warranted when using these agents in patients with renal insufficiency or other disorders that impair renal K^+ excretion.

HYPERKALEMIA

Definition

As in the hypokalemic disorders, a high serum K^+ concentration can occur in the setting of normal or altered body stores of K^+. The body has a marked ability to protect against hyperkalemia. This includes regulatory mechanisms that excrete excess K^+ quickly and mechanisms that redistribute excess K^+ into cells until it is excreted. All causes of hyperkalemia involve abnormalities in these mechanisms.

Pseudohyperkalemia is an in vitro phenomenon caused by the mechanical release of K^+ from cells during a phlebotomy procedure, specimen processing, or in the setting of marked leukocytosis and thrombocytosis.

Excessive Dietary Potassium Intake

In the setting of normal renal and adrenal function, it is difficult to ingest sufficient K^+ in the diet to produce hyperkalemia. Dietary intake of K^+ as a contributor to hyperkalemia is usually observed in patients with impaired kidney function. Dietary sources particularly enriched with K^+ include melons, citrus juice, and commercial salt substitutes containing KCl.

Cellular Redistribution

Cellular redistribution is a more important cause of hyperkalemia than as a cause of hypokalemia. Tissue damage is probably the most important cause of hyperkalemia due to redistribution of K^+ out of cells. This can be caused by rhabdomyolysis, trauma, burns, massive intravascular coagulation, and tumor lysis (spontaneous or after treatment).

The effect of metabolic acidosis in causing K^+ to exit from cells depends on the type of acid. Mineral acidosis (i.e., ammonium chloride [NH_4Cl] or hydrogen chloride [HCl]), by virtue of the relative impermeability of the chloride anion, results in the greatest efflux of K^+ from cells. In contrast, organic acidosis (lactic or β-hydroxybutyric) results in no significant efflux of K^+.

Increased osmolality, as occurs in uncontrolled diabetics, causes K^+ to move out of cells. The hypertonic state and insulin deficiency account for hyperkalemia often seen in patients with diabetic ketoacidosis who are total body K^+ depleted. β-Adrenergic blocking agents can interfere with the disposal of acute K^+ loads. Other drugs that can result in hyperkalemia include the depolarizing muscle relaxant succinylcholine and digitalis in cases of severe poisoning.

Decreased Renal Excretion of Potassium

Decreased renal excretion of K^+ can occur because of three abnormalities: a primary decrease in distal delivery of salt and water, abnormal cortical collecting duct function, and a primary decrease in mineralocorticoid levels.

Primary Decrease in Distal Delivery of Salt and Water

Acute decreases in the glomerular filtration rate (GFR), as occur in acute kidney injury, may lead to marked decreases in the distal delivery of salt and water, which may secondarily decrease distal K^+ secretion. When acute kidney injury is oliguric, distal delivery of NaCl and volume are low, and hyperkalemia is a frequent problem. When acute kidney injury is nonoliguric, distal delivery is usually sufficient, and hyperkalemia is unusual.

In chronic kidney disease patients, hyperkalemia is unusual until the GFR falls to less than 10 mL/min. Hyperkalemia with a GFR of more than 10 mL/min raises the question of decreased aldosterone levels or a specific lesion of the cortical collecting duct.

Primary Decrease in Mineralocorticoid Activity

Decreased mineralocorticoid activity can result from disturbances that originate at any point along the renin-angiotensin-aldosterone system. These disturbances can be the result of a disease state or various drugs. Hyperkalemia most commonly develops when one of more of these drugs are administered when the renin-angiotensin-aldosterone system is already impaired. A common example is the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) in diabetics with hyporeninemic hypoaldosteronism.

Distal Tubular Defects

Certain interstitial renal diseases can affect the distal nephron specifically and lead to hyperkalemia despite mild decreases in the GFR and normal aldosterone levels. Amiloride and triamterene inhibit Na^+ transport, which makes the luminal potential more positive and secondarily inhibits K^+ secretion. A similar effect occurs with trimethoprim and accounts for the development of hyperkalemia after the administration of the antibiotic sulfamethoxazole-trimethoprim. Spironolactone and eplerenone compete with aldosterone and block the mineralocorticoid effect.

Clinical Presentation

Hyperkalemia leads to depolarization of the resting membrane because the potential across cell membranes is in part determined by the ratio of intracellular to extracellular K^+. The heart is particularly sensitive to this depolarizing effect. The progressive changes of hyperkalemia on the electrocardiogram are peaking of T waves, widening of the PR and QRS interval, development of a sine wave pattern, and eventually, ventricular fibrillation and asystole.

ECG changes appear at a serum K^+ level of 6 mEq/L with acute onset of hyperkalemia, whereas the ECG may remain normal up to a concentration of 8 to 9 mEq/L with chronic hyperkalemia. Hyperkalemia can also cause neuromuscular manifestations such as ascending paralysis and flaccid quadriplegia.

Treatment

Acute Hyperkalemia

The immediate treatment for life-threatening hyperkalemia is the administration of calcium usually in the form of calcium gluconate or calcium chloride. ECG changes such as an increasing PR interval or a widening QRS complex warrant treatment with calcium. Glucose and insulin therapy shift K^+ into cells. Acute administration of glucose without insulin can potentially worsen