CHAPTER 57

Disorders of Potassium and Magnesium

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OBJECTIVES

This chapter will:

1. Discuss mechanisms of potassium and magnesium absorption and excretion.
2. Review main causes of altered serum potassium and magnesium concentrations.
3. Describe clinical manifestations of disorders of potassium and magnesium.
4. Summarize modalities of treatment of altered serum potassium and magnesium.

The total corporal potassium (K^+) stores are approximately 3000 to 4000 mEq (50 mEq/kg), and potassium is essentially an intracellular cation, with 95% to 98% found intracellularly. In humans, maintaining extracellular potassium in a narrow range is crucial for survival. Complex renal and extrarenal mechanisms are involved in potassium homeostasis. Although extrarenal mechanisms are able to rapidly shift potassium into cells, the kidney is responsible mainly for elimination of potassium from the body.

Magnesium (Mg^{++}) is the second most abundant intracellular cation and the fourth most prevalent cation in the body. The human body normally contains 1750 to 2400 mEq of magnesium. Magnesium is concentrated in bone (67%), muscles (20%), and nonmuscle soft tissues (11%). Only 1.3% of the total magnesium pool is extracellular (Fig. 57.1).

PHYSIOLOGIC ROLE OF POTASSIUM

Potassium has a major role in maintaining cellular function in excitable tissues (e.g., nerve and muscle), where it maintains the negative voltage across cell membranes. The Na^+-K^+-ATPase in a ubiquitous pump accomplishes this role by actively pumping Na^+ out of the cell and K^+ into the cell in a 3:2 ratio. This ratio of the potassium concentration in the cell and out of the cell is a major factor of the resting membrane potential. Variations in this negative voltage across cell membranes can cause dramatic cardiac arrhythmias. The negative voltage across cell membranes has other effects by modifying the ionized calcium concentration. Thus subtle changes in the resting potential may alter physiologic activity related to intracellular calcium (e.g., release of insulin by the pancreas).

REGULATION OF POTASSIUM

Absorption

The normal potassium intake in the diet usually varies between 100 and 500 mmol/day. Absorption of potassium by the gastrointestinal tract is fast, requiring a close control of the extracellular concentration. Renal excretion of potassium requires several hours to occur, so movement of potassium into muscle cells is necessary to maintain extracellular

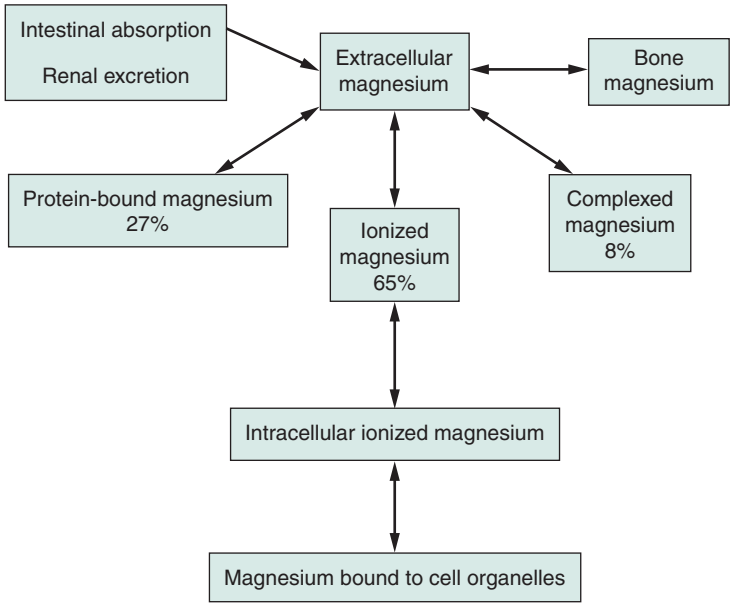

FIGURE 57.1 Magnesium homeostasis.

concentration within normal limits. The Na^+-K^+-ATPase pump plays a major role in this control by pumping K^+ into cells. Some evidence delineates a reactive feed-forward control system to induce kaliuresis after an oral load of potassium before any increase in serum potassium level.[1] The circadian clock has also an important role in regulating potassium homeostasis.[1,2]

Excretion

Potassium excretion is accomplished by several complex mechanisms in different parts of the nephron.[1,3–6] Most of filtered potassium is reabsorbed primarily by passive mechanisms in the proximal tubule. Potassium reabsorption occurs by the paracellular pathway. Potassium reabsorption occurs through a solvent drag mechanism and by a shift in transepithelial voltage. Less than 10% of the filtered load continues to the distal part of the nephron.

Potassium reabsorption in the thick ascending limb of Henle occurs using paracellular and transcellular pathways. The basolateral Na^+-K^+-ATPase pump creates a lumen-positive potential that drives the apical Na^+-K^+-$2Cl^-$ (NKCC2) cotransporter. This transcellular electroneutral cotransport allows reabsorption of one K^+ ion with one Na^+ ion and 2 Cl^- ions. The potassium recycling from the cell to the lumen is required for NKCC2 cotransport. The apical renal outer medullary K^+ (ROMK) channel provides this potassium supply to NKCC2. A lumen-positive potential is also created by the ROMK activity, which enhances passive paracellular potassium reabsorption.

The distal convoluted tubule (DCT), in its early part, is characterized by sodium reabsorption by the apical thiazide-sensitive Na^+-Cl^- (NCC2) cotransporter. NCC2 cotransport is driven by the low intracellular sodium concentration maintained by the basolateral Na^+-K^+-ATPase. ROMK is present in all parts of the DCT. In the DCT2, the amiloride-sensitive epithelial Na^+ channel (ENaC) expression begins and continues throughout the connecting tubule and the cortical collecting duct. It modulates the final excretion of potassium via the ROMK channel. Aldosterone affects potassium secretion through several mechanisms: it mainly increases basolateral Na^+-K^+-ATPase activity and the number of open sodium and potassium channels.[7] Potassium reabsorption occurs through the H^+-K^+-ATPase, which secretes one H^+ and reabsorbs one K^+ using ATP hydrolysis.

HYPOKALEMIA

Hypokalemia is defined as plasma potassium below 3.5 mmol/L. It is a common electrolyte disorder in the critical care setting. Hypokalemia usually results from a transcellular shift of potassium or depletion in total body potassium resulting from renal or gastrointestinal losses.

Causes

Major causes of hypokalemia (see Table 57.1) can be classified according to whether a transcellular shift is present or whether total body potassium loss occurred. Decreased intake of potassium is normally not sufficient to develop significant hypokalemia, unless very severe. In this circumstance, another concomitant cause of hypokalemia is usually present, such as increased urinary excretion induced by diuretics.

TABLE 57.1

Principal Causes of Potassium Deficiency

Gastrointestinal	Diarrhea of any cause
	Vomiting
	Nasogastric drainage
	Inadequate intake (very low and prolonged)
Renal	Diuretics (loop or thiazide)
	Hyperaldosteronism
	Nonreabsorbable anions
	Renal tubular acidosis
	Hypomagnesemia
Shift of K^+ into cells	Hormones (e.g., insulin, elevated β-adrenergic activity)
	Alkalemia
	Anabolic state (e.g., recovery from diabetic ketoacidosis)
	Anesthesia
	Hypothermia

All kinds of gastrointestinal fluids (gastric, pancreatic, biliary, and intestinal) contain potassium. Thus decreased absorption or increased secretion of those fluids can cause hypokalemia when it occurs over a prolonged period of time or is acute and massive. Otherwise, another concomitant cause of hypokalemia should be suspected because the nephron adapts very well to potassium deprivation by decreasing urinary excretion to 15 to 25 mmol/day.

Hypokalemia related to diuretics use is a relatively common problem in everyday clinical practice and in the intensive care unit setting. Loop and thiazide-type diuretics are known to cause hypokalemia by two main mechanisms: (1) an increased flow to the distal nephron by inhibiting NKCC2 or NCC2 cotransporters and (2) volume depletion. Volume deprivation leads to increased potassium excretion by activation of the renin-angiotensin-aldosterone system. Diuretics also can lead to hypomagnesemia, which by itself is a cause of hypokalemia.

Other conditions associated with an enhanced secretion of aldosterone are related to hypokalemia. Indeed, aldosterone increases absorption of sodium by the distal nephron and stimulates secretion of potassium. The major causes of mineralocorticoid excess are primary hyperaldosteronism, hyperreninism, glucocorticoid-remediable hyperaldosteronism, and syndrome of apparent mineralocorticoid excess.

Hypokalemia also is caused by potassium shift into cells. Several hormones are implicated in internal potassium balance. Activation of the insulin receptor increases Na^+-K^+-ATPase activity. β-adrenergic receptor stimulation triggers potassium entry into cells. Alkalosis also promotes cellular entry of potassium into cells.

Other causes of hypokalemia include hypokalemic periodic paralysis, mutations of the NKCC2 (Bartter syndrome) or the NCC2 (Gitelman syndrome) cotransporters, licorice, amphotericin B, and chloroquine intoxication.

Clinical Manifestations

Hypokalemia is an electrolyte disorder that is common in various disease states. A decreased serum level of potassium (less than 3.5 mmol/L) can seriously alter the negative voltage in cells. This effect on cell homeostasis may have dramatic effect in cardiac and respiratory muscles, leading to cardiac arrhythmia and respiratory failure by muscle weakness. Symptoms resulting from hypokalemia are usually

not present when serum potassium is not below 3.0 mmol/L. Cardiac arrhythmias associated with hypokalemia are diverse and include ventricular tachycardia or fibrillation, sinus bradycardia, paroxysmal atrial or junctional tachycardia, atrioventricular block, and premature atrial and ventricular beats. Typical changes on the echocardiogram (ECG) are ST segment depression, decreased amplitude of the T wave, and increased amplitude of the U wave. Severe hypokalemia (<2.5 mmol/L) may result in muscle cramps, rhabdomyolysis, and myoglobinuria. Gastrointestinal muscles also can be involved and lead to ileus (e.g., nausea, vomiting).

Treatment

Potassium preparation to correct hypokalemia can be administered either orally or intravenously. The oral route usually is preferred because it is safer and does not require venous access. In most cases, potassium chloride preparation is the preferred choice because it increases serum potassium faster than potassium bicarbonate preparation and corrects chloride depletion in concomitant metabolic alkalosis. In mild to moderate hypokalemia (serum potassium 3.0 to 3.5 mmol/L), 20 to 80 mmol per day are usually given in two to four divided doses. In more severe hypokalemia (serum potassium 2.5 to 3.0 mmol/L), a 40 mmol dose is usually given, up to four times per day. When hypokalemia is considered life threatening in presence of severe symptoms, an aggressive therapy is required. Cardiac arrhythmia and extreme weakness of respiratory muscles are two circumstances for which a rapid raise in plasma potassium is needed. In those situations, potassium should be administrated intravenously through a central vein catheter under cardiac monitoring. An initial bolus of 20 mmol of KCl usually is administered rapidly. Potassium-sparing diuretics can be useful for the treatment of chronic hypokalemia by diminishing the renal loss of potassium, such as in primary hyperaldosteronism. Amiloride, triamterene, eplerenone, and spironolactone are potential useful agents.

HYPERKALEMIA

Hyperkalemia is defined as a plasma potassium above 5.0 mmol/L and is a common electrolyte disorder in the critical care setting, especially in patients with acute kidney injury and oliguria.[8] Besides decreased renal elimination, several mechanisms trigger potassium release from cells (e.g., rhabdomyolysis) in acute care patients.

The first step when assessing the presence of hyperkalemia is to exclude pseudohyperkalemia, which relates to different clinical settings in which the elevated serum potassium is caused by potassium shifting out of the cell during or after blood drawing.[9] There are also a variety of other conditions in which pseudohyperkalemia can manifest: after clotting, in acute leukemia, with high white blood cell count, and in diseases associated with increased potassium permeability of red blood cells.

Clinical Manifestations

Hyperkalemia is associated with muscle weakness or paralysis, cardiac conduction abnormalities, and cardiac arrhythmia. Its detrimental potential and the degree of elevation in potassium are not well correlated. Therefore the first step when faced with a patient with hyperkalemia is to determine if an emergency is present by assessing changes in the ECG. Classically, hyperkalemia is associated with tall peaked T waves and shortened QT interval as the first findings. When it gets more severe, there is a lengthening of the PR interval and QRS duration, and the P wave may disappear. Ultimately, the QRS widens until it reaches a sinusoid wave pattern.

TABLE 57.2

Principal Causes of Potassium Excess

Gastrointestinal	High intake combined with decreased excretion
Renal	Renal failure
	Hypoaldosteronism
	Hyporeninemic hypoaldosteronism (e.g., diabetic nephropathy, NSAIDs, calcineurin)
	Angiotensin inhibitors
	Heparin therapy
	Inherited disorders (e.g., congenital hypoaldosteronism, pseudohypoaldosteronism type 2)
	Blockade of the aldosterone receptor
	Blockade of ENaC
	Reduced distal sodium delivery
Shift of K^+ out of cells	Cell necrosis (e.g., rhabdomyolysis)
	Lack of insulin
	Metabolic acidosis
	Use of nonselective β-blockers

ENaC, epithelial Na+ channel; *NSAIDs,* nonsteroidal antiinflammatory drugs.

Causes

One of the most common causes (see Table 57.2) of hyperkalemia is an increased intake (oral or intravenous), especially in patients with impaired kidney function.[10]

Several clinical conditions are associated with movement of potassium in the extracellular compartment. Those transcellular shifts of potassium out of the cells are often fast and cannot be compensated by an increase in urinary potassium excretion. Several factors regulate internal potassium distribution by modulating the Na^+-K^+-ATPase pump. Insulin is a well-known promoter of potassium shift into cells.[11] Catecholamines also can alter potassium uptake by the cells.[12] Metabolic acidosis (other than organic acidosis such as lactic acidosis or ketoacidosis) is associated with potassium movement out of the cell by apparent coupling to maintain electroneutrality. Intracellular potassium also can be released with a high rate of tissue breakdown in a variety of catabolic states such as in malignancy. Exercise is related to release of potassium by muscle cells, the extreme case being severe rhabdomyolysis.

Aldosterone in an important mineralocorticoid in humans by its role in urinary potassium excretion. Conditions affecting aldosterone secretion and response can lead to hyperkalemia. A frequent cause of hyperkalemia in that setting includes angiotensin inhibitors. In adults, hyporeninism and primary adrenal insufficiency are common causes of hypoaldosteronism. Hyporeninism has been seen in several conditions including renal insufficiency, most likely caused by diabetes, nonsteroidal antiinflammatory drug use, calcineurin inhibitor nephrotoxicity, acquired immune deficiency syndrome, and volume expansion. Reduced aldosterone synthesis is also seen in chronic heparin use, primary adrenal insufficiency, severe illness,

and inherited disorders such as congenital hypoaldosteronism and pseudohypoaldosteronism type 2 (Gordon syndrome). The most common cause of aldosterone resistance is potassium-sparing diuretics (spironolactone, eplerenone, amiloride, and triamterene). Antibiotics trimethoprim and pentamidine also are associated with inhibition of the ENaC channel. Hyperkalemia also is seen in decreased effective arterial blood volume, where an increase in proximal sodium reabsorption occurs, leading to decreased distal sodium delivery and reduced potassium secretory capacity.[13]

Other rare causes of hyperkalemia include digitalis overdose, hyperkalemic periodic paralysis, red cell transfusion, and administration of succinylcholine to patients with burn or extensive trauma.

Treatment

Patients with high serum potassium (>7 mmol/L) must be treated rapidly to avoid fatal complications. Treatment of hyperkalemia aims to antagonize cardiac irritability, induce a transcellular shift of potassium into the cells, decrease gastrointestinal absorption of potassium, and increase elimination by the kidney. Nonetheless, the treatment of hyperkalemia should always focus on the disorder causing the raise in potassium concentration, such as hypovolemia, angiotensin inhibitors, nonsteroidal antiinflammatory drugs, and urinary tract obstruction.

Patients with ECG abnormality associated with hyperkalemia should be treated promptly. Calcium is the best agent to antagonize the cardiac effect of hyperkalemia. It usually is given as 10% calcium gluconate solution, with initial dose of 1 g (10 mL of 10% solution) infused over 2 to 3 minutes under cardiac monitoring. The dose can be repeated 5 minutes later if ECG changes persist. Calcium chloride contains three times more elemental calcium than calcium gluconate; therefore it should be given via a central catheter to avoid irritation of peripheral veins.

Insulin is used as the first therapy to induce a transcellular shift of potassium into cells by increasing Na-K-ATPase activity. An initial bolus of 10 units of regular insulin usually is given to induce a shift of potassium into cells. Insulin should be given with glucose, usually 50 mL of 50% dextrose (25 g of glucose), to avoid hypoglycemia. Glycemia should be monitored closely after the insulin bolus. A 10% dextrose infusion also may be given subsequently (75 mL per hour) to prevent hypoglycemia. The value of sodium bicarbonate to induce transcellular shift of potassium into cells remains unproven based on several studies.[14–16] Sodium bicarbonate should be considered as an adjunct therapy in patients with significant acidosis if therapy was considered to treat metabolic acidosis regardless of the presence of hyperkalemia. β2 agonists also may play a role in the treatment of hyperkalemia as a second-line agent to promote transcellular shift into cells.

Use of cation exchange resins has not been shown to reduce serum potassium in an acute setting.[17] Dialysis remains the therapy of choice when hyperkalemia cannot be reversed with other treatment modalities.

PHYSIOLOGIC ROLE OF MAGNESIUM

Magnesium actions affect primarily the cardiovascular system and derive from its effects on calcium channels and pumps to regulate transmembrane and intracellular ionic flows. Magnesium has recognized vasodilatory effects, predominantly on the arteriolar vasculature, and modulates calcium fluxes, causing smooth muscle cell contraction. Magnesium exerts a "calcium antagonist" effect on myocytes by inhibiting calcium uptake and reducing cardiac contractility.

REGULATION OF MAGNESIUM

Absorption

The average daily intake of magnesium is 250 to 370 mg (10–15 mmol). One third is absorbed mainly in the distal portion of the small bowel through paracellular pathways and a saturable transport system. Intestinal absorption may vary according to the dietary magnesium content and total body magnesium level.

Excretion

Between 70% and 80% of total plasma magnesium is ultrafiltered by the glomerulus, and 15% to 25% is reabsorbed at the proximal tubule through passive diffusion down a favorable concentration gradient, because the concentration of magnesium rises to 1.5 times that of the glomerular filtrate.

The thick ascending limb of the loop of Henle is the principal site of magnesium reabsorption. Paracellular diffusion of magnesium is passive and depends on the sodium chloride-generated transmembrane potential. Passive diffusion is facilitated by paracellin-1, a protein present in renal tight junctions. Changes in paracellular permeability and transmembrane potential affect magnesium reabsorption. Loop diuretics reduce magnesium reabsorption by blocking sodium chloride reabsorption and inhibiting the creation of an electrical gradient.

Magnesium transport in the cortical collecting tubule is active and transcellular. Magnesium channels in the apical membrane allow entry of Mg^{++} into the distal tubular cells via a favorable transmembrane voltage and a low intracellular free magnesium concentration (0.5 mmol/L). Magnesium exit from the basolateral side could occur via sodium-magnesium exchange favored by a lower intracellular (10–15 mmol/L) rather than extracellular fluid sodium concentration.

HYPOMAGNESEMIA

A serum total magnesium concentration less than 0.75 mmol/L usually is considered abnormally low. However, serum total magnesium concentrations are not well correlated with serum ionized concentrations in acutely ill patients because of alterations in serum proteins, acid-base disturbances, and the potential influence of concomitantly administered drugs on magnesium balance. A low serum total magnesium concentration may well represent pseudohypomagnesemia in a severely hypoalbuminemic patient. The normal serum ionized magnesium concentration is between 0.52 and 0.60 mmol/L. In critically ill patients, serum total magnesium concentration has been found to be sensitive (75%) but not specific (<40%) in predicting ionized hypomagnesemia; on the other hand, studies have found serum ionized magnesium concentrations to be normal in more than 70% of patients who had low total serum

magnesium concentrations.[18,19] The potential consequences of various magnesium measures for the outcome of different subpopulations of critically ill patients are undefined at present. Nonetheless, mortality has been shown to be increased in acutely ill patients who have hypomagnesemia at admission.[20]

Clinical Manifestation

Concurrent hypokalemia is present in 60% to 65% of hypomagnesemic patients, because the underlying cause frequently induces potassium and magnesium wastage. Hypomagnesemia can also cause hypokalemia secondary to increased tubular secretion of potassium; in such case, hypokalemia is refractory to supplementation unless hypomagnesemia is corrected. Hypocalcemia is also common and is induced by a suppressive effect of hypomagnesemia on PTH secretion, a resistance to vitamin D, and end-organ resistance to PTH action.

Central neuronal excitability and neuromuscular transmission are increased in situations of magnesium depletion. Clinical manifestations include tremor, myoclonic jerks, seizures, Chvostek and Trousseau signs, spontaneous carpopedal spasm, ataxia, nystagmus, and dysphagia. Various psychiatric abnormalities may manifest, from delirium to apathy to coma.[21]

In severe hypomagnesemia, PR and QT intervals are prolonged, predisposing to ventricular arrhythmias, tachycardia, and abnormal T wave. Increased arteriolar tone is also common when extracellular magnesium is low, because calcium uptake is enhanced and intracellular calcium concentration is increased.

Causes

Hypomagnesemia can be induced by gastrointestinal losses, renal losses, or cellular redistribution of magnesium (Table 57.3). Gastrointestinal losses are not regulated and are more important with small bowel disease (diarrhea, malabsorption, short-bowel syndrome, small bowel bypass surgery). Diarrheal fluids and fistula drainage contain as much as 7 to 8 mmol/L total magnesium ions (or 15 mEq/L). Losses via nasogastric suctioning are not large but are associated with poor magnesium intake, contributing to progressive depletion. Magnesium content of upper gastrointestinal fluids is about 0.5 mmol/L (or 1 mEq/L).

Two mechanisms may cause renal losses of magnesium: an intrinsic defect in tubular magnesium reabsorption and an extrinsic defect that causes renal magnesium wasting. Tubular dysfunction in the recovery phase of acute tubular necrosis is not unusual and may be associated with magnesium wastage. Tubular dysfunction with hypomagnesemia also may be present in acute interstitial nephropathy and postobstructive diuresis as well as after renal transplantation. In alcoholics, hypomagnesemia is not unusual because magnesium intake is often decreased and an alcohol-induced (but reversible) tubular dysfunction increases magnesium excretion.

Loop diuretics and long-term administration of thiazide diuretics and mannitol may induce hypomagnesemia. The other most common therapeutic agents that cause hypomagnesemia by increasing renal magnesium losses are aminoglycosides, cisplatin, amphotericin B, cyclosporine, pentamidine, insulin, carbenicillins, and digoxin.

In patients with severe head injury, particularly those with hypothermia, severe electrolyte depletion, including hypomagnesemia, is common and is related in part to the greater urinary excretion through polyuria.[22,23] Increased magnesuria has been observed in severe phosphate depletion and thyrotoxicosis.

The infusion of citrate with massive tranfusions, particularly during liver transplantation or apheresis, may affect levels of ionized magnesium.[24,25] During acute pancreatitis or after pancreatic surgery, saponification of magnesium in necrotic fat and by free fatty acids can occur, resulting in hypomagnesemia. Hypomagnesemia, because of large cutaneous magnesium losses, also is observed after severe burns.[26]

TABLE 57.3

Principal Causes of Magnesium Deficiency

Gastrointestinal	Diarrhea
	Malabsorption syndromes
	Prolonged nasogastric suction
	Inadequate intake
	Malnutrition
	Refeeding syndrome
	Intestinal and biliary fistulas
Renal	Osmotic diuresis
	Diuretic (loop or thiazides)
	Volume expansion
	Hypercalcemia and hypercalciuria
	Posttransplantation
	Polyuric phase (after acute tubular necrosis or obstruction)
	Drugs (cyclosporine, amphotericin B, cisplatin, foscarnet, pentamidine, aminoglycosides)
	Hypophosphatemia
Redistribution	Acute pancreatitis
	Hungry bone disease
	Correction of chronic systemic acidosis
	Severe burns
	Massive blood transfusion

Treatment

The modality and rapidity of magnesium repletion are functions of the symptoms and serum magnesium concentration. In the patient with seizures or cardiac arrhythmias, 8 to 12 mmol of magnesium should be given rapidly in 5 to 10 minutes, followed by a perfusion over several hours. Because renal magnesium reabsorption is slow and inversely proportional to serum magnesium concentration, rapid magnesium infusion will result in excretion of up to 50% of the dose given. Thus oral supplementation may be preferred over intravenous supplementation for asymptomatic patients. However, several magnesium salts induce diarrhea when given by the enteral route. Patients with hypomagnesemia induced by renal wastage may benefit from the use of a potassium-sparing diuretic (amiloride, triamterene) to improve magnesium reabsorption at the collecting tubule.

Before initiation of magnesium supplementation, the patient's renal function should be assessed, and doses reduced by 25% to 50% in patients with moderate to severe renal failure. Moreover, because magnesium has a calcium antagonist effect, with a potential for severe heart block and cardiac conduction defects, caution is mandatory.

HYPERMAGNESEMIA

Hypermagnesemia corresponds to a serum concentration in excess of 0.95 mmol/L. Because the efficacy of the kidneys to excrete a magnesium load is very good, more than 250 mmol/day or nearly 100% of the filtered load can be eliminated by the person with increased plasma magnesium concentration, and hypermagnesemia is rarely seen.

Clinically significant hypermagnesemia is rare in the absence of acute or chronic renal failure and/or administration of a massive magnesium load. In chronic renal failure, urinary magnesium excretion falls, but plasma magnesium concentration usually stabilizes at approximately 1 to 1.5 mmol/L. Because there is no regulatory system other than renal excretion and also no protection mechanism against hypermagnesemia with loss of renal function, magnesium-containing antacids and cathartics, as well as large doses of magnesium salts supplementation, are contraindicated in the patient with renal failure.

The prevalence of hypermagnesemia has been reported as 0.8% to 9.3% among hospitalized patients, and 13.5% at admission to intensive care.[27–29]

Clinical Manifestations

Symptoms of hypermagnesemia are uncommon when serum magnesium levels are less than 2 mmol/L. The first symptoms to appear are nausea, vomiting, and flushing with reduced tendon reflexes. Neurologic manifestations include flaccid paralysis, lethargy, coma, and respiratory depression. Cardiovascular effects of hypermagnesemia occur with serum magnesium concentrations above 2 to 2.5 mmol/L. Calcium antagonist properties of magnesium induce bradycardia and hypotension. Prolongation of PR interval, QRS complex, and QT interval may be seen at higher concentrations, between 2.5 and 5 mmol/L. With further increases in magnesemia, evolution toward complete heart block and cardiac arrest is possible.

Causes

Severe hypermagnesemia may occur after multiple doses of a magnesium-containing cathartic for treatment of drug overdose. The usual total average dose of magnesium citrate (9.22 g magnesium) induces an increment in serum magnesium concentration.[30] Forty-seven percent of patients experience hypermagnesemia (>1.2 mmol/L), and 12% severe hypermagnesemia (>1.5 mmol/L), although there is no correlation between the total amount of magnesium citrate administered and the rise in serum magnesium concentration. Magnesium enemas also may induce hypermagnesemia. Laxative abuse and accidental ingestion of Epsom salts are other reported causes. Elderly patients and patients with bowel disorders associated with enhanced absorption (active ulcer disease, gastritis, colitis, perforated viscus, or massive gastric dilatation) are particularly at risk for hypermagnesemia with oral ingestion of magnesium-containing antacids and cathartics, even though the amount of magnesium ingested is not excessive.[31]

Hypermagnesemia is one of the metabolic complications of tumor lysis syndrome, massive tissue damage, from sustained seizure, and severe ischemia. Some cases of hypermagnesemia associated with diabetic ketoacidosis have been documented.

Treatment

Discontinuation of magnesium intake (supplementation, medication, parenteral nutrition) is the first step in management of hypermagnesemia. In patients with normal kidney function, discontinuing magnesium intake allows hypermagnesemia to correct itself; in patients with renal failure or with severe symptomatic hypermagnesemia, renal replacement therapy may be necessary. Hemodialysis is preferable to hemofiltration because the decline in magnesium serum concentration occurs faster with the former. When severe symptoms are present, calcium may be given as a magnesium antagonist to reverse cardiac arrhythmias, hypotension, and respiratory depression. The usual dose is 50 to 100 mg elemental calcium over 5 to 10 minutes, but larger amounts may be required.

CONCLUSION

Potassium homeostasis implies complex renal and extrarenal mechanisms. Regulation of extracellular potassium in a narrow range is crucial. Magnesium metabolism has not been as well defined as metabolism of other ions, and interest in further research should be encouraged.

Key Points

1. Potassium plays a major role in maintaining cellular function in excitable tissues.
2. Magnesium has several important physiologic roles.
3. Hypokalemia usually results from increased gastrointestinal or renal losses.
4. Hyperkalemia usually results from increased intake, transcellular shift of K^+ out of the cells, and decreased renal excretion.
5. Hypomagnesemia usually results from increased gastrointestinal or renal losses.

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