correct volume deficit.

- Administer isotonic saline, until improvement of orthostasis, tachycardia occurs.
- Treat etiology of losses

Correction of water deficit

- Calculate water deficit
- Administer 0.45% saline, replacing deficit and ongoing losses

Euvolemic Hypernatremia

Correction of water deficit

- Calculate water deficit
- Administer 0.45% saline, replacing deficit and ongoing losses
- Follow serum Na^+ carefully to avoid water intoxication

Long Term Therapy

Central Diabetes Insipidus

- DDAVP (Complete Central DI)
- Clofibrate, Carbamazepine, Chlorpropamide and Aqueous vasopressin. (Partial Central DI)

Nephrogenic Diabetes Insipidus

- Correction of K^+ and Ca^+
- Removal of offending drug
- Low sodium diet
- Drugs; Thiazide diuretics, Amelorida

Hypervolemic Hypernatremia

Removal of sodium

- Discontinue offending drug
- Furosemide
- Hemodialysis as required for renal insufficiency

Hyponatremia

Incidence of hyponatremia is approximately 30% in intensive care units. Hyponatremia occurs when serum Na⁺ values are < 135 mEq/L. Studies have shown that mortality with acute hyponatremia is as high as 50%, whereas with chronic hyponatremia is 10% to 20%. The problem in hyponatremia is a water problem and not a sodium problem. There is excess of water relative to sodium when hyponatremia is present.

Etiology

Hyponatremia may present as,

Hypoosmolar Hyponatremia

Increased ECF (Hypervolemia)

- CCF
- Cirrhosis of Liver
- Renal failure
 - Normal ECF volume and no edema. (Euvolemia).
- SIADH
- Hypothyroidism
- Psychogenic Polydipsia
- Glucocorticoid Deficiency
 - Decreased ECF Volume (Hypovolemia). (Estimate Urinary Na⁺ Levels)
 - Salt/water losses replaced with hypotonic fluids.
 - Diuretics, Adrenal Insufficiency, Bowel Obstruction, Renal Injury.

Normosmolar Hyponatremia (Pseudo hyponatremia).

- Hyperlipidemia
- Hyperproteinemia

Hyperosmolar Hyponatremia

- Mannitol
- Hyperglycemia

Management of Hyponatremia

Management of hyponatremia would be reflected by the clinical presentation of the patient and the underlying etiology

Acute Symptomatic Hyponatremia

- 3% hypertonic saline with loop diuretic
- Correct at rate not more than 2 mEq/L/h
- Correct not more than 12 mEq/L over first 24 hours.

Chronic Symptomatic Hyponatremia (> 48 hours, or unknown duration)

- 3% hypertonic saline with loop diuretic
- Correct at rate not more than 1-5 mEq/L/h.
- Correct not more than 12 mEq/L over first 24 hours.
- Correct till patient asymptomatic or 10% correction of serum sodium.
- Close monitoring of electrolytes and neurologic status.

Asymptomatic Hyponatremia

Euvolemia

- Treat underlying cause
- Restrict water intake
- Rarely hypertonic saline indicated

Hypovolemia

- Treat underlying cause of hypovolemia
- Normal saline

Hypervolemia

- Treat underlying cause of decreased effective circulating volume
- Salt and water restriction
- Loop diuretics for some patients

Potassium Abnormalities

Potassium abnormalities occur due to a wide range of causes in sick patients. Unfortunately the exact quantification of extent of the abnormality

in critically ill patients is a trifle difficult, which goes to show the relatively high incidence. Potassium abnormalities occur as hypokalemia and hyperkalemia. Prompt correction of either of the two situations is essential to minimize morbidity and mortality.

Hyperkalemia

Hyperkalemia occurs when serum K^+ values are above the prescribed upper limit of the normal range of the given laboratory values, i.e. > 5.4 mEq/L. Hyperkalemia is less frequent than hypokalemia, but is more likely to cause serious complications in critically ill patients due to serious cardiovascular side effects. Correction therefore should be rapid.

Etiology

Increased intake (usually coupled with decreased excretion)

- Unusual diet (low Na^+ , K^+ supplement, salt substitute)
- Excessive parenteral administration

Decreased Excretion

- Renal failure
- Decreased mineralocorticoid effect
 - Addison's disease
 - RTA – Type IV
 - Urinary obstruction
 - Drugs e.g. ACE inhibitors, K^+ sparing diuretics, NSAIDs

Extracellular shift

- Hormonal
 - Glucagon
 - β -Blockade
 - α -Adrenergics
 - Insulin deficiency
- Physical
 - Acidemia
- Miscellaneous

- Hyperkalemic periodic paralysis
- Digoxin Toxicity

Management of Hyperkalemia

Correction of hyperkalemia is very vital as mentioned above. Approach to correction depends on the severity of hyperkalemia and the underlying etiology.

Mild Hyperkalemia

- Search cause of hyperkalemia
- Discontinue offending drugs, (K. salts of penicillin, ACE inhibitors, K sparing diuretics), iv infusions, diet
- Optimize Renal excretion of K^+ by use of diuretics e.g. furosemide
- Administration of small doses of exchange resins orally or rectally e.g. sodium polystyrene sulfonate (Kayexalate)
- Monitor serum K^+ values at regular intervals

Severe Hyperkalemia

- Emergency
- Cardiac Protection – Cal gluconate 10 ml 10% iv slow bolus
- 2 approaches
 - A. Enhance K^+ movement into the cells.
 - $NaHCO_3$ IV
 - Glucose Insulin drip
 - Albuterol (by nebulization)
 - B. Remove K^+ from body
 - Furosemide or another loop diuretic iv
 - Per Rectal administration of Exchange Resin

Refractory Hyperkalemia

- Dialysis

Hyperkalemia associated with Digoxin Toxicity

- Do not administer calcium

- Give MgSO_4 (e.g. 2 gm iv) if no contra-indication.
- Consider digoxin-specific antibody fragment treatment

Hypokalemia

Hypokalemia is said to occur when serum K^+ values are < 3.5 mEq/L. It is a more serious complication in critically ill patients, as severe hypokalemia can lead to significant complications. In critically ill patients it should be realised that increased losses are more commonly responsible for K^+ depletion than inadequate ingestion. Losses are commonly due to use of diuretics, though several other causes are also responsible for hypokalemia. In general hypokalemia occurs when serum K^+ falls below 3.6 mEq/L.

Etiology

Decreased Intake

- Unusual diet (e.g. tea and toast)
- Parenteral fluids deficient in K^+

Increased Excretion

Renal - Increased Mineralocorticoid Effect

- Primary Hyperaldosteronism
- Secondary Hyperaldosteronism

Volume depletion, Vomiting, CCF, Cirrhosis, Mineralocorticoid administration.

- Osmotic Diuresis
- Tubular defects
- Hypomagnesemia

GastroIntestinal

- Diarrhea

Intracellular Shift

Hormonal

- Insulin
- β -Adrenergics
- Aldosterone

Physical

Alkalemia

Miscellaneous

- Hypokalemic Periodic Paralysis
- Thyrotoxic Periodic Paralysis

Management of Hypokalemia

The immediate goal is to correct cardiac arrhythmias and neuromuscular disturbances. Reduction of 1 mmol/L in plasma K^+ conc (from 4.0 to 3.0 mmol/L) may represent a total body deficit of 200 – 400 mmol. Plasma levels under 3 mmol/L often require in excess of 600 mmol of K^+ to correct the deficit.

Non life threatening Hypokalemia

- Oral replacement therapy ideal.
- If oral cannot be tolerated. IV Therapy : KCl infusion rate should not exceed 20 mmol/ hr unless paralysis or malignant ventricular arrhythmias are present.

Severe Hypokalemia

- IV Therapy :
upto 40 mmol / liter via peripheral vein.
upto 60 mmol / liter via central vein.

KCl infusion rate should not exceed 20 mmol/hr unless paralysis or malignant ventricular arrhythmias are present. Use saline containing drips initially to avoid glucose induced insulin mediated K^+ movement into cells causing increase in Hypokalemia. KCl preparation of choice will promote more rapid correction of hypokalemia and metabolic alkalosis. KHCO_3 and Citrate (metabolized to HC03^-) appropriate for Hypokalemia tend to alkalinize the patient and would be more appropriate to treat hypokalemia due to chronic diarrhea or RTA. Rapid iv administration of K^+ should be used judiciously and requires close clinical observation and ECG monitoring and serial monitoring of K^+ values. High concentration of potassium infusion should be given through a central line with controlled rates and cardiac monitoring. If magnesium levels are low,

they should be corrected, because hypomagnesemia promotes renal loss of K^+ , making correction of hypokalemia more difficult. Post correction of hypokalemia it is mandatory that, prevention of further losses should be prevented by continuous supplementation of K^+ , with monitoring of serum K values. Use of potassium sparing diuretics can be also used according to clinical situation, but caution should be exercised, because of development of hyperkalemia can occur causing adverse consequences. It is therefore imperative to monitor; ECG, serum K^+ and serum Mg^+ values.

Conclusion

Metabolic abnormalities constitute a major chunk of problems in critical care units. Setting the parameters right can influence in a positive way, the outcomes in a critically ill patient. The success

lies in recognition of the problem, and employing prompt measures in correcting the problems in a scientific manner, thereby preventing morbidity and mortality.

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