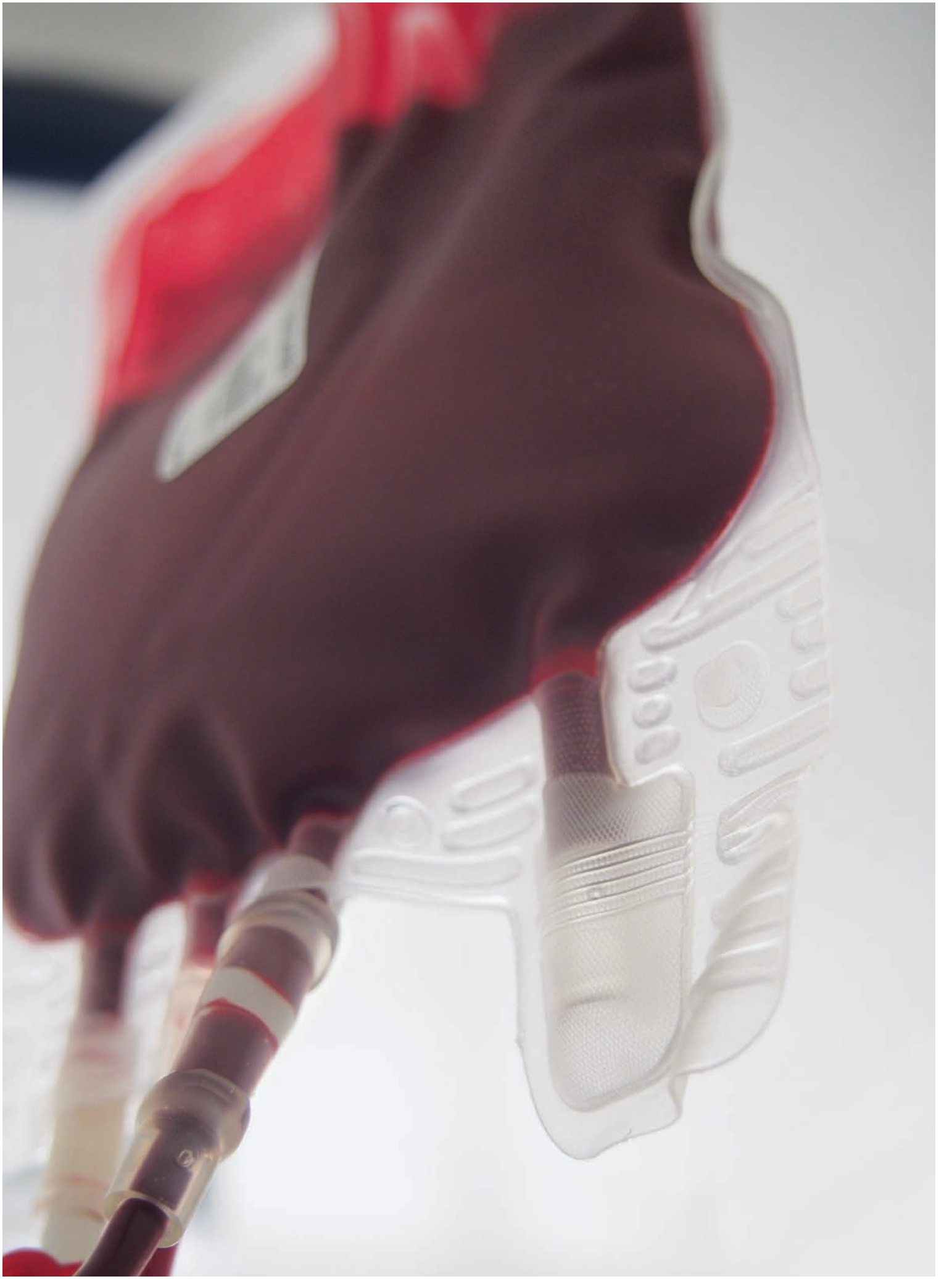

Managing hypocalcemia in massive blood transfusion

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MR. P, 56, had a history of cirrhosis, pancreatitis, and peptic ulcer disease. He was admitted to the ED with hematemesis (estimated at about 1 L). On presentation, he was responsive to painful stimuli only. He was immediately placed on a cardiac monitor. His initial vital signs were: BP 70/40, heart rate 134/minute sinus tachycardia, respiratory rate 28/minute, temperature 35.5 °C (95.9° F), and SpO_2 89% on room air. His mild hypothermia was likely related to losing a significant amount of blood and being hypotensive for an unknown period.[1]

Mr. P was immediately endotracheally intubated to protect the airway and two large-bore peripheral I.V. catheters, a large-bore orogastric tube (OGT), and an indwelling urinary catheter were inserted. An arterial line was inserted and 3 L of 0.9% sodium chloride was administered I.V. bolus.

Initial lab values revealed hemoglobin (Hgb) 4.4 g/dL (normal, 14 to 17.4 g/dL) and hematocrit (Hct) 13.2% (normal, 42% to 52%). For other assessment findings, see Mr. P's initial lab results *and* Mr. P's initial ABGs.

Mr. P underwent an emergency upper endoscopy, which showed acute variceal hemorrhage. I.V. octreotide was initiated and endoscopic variceal ligation was attempted. Mr. P remained hypotensive at 90/50 mm Hg in spite of ongoing treatment with normal saline boluses, blood transfusions, and vasopressor therapy. His OGT drained about 2.5 L of bright red blood.

At this time, the hospital's massive transfusion (MT) protocol was initiated.

Nursing care for patients receiving MT is challenging because MT is associated with serious and potentially fatal consequences such as hypocalcemia, hypothermia, dilutional coagulopathy, hypomagnesemia, citrate toxicity, lactic acidosis, and air embolism.[2] Clinically significant hypocalcemia, a common complication of MT, can cause neurologic and cardiovascular dysfunction that can further compromise survival. Mortality for patients receiving MT to treat hemorrhage from nontraumatic causes has been estimated at about 23%.[3]

Based on a discussion of Mr. P's case history, this article focuses specifically on the nurse's role in caring for patients with hypocalcemia related to MT.

Defining MT

Depending on facility protocol, MT may be defined in several ways:[4]

- the transfusion of 10 or more RBC units in a 24-hour period

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• transfusion of 5 RBC units over 3 or 4 hours
• transfusion of 3 RBC units in 1 hour.

The last two definitions aim to include patients who might die early or those in the acute resuscitation phase.[5] Clinicians are encouraged to review their facility's MT protocol, including facility-specific MT criteria.

A comprehensive discussion of MT protocols is beyond the scope of this article. However, given that MT is a low-frequency but high-impact clinical event, the multidisciplinary team is encouraged to maintain familiarity with their facility's MT protocol through regular trainings (such as clinical simulation) and debriefing postevent for continuous quality improvement.[6] (See *Key elements of an MT protocol*.)

Understanding calcium's role

Calcium (Ca^{++}) is the major divalent cation in the body. Almost all (99%) of Ca^{++} in the human body is stored in the bones, where it provides strength and stability for the skeletal system and serves as an exchangeable source to maintain extracellular fluid (ECF) calcium levels. Most of the remaining calcium (approximately 1%) is located in the intracellular fluid. Only 0.1% to 0.2% (approximately 8.5 to 10.5 mg/dL, or 21 to 26 mmol/L) of the remaining calcium is present in the ECF.[7]

The total serum calcium concentration consists of three forms: ionized, complexed, and protein-bound.[7] Approximately 50% of total serum Ca^{++} is ionized or free, meaning that the Ca^{++} molecule is metabolically active.[8] Only the ionized form of Ca^{++} (normal, 4.65-5.28 mg/dL [1.16-1.32 mmol/L]) is free to leave the vascular compartment and participate in cellular functions. As discussed in more detail later, these wide-ranging effects are involved in blood coagulation, membrane potentials, and neuronal excitability; skeletal, cardiac, and smooth muscle function; and release of various hormones and neurotransmitters. Ionized serum Ca^{++} concentration is tightly regulated by parathyroid hormone (PTH) and vitamin D.[7] (See *Understanding Ca^{++} homeostasis*.)

About 10% of serum Ca^{++} is complexed, or bound to organic and inorganic acids such as citrate and phosphate. The remaining 40% of serum Ca^{++} is bound to protein, primarily albumin.[9] For this reason, total serum Ca^{++} levels are strongly influenced by serum albumin levels. Ionized Ca^{++} levels are also inversely affected by the blood's pH; when arterial pH increases, more calcium is bound to protein.[7]

Formulas have been proposed to obtain a corrected Ca^{++} level based on total serum Ca^{++} and serum albumin levels, but the most accurate method of measuring metabolically active serum calcium is to obtain an ionized Ca^{++} level. However, this may not be standard protocol in all settings.[8,9]

How hypocalcemia develops

Hypocalcemia represents a total serum calcium level of less than 8.8 mg/dL (2.2 mmol/L) and an ionized Ca^{++} level of less than 4.65 mg/dL (1.16 mmol/L). A pseudohypocalcemia is caused by hypoalbuminemia. It results in a decrease in protein-bound rather than ionized Ca^{++} and usually is asymptomatic. Before a diagnosis of hypocalcemia can be made, the total serum calcium should be corrected for low albumin levels.[7]

The most common causes of hypocalcemia are abnormal losses of calcium by the kidney, impaired ability to mobilize calcium from bone due to hypoparathyroidism, and increased protein binding or chelation such that higher proportions of calcium are in the nonionized form. In renal failure, an important cause of hypocalcemia, decreased production of activated vitamin D and hyperphosphatemia both play a role. Because of the inverse relationship between calcium

Mr. P's initial lab results

On admission to the ED, Mr. P's initial lab values were as follows:
- white blood cell count 16,000 cells/mm^3 (normal, 5,000-10,000 cells/mm^3)
- red blood cell (RBC) count 2.0 x 10^6/mm^3 (normal, 4.5-5.5 x 10^6/mm^3)
- Hgb 4.4 g/dL (normal, 14-17.4 g/dL)
- Hct 13.2% (normal, 42%-52%)
- platelets 86,000/mm^3 (normal,140,000-400,000/mm^3)
- activated partial thromboplastin time (aPTT) >60 seconds (normal, 21.0-35.0 seconds)
- prothrombin time (PT) 30 seconds (normal, 11.0-13.0 seconds)
- international normalized ratio (INR) 2.10 (normal, 0.8-1.2)
- serum sodium 148 mEq/L (normal, 135-145 mEq/L)
- potassium 4.8 mEq/L (normal, 3.5-5.2 mEq/L)
- chloride 105 mEq/L (normal, 96-106 mEq/L)
- carbon dioxide 17 mEq/L (normal, 23-30 mEq/L)
- total Ca^{++} 7.8 mg/dL (normal, 8.8-10.4 mg/dL; ionized Ca^{++} was not measured for this patient)
- phosphate 5.1 mg/dL (normal, 2.7-4.5 mg/dL).

Reference for normal lab values: Fischbach F, Dunning III MB. *A Manual of Laboratory and Diagnostic Tests.* 9th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014.

Mr. P's initial ABGs

- pH, 7.30 (normal, 7.35 to 7.45)
- $PaCO_2$, 33 mm Hg (normal, 35 to 45 mm Hg)
- HCO_3, 16 mEq/L (normal, 21 to 27 mEq/L)
- PaO_2 65 mm Hg (normal, greater than 80 mm Hg)
- SaO_2 89% (normal, greater than 95%).

Reference for normal values: Theodore AC. Arterial blood gases. UpToDate. 2015. www.uptodate.com.

and phosphate, serum Ca^{++} levels fall as phosphate levels rise.[7]

Magnesium levels also affect serum Ca^{++} levels by influencing PTH secretion and intestinal reabsorption of Ca^{++}.[10] Severe hypomagnesemia has been shown to cause secondary hypocalcemia.[8] In cases of chronic hypomagnesemia, the decreasing effect on serum calcium is due to an inhibitory effect on PTH secretion. However, in acute-onset hypomagnesemia, the mechanism hasn't yet been fully elucidated.[11]

Hospitalized patients are at risk for hypocalcemia due to both their disease state and iatrogenic causes. For example, sepsis and other proinflammatory states are associated with hypocalcemia. Many inflammatory cytokines such as tumor necrosis factor alpha have been shown to inhibit PTH, which leads to hypocalcemia. Acute kidney injury and fluid overload, which are both common disorders in critically ill patients, can also contribute to hypocalcemia.[9]

As in Mr. P's case, acute pancreatitis is often associated with hypocalcemia. The combination is associated with poorer outcomes (see *Pancreatitis and hypocalcemia: A deadly combination*).[12]

Why MT can lead to hypocalcemia

Iatrogenic causes of hypocalcemia in critically ill patients include volume overload from aggressive fluid resuscitation and blood transfusions.[9] The association between blood transfusion and hypocalcemia has long been recognized.[13] In one retrospective study of trauma patients who received MT, 97% (n = 152) of patients were noted to have hypocalcemia. Of these patients, 71% had severe hypocalcemia, defined as ionized calcium <3.6 mg/dL (0.90 mmol/L).[14] Severe hypocalcemia was associated with worse outcomes.

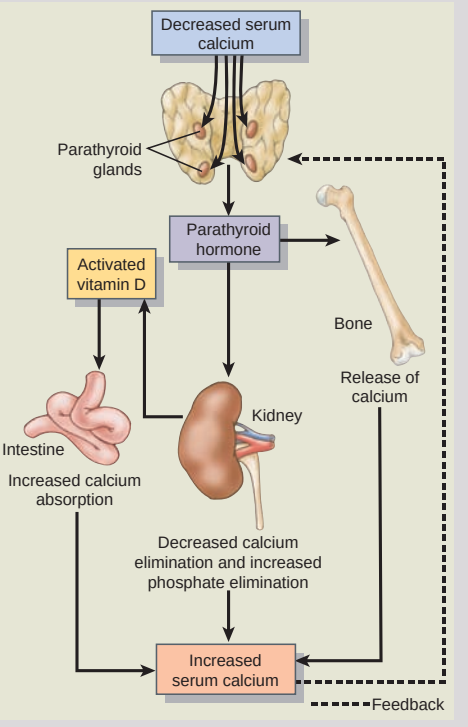
In patients receiving blood transfusions, hypocalcemia results from the citrate chelation of serum Ca^{++}.[15] Each unit of packed RBCs (PRBC) and fresh frozen plasma (FFP) contains approximately 3 g of citrate used as a preservative and anticoagulant. Normally, the liver metabolizes and clears citrate in a matter of minutes. However, in patients who are in hemorrhagic shock and require MT, as in the case of Mr. P, liver function is often impaired due to hypoperfusion.[14] In Mr. P's case, a history of cirrhosis and pancreatitis both raised the risk of hypocalcemia. In context of hemorrhagic shock, hepatic hypoperfusion led to critical levels of hypocalcemia due to citrate binding.

Hypocalcemia in critically ill patients requiring MT is exceptionally detrimental because Ca^{++} plays a crucial role in normal coagulation.[15] Ca^{++} is a cofactor in factor II, VII, IX, and X along with protein C and protein S of the coagulation cascade, and it also contributes to platelet adhesion at the site of vessel injury.[14] In combination with transfusion of a large amount of cold temperature blood products, MT can worsen the lethal triad of hypothermia, acidosis, and coagulopathy, placing patients in hemorrhagic shock at a higher risk for death.[16] In Mr. P's case, hypothermia was addressed by using a blood warmer during transfusion and avoiding unnecessary exposure of Mr. P's body surface. Metabolic acidosis in MT results from hypoperfusion of end organs (anaerobic metabolism) and liver dysfunction, which prevents the conversion of citrate to bicarbonate and causes lactic acidosis.[17]

Hypocalcemia and cardiac dysfunction

Besides coagulation, Ca^{++} plays an important role in neuromuscular and cardiovascular membrane stability, cardiac conduction, and myocardial contractility.[18] Ca^{++} supplementation

Understanding Ca^{++} homeostasis[7]



Homeostatic mechanisms that regulate serum calcium and phosphorus levels involve the intestine, kidney, and bone, principally through the complex interaction of PTH and vitamin D. The main function of PTH is to maintain ECF calcium concentrations by stimulating the release of calcium and phosphorus from bone into the ECF; increasing renal reabsorption of calcium and excretion of phosphorus; and enhancing the gastrointestinal absorption of calcium and phosphorus through its effects on vitamin D synthesis. Vitamin D, which functions as a hormone, is synthesized by the skin and converted to its active form, calcitriol, in the kidney. The active form of vitamin D has several effects on the intestines, kidneys, and bone that increase serum levels of calcium and phosphorus and contribute to their feedback regulation. It stimulates the absorption of calcium, and to a lesser extent phosphorus, from the intestine; it increases calcium and phosphorus reabsorption by the renal tubules; and it inhibits PTH synthesis by the parathyroid glands.

has been shown to improve signs and symptoms of heart failure and hypotension in critically ill patients both with and without chronic hypocalcemia.[9]

Because Ca^{++} plays a role in myocardial contractility, hypocalcemia has been associated with cardiac dysfunction. Newman et al. conducted a systematic review and meta-analysis of case reports from 1948 through 2011 that described hypocalcemia-associated cardiac dysfunction.[19] The review showed that the most commonly reported cardiac dysfunctions associated with hypocalcemia are heart failure, prolonged corrected QT interval (QTc), and sinus tachycardia. Although a definite causal relationship can't be established, 98% of the cardiac dysfunctions described resolved after treatment with calcium infusions. And in a small study that used echocardiography to evaluate cardiac function postdialysis in patients with end-stage renal disease, an acute decrease in systolic function was associated with a decreased ionized Ca^{++} level.[19]

Key elements of an MT protocol[6]

The American College of Surgeons Trauma Quality Improvement Program provides guidelines for developing and initiating a massive transfusion protocol (MTP) in trauma. The guidelines specify that MTPs should be written documents accessible and familiar to all. All staff should receive initial training and regular drills to maintain proficiency. The guidelines state that this is particularly important in smaller facilities where MT is rare.

The MTP should address:

- triggers for initiating MT in trauma. Triggers should include at least one of the following: Assessment of Blood Consumption score of two or more, persistent hemodynamic instability, active bleeding requiring surgery or angioembolization, and blood transfusion in the trauma bay.
- resuscitation in the trauma bay, including MTP product availability, delivery, and transfusion.
- continuing MTP in the OR, angiography suite, and ICU.
- transfusion service processes for delivery of blood products.
- transfusion targets.
- termination of the MTP.
- performance improvement monitoring.

The guidelines discuss each element in detail and provide performance indicators such as time from calling MTP to infusion of first RBC unit and wastage rates for blood products.

Mr. P's signs

While in the ICU, Mr. P was lethargic and had jerky movements of his upper extremities (questionable focal seizures). He also exhibited Trousseau sign, which is carpopedal spasm induced by inflation of a sphygmomanometer cuff above systolic BP for 3 minutes. (See Trousseau sign in hypocalcemia.*) Carpopedal spasm is characterized by adduction of the thumb, flexion of the metacarpophalangeal joints, extension of the interphalangeal joints, and flexion of the wrist, and is a sign of hypocalcemia.[20] His total serum calcium level at this time was 6.8 mg/dL and the ionized Ca^{++} level was 3.0 mg/dL. His ECG showed sinus tachycardia and a prolonged QTc. Hypocalcemia characteristically causes prolongation of the QTc, which increases the risk of torsades de pointes, a life-threatening cardiac dysrhythmia.[20] In addition, bedside echocardiography showed new moderate left-ventricular systolic dysfunction. His ejection fraction was 50% (normal, ≥55%).*

Pancreatitis and hypocalcemia: A deadly combination

Acute pancreatitis is often associated with hypocalcemia due to autolipolysis from the pancreatic enzymes and fat saponification (hydrolysis of the fatty acid esters, turning it into calcium salts or "soap").[15] Hypocalcemia in pancreatitis is a well-recognized phenomenon but an understanding of the mechanism of injury is still evolving. The current theory is that in the acute phase of pancreatitis, the injured acinar cells in the pancreas release lipid-dissolving enzymes that digest mesenteric fat and release fatty acids. These fatty acids can form calcium salts that aren't absorbed, leading to hypocalcemia.[28]

Inflammatory markers released from acute pancreatitis also compound hypocalcemia by inhibiting PTH. Hypocalcemia in acute pancreatitis is an indicator of severity and is associated with worse outcomes.[12]

Mr. P was exhibiting signs of severe hypocalcemia related to MT and compounded by preexisting hypocalcemia and comorbidities, including cirrhosis and pancreatitis.

The clinical manifestations of hypocalcemia depend upon its severity and chronicity. Nonspecific signs and symptoms include fatigue, hyperirritability, anxiety, and depression. Specific signs such as Trousseau sign (as in Mr. P) and Chvostek sign indicate neuromuscular excitability.[20]

Chvostek sign is contraction of the ipsilateral facial muscles elicited by tapping the facial nerve just anterior to the ear. The response ranges from twitching of the lip to spasm of all facial muscles and depends upon the severity of the hypocalcemia.[8,20]

Severe signs of hypocalcemia include seizures, laryngospasm, and bronchospasm. Because these compromise a patient's airway, immediate intervention is indicated.[9]

Calcium correction best practices

No published guidelines for correcting hypocalcemia secondary to MT are currently available. Clinical

practice is mainly derived from the general management of hypocalcemia.[21] General guidelines include closely monitoring the patient's serum ionized Ca^{++} levels and assessing for signs and symptoms of hypocalcemia.

MT-induced hypocalcemia with ionized Ca^{++} levels below 3.6 mg/dL (0.9 mmol/L) or serum total corrected calcium levels of 7.5 mg/dL or less, especially in patients with neurologic and cardiac manifestations, requires prompt calcium replacement.[15,21,22] Ionized Ca^{++} levels below 3.6 mg/dL are associated with increased mortality in critically ill adults; furthermore, ionized Ca^{++} levels less than 3.2 mg/dL (0.8 mmol/L) are associated with cardiac dysrhythmias.[22-24]

Calcium gluconate or calcium chloride?

Calcium gluconate is generally the preferred I.V. calcium salt because it's less likely than calcium chloride to cause tissue necrosis if extravasated.[22] However, calcium chloride may be preferable to calcium gluconate in the presence of abnormal liver function (as in Mr. P's case), because decreased citrate metabolism results in slower release of ionized calcium.[25] Ten percent calcium gluconate contains 90 mg of elemental calcium per 10 mL, while 10% calcium chloride contains 270 mg of elemental calcium per 10 mL.[22]

Calcium chloride replacement is generally reserved for severe symptomatic hypocalcemia, with ionized Ca^{++} levels less than 4 mg/dL (1 mmol/L).[21] To avoid extravasation and tissue necrosis, calcium chloride should be administered via a central venous access device.

In Mr. P's case, 2 g of calcium gluconate was infused over 2 hours. I.V. lorazepam was also administered to manage his possible seizure activity. His jerky arm movements resolved after the first hour and his QTc returned to normal, although he remained hypotensive with a systolic BP of 85 to 92 mm Hg.

Calcium replacement infusions should be administered slowly at a maximum infusion rate of 100 mg/min except in emergency situations, because adverse reactions to both Ca^{++} I.V. preparations are associated with rapid infusion.[22] Calcium should be diluted in dextrose and water or saline because concentrated calcium solutions are irritating to veins. In addition, the I.V. solution shouldn't contain bicarbonate or phosphate, which can form insoluble calcium salts. Use caution to avoid administering too much calcium and causing hypercalcemia by monitoring the ionized calcium concentration. Patients with critically low serum Ca^{++} levels require continuous cardiac monitoring and frequent QTc measurements.[22]

Keeping an eye on electrolytes

MT leads to a host of interrelated metabolic derangements due to rapid infusion of a large amount of blood products in a short time period. In addition to hypocalcemia, potential electrolyte and pH imbalances include hyperkalemia (due to RBC hemolysis in stored blood), hypokalemia (from reentry of potassium into transfused RBCs), hypomagnesemia (from citrate binding), metabolic acidosis (due to potassium leakage from stored RBCs, particularly irradiated blood), and metabolic alkalosis (due to citrate overload; citrate generates bicarbonate).[17] Serial metabolic panels or electrolyte point-of-care testing and arterial blood gas (ABG) trending are part of best practices for patients receiving MT.

After receiving 2 g of I.V. calcium gluconate, Mr. P's ABGs demonstrated partially compensated metabolic acidosis in addition to hyperkalemia and hypomagnesemia. His serum total Ca^{++} level remained at 7.8 mg/dL and the ionized Ca^{++} was 2.3 mg/dL. He continued to drain significant amounts of blood from his OGT. His metabolic acidosis and cirrhosis may have played a role in his poor response to I.V. Ca^{++} replacement.

Rapid MT in patients with hepatic dysfunction can cause more severe and prolonged ionized hypocalcemia compared with patients with normal liver function.[26] Chelation of Ca^{++} with citrate in donor blood forms a Ca^{++}-citrate complex that's metabolized in the liver. Some evidence indicates that ionized Ca^{++} <2.4 mg/dL (0.60 mmol/L) may lead to cardiac arrest.[27]

In Mr. P's case, liver dysfunction may have delayed the correction of his serum Ca^{++} levels. Additionally, his pancreatitis may have also worsened his hypocalcemia secondary to sequestration of Ca^{++} by saponification. As part of comprehensive management of MT-induced hypocalcemia, simultaneous interventions to correct hypomagnesemia, hyperphosphatemia, and hypoalbuminemia must be initiated.[15,26]

In total, Mr. P received 14 units of PRBC, 12 units of FFP, and 10 units of platelets in a 12-hour period. Posttransfusion lab results included Hgb 5.8 g/dL; Hct 16.0%; platelets 60,000/mm^3; aPTT >100 seconds; and INR 2.3. His serum Ca^{++} remained at 7.8 mg/dL and the ionized Ca^{++} was 2.3 mg/dL.

Trousseau sign in hypocalcemia[20]

Trousseau sign is carpopedal spasm induced by inflation of a sphygmomanometer cuff above systolic BP for 3 minutes. The wrist and metacarpophalangeal joints are flexed, the interphalangeal joints hyperextended, and the thumb adducted.

Mr. P went into pulseless ventricular tachycardia a few hours later, most likely from the combination of severe hypocalcemia and metabolic acidosis. During an unsuccessful resuscitation attempt, massive hematemesis continued.

Meeting the challenge

Whether indicated due to traumatic or nontraumatic causes, MT is associated with serious complications and high mortality. Nurses should be familiar with their facility's MT protocol and participate in training and drills to maintain competence.[6] ■

REFERENCES

1. Kheirbek T, Kochanek AR, Alam HB. Hypothermia in bleeding trauma: a friend or a foe? *Scand J Trauma Resusc Emerg Med*. 2009;17:65.
2. Mitra B, Olaussen A, Cameron PA, O'Donohoe T, Fitzgerald M. Massive blood transfusions post trauma in the elderly compared to younger patients. *Injury*. 2014;45(9):1296-1300.
3. DeSimone RA, Goss CA, Hsu YMS, Haas T, Cushing MM. Massive transfusion protocols: indications, ratios and mortality in the non-trauma setting. *Blood*. 2015;126(23)2348.
4. Paterson TA, Stein DM. Hemorrhage and coagulopathy in the critically ill. *Emerg Med Clin North Am*. 2014;32(4):797-810.
5. Mitra B, Cameron PA, Gruen RL, Mori A, Fitzgerald M, Street A. The definition of massive transfusion in trauma: a critical variable in examining evidence for resuscitation. *Eur J Emerg Med*. 2011;18(3):137-142.
6. ACS TQIP. Massive transfusion in trauma guidelines. https://www.facs.org/~/media/files/quality%20programs/trauma/tqip/massive%20transfusion%20in%20trauma%20guildelines.ashx.
7. Porth CM. *Essentials of Pathophysiology: Concepts of Altered Health States*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:182-183.
8. Chang WT, Radin B, McCurdy MT. Calcium, magnesium, and phosphate abnormalities in the emergency department. *Emerg Med Clin North Am*. 2014;32(2):349-366.
9. Kelly A, Levine MA. Hypocalcemia in the critically ill patient. *J Intensive Care Med*. 2013;28(3):166-177.
10. Goltzman D. Etiology of hypocalcemia in adults. UpToDate. 2016. www.uptodate.com.
11. Yamamoto M, Yamaguchi T, Yamauchi M, Yano S, Sugimoto T. Acute-onset hypomagnesemia-induced hypocalcemia caused by the refractoriness of bones and renal tubules to parathyroid hormone. *J Bone Miner Metab*. 2011;29(6):752-755.
12. Zhang Y, Wu H, Wang C. Serum calcium as an indicator of persistent organ failure in acute pancreatitis. *Am J Emerg Med*. In press.
13. Denlinger JK, Nahrwold ML, Gibbs PS, Lecky JH. Hypocalcaemia during rapid blood transfusion in anaesthetized man. *Br J Anaesth*. 1976;48(10):995-1000.
14. Giancarelli A, Birrer KL, Alban RF, Hobbs BP, Liu-DeRyke X. Hypocalcemia in trauma patients receiving massive transfusion. *J Surg Res*. 2016;202(1):182-187.
15. Shoback DM. Hypocalcemia management. Endotext [Internet]. 2015. www.endotext.org.16. Van Wessem KJP, Twigt BA, ten Duis K, Leenen LPH. Massive transfusion in multi-trauma patients. *Int J Case Rep Imag*. 2014;5(7):474-481.
17. Pham HP, Shaz BH. Update on massive transfusion. *Br J Anaesth*. 2013;111(suppl 1):i71-i82.
18. Elmer J, Wilcox SR, Raja AS. Massive transfusion in traumatic shock. *J Emerg Med*. 2013;44(4):829-838.
19. Newman DB, Fidahussein SS, Kashiwagi DT, et al. Reversible cardiac dysfunction associated with hypocalcemia: a systematic review and meta-analysis of individual patient data. *Heart Fail Rev*. 2014;19(2):199-205.
20. Goltzman D. Clinical manifestations of hypocalcemia. UpToDate. 2015. www.uptodate.com.
21. Kraft MD. Phosphorus and calcium: a review for the adult nutrition support clinician. *Nutr Clin Pract*. 2015;30(1):21-33.
22. Goltzman D. Treatment of hypocalcemia. UpToDate. 2015. www.uptodate.com.
23. Lier H, Krep H, Schroeder S, Stuber F. Preconditions of hemostasis in trauma: a review. The influence of acidosis, hypocalcemia, anemia, and hypothermia on functional hemostasis in trauma. *J Trauma*. 2008;65(4):951-960.
24. Cecchi E, Grossi F, Rossi M, Giglioli C, De Feo ML. Severe hypocalcemia and life-threatening ventricular arrhythmias: case report and proposal of a diagnostic and therapeutic algorithm. *Clin Cases Miner Bone Metab*. 2015;12(3):265-268.
25. Hess JR. Massive blood transfusion. UpToDate. 2017. www.uptodate.com/contents/massive-blood-transfusion.
26. Chung HS, Cho SJ, Park CS. Effects of liver function on ionized hypocalcaemia following rapid blood transfusion. *J Int Med Res*. 2012;40(2):572-582.
27. Meikle A, Milne B. Management of prolonged QT interval during a massive transfusion: calcium, magnesium or both? *Can J Anaesth*. 2000;47(8):792-795.
28. Ahmed A, Azim A, Gurjar M, Baronia AK. Hypocalcemia in acute pancreatitis revisited. *Indian J Crit Care Med*. 2016;20(3):173-177.

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