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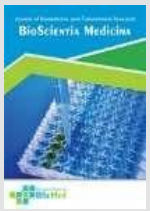

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Clinical Overview and Treatment of Hypokalemia in Pediatric Patients: A Narrative Literature Review

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A B S T R A C T

Hypokalemia is a condition in which the blood potassium levels are below the normal range, which is typically between 3.5 and 5.0 mEq/L. Potassium is an essential electrolyte that plays a critical role in many physiological processes in the body, including nerve and muscle function, heart rhythm, and acid-base balance. This literature review aimed to describe the clinical and current management aspects of hypokalemia in pediatric patients. The pathophysiology of hypokalemia involves a disturbance in the balance of potassium in the body, which can occur due to several mechanisms, including reduced intake of potassium-rich foods, increased loss of potassium, and redistribution of potassium. In children, clinical symptoms of hypokalemia may include weakness and fatigue, abdominal discomfort, cardiac symptoms, respiratory symptoms, neurological symptoms, polyuria, and renal symptoms. There are several diseases and conditions that can cause hypokalemia in children, including renal tubular acidosis, prolonged diarrhea, cystic fibrosis, hyperaldosteronism, malnutrition, medication, type 1 Bartter syndrome, type 2 Bartter syndrome, and Liddle syndrome. Some options for hypokalemia treatment are potassium supplements, a potassium-rich diet, intravenous potassium, and treating underlying conditions. In conclusion, hypokalemia is an overview of the underlying disease and requires immediate management. Understanding the pathophysiology of hypokalemia will increase the accuracy of diagnosis and accelerate hypokalemia intervention in children, as well as prevent complications due to hypokalemia.

1. Introduction

Hypokalemia is a condition characterized by a low level of potassium in the blood (less than 3.5 mmol/L) and is a common electrolyte disorder in pediatric and adult patients.[1] Potassium is an important mineral that helps regulate muscle and nerve function, maintain proper fluid balance in the body, and support normal heart function.[2] In children, hypokalemia can be caused by a variety of factors, such as inadequate potassium intake, excessive loss of potassium through vomiting or diarrhea, certain medications, or underlying medical conditions.[3] Symptoms of hypokalemia in children may include weakness, fatigue, muscle cramps, constipation, abdominal pain, and irregular heartbeat. Understanding the symptoms, diagnosis, and treatment of hypokalemia is very important in preventing complications or worsening of the patient's condition due to hypokalemia. This literature review aimed to describe the clinical and current management aspects of hypokalemia in pediatric patients.

Definition and pathophysiology of hypokalemia

Hypokalemia is a condition in which the blood potassium levels are below the normal range, which is typically between 3.5 and 5.0 mEq/L.[4] Potassium is an essential electrolyte that plays a critical role in many physiological processes in the body, including

nerve and muscle function, heart rhythm, and acid-base balance. Potassium's primary role is in its involvement in the Na^+-K^+-ATPase pathway, an electrogenic enzyme that mediates transcellular ion transport.[5,6]

The pathophysiology of hypokalemia involves a disturbance in the balance of potassium in the body, which can occur due to several mechanisms, including reduced intake of potassium-rich foods, increased loss of potassium, and redistribution of potassium.[7] A diet low in potassium or an inadequate intake of potassium-rich foods such as fruits, vegetables, and dairy products can lead to hypokalemia.[8] Potassium can be lost from the body through various routes, including urine, feces, sweat, and vomit. Conditions that increase the loss of potassium from the body include excessive sweating, diarrhea, vomiting, and the use of diuretic medications. In certain conditions, such as metabolic alkalosis, insulin excess, or beta-adrenergic stimulation, potassium may shift from the extracellular fluid to the intracellular compartment, leading to hypokalemia.[9-11]

The consequences of hypokalemia depend on the severity and duration of the condition. Mild hypokalemia may not cause any symptoms, while more severe cases can lead to muscle weakness, cramping, and cardiac arrhythmias. Muscle weakness occurs due to impaired nerve function, as potassium is essential for proper nerve conduction. The heart is particularly sensitive to changes in potassium levels, and hypokalemia can cause various cardiac arrhythmias, including ventricular tachycardia, ventricular fibrillation, and atrial fibrillation. These arrhythmias can lead to life-threatening complications such as sudden cardiac arrest.[12,13]

Etiology of hypokalemia

There are several possible etiologies or causes of hypokalemia, which include increased loss of potassium, inadequate intake of potassium, redistribution of potassium, increased cellular uptake of potassium, renal causes, and genetic causes. Increased loss of potassium can be due to excessive sweating, vomiting, diarrhea, or the use of certain medications such as diuretics or laxatives.[14]

Inadequate intake of potassium occurs with diets low in potassium or with malabsorption syndromes. Generally, the daily intake of potassium in children and adults ranges from 80 mmol per day. The digestive system will absorb 75 mmol, and the rest will be excreted in the feces. Nutritional deficiencies are generally not significant in causing hypokalemia. Diarrhea is a common cause of hypokalemia in children.[1,15]

Redistribution of potassium occurs when potassium is shifted from the extracellular fluid to the intracellular fluid due to insulin therapy, alkalosis, or excessive beta-adrenergic stimulation. Increased cellular uptake of potassium occurs with increased insulin levels or in response to beta-agonist medications. Certain kidney diseases can cause hypokalemia by impairing potassium reabsorption in the kidneys. Excessive adrenocorticotropic hormone (ACTH) stimulation due to pituitary adenoma and carcinoid tumors causes refractory hypokalemia and hypertension. Some genetic disorders, such as Bartter's syndrome or Gitelman's syndrome, can cause hypokalemia due to abnormalities in the kidney's ability to reabsorb potassium.[16,17]

Clinical symptoms of hypokalemia in children

In children, clinical symptoms of hypokalemia may include weakness and fatigue, abdominal discomfort, cardiac symptoms, respiratory symptoms, neurological symptoms, polyuria, and renal symptoms. Low potassium levels can cause muscle weakness, fatigue, and overall lethargy in children. Children may experience abdominal discomfort or cramp due to decreased gastrointestinal motility. Hypokalemia can cause irregular heartbeat, palpitations, and decreased blood pressure. Children with hypokalemia may experience shallow breathing, shortness of breath, and decreased lung function. Hypokalemia can lead to neurological symptoms such as tremors, muscle twitching, and numbness or tingling in the extremities. Children with hypokalemia

may experience increased urine output and increased thirst. Hypokalemia can also cause renal symptoms such as kidney stones, renal tubular acidosis, and polyuria. It is important to note that hypokalemia may be asymptomatic in some cases, and symptoms may vary depending on the severity of the condition.[18]

Conditions and diseases that cause hypokalemia in children

Hypokalemia is a medical condition that occurs when the level of potassium in the blood is lower than normal. There are several diseases and conditions that can cause hypokalemia in children, including renal tubular acidosis, prolonged diarrhea, cystic fibrosis, hyperaldosteronism, malnutrition, medication, type 1 Bartter syndrome, type 2 Bartter syndrome, and Liddle syndrome.

Renal tubular acidosis

Renal tubular acidosis (RTA) is a condition that occurs when the kidneys are unable to remove acid from the body. This can lead to hypokalemia because potassium is lost in the urine as the kidneys try to remove the excess acid. Distal RTA (d-RTA) is caused by defects in H+ secretion. Genetic mutations in children can cause $Cl\text{-}HC0_3^-$ basolateral exchanger deficiency, apical ATPase H^+, and apical ATPase H+ pumps in the distal convoluted tubule (DCT).[19]

Proximal RTA (p-RTA) is caused by a decrease in the absorption threshold of HCO_3^- filtered by the proximal tubule. This led to the delivery of a large amount of HCO_3- to DCT, exceeding its reabsorption capacity. Gene mutations for Na^+-$HC0_3^-$ exchangers result in isolated p-RTA. Na+ load delivery in DCT enables secondary aldosteronism and K^+ disposal.[19]

Diarrhea and malnutrition

Prolonged diarrhea can lead to hypokalemia because the body loses potassium through the stool (K^+ feses 20–50 mmol/L). Malnutrition can cause hypokalemia because the body may not be receiving enough potassium in the diet. The cause of mortality due to acute malnutrition is especially if it is accompanied by potassium loss due to diarrhea. Nutritional rehabilitation after the anabolic phase of severe malnutrition can result in a potentially fatal refeeding syndrome. The renewed supply of glucose causes hyperglycemia and excessive insulin response. Death from severe hypokalemia can occur as a result of respiratory muscle weakness and ventricular arrhythmias.[20]

Hyperaldosteronism

Hyperaldosteronism is a condition that occurs when the adrenal gland produces too much aldosterone hormone. This hormone can cause the kidneys to excrete potassium, leading to hypokalemia. Aldosterone stimulation is the main physiological mechanism for defending against hypovolemia. A lower glomerular filtration rate (GFR) leads to proximal renal sodium reabsorption. Lower delivery of sodium and chloride to macula densa increases plasma renin secretion, angiotensin II, and aldosterone. Aldosterone activates the epithelial sodium channel (ENaC) in DCT, restoring blood volume.[21]

Drugs

Some medications, such as diuretics, can cause the kidneys to excrete potassium, leading to hypokalemia. Overdosage of certain drugs and toxins can cause severe hypokalemia leading to cardiac arrhythmias and death. β-adrenergic agonist drugs, theophylline, and caffeine increase endogenous catecholamines, cationic barbiturates, barium chloride, and chloroquine, impairing potassium release by the sarcolemma. Hypokalemia may result from the therapeutic use of insulin or after overdosage in a suicide attempt. Hypoglycemia potentiates cellular potassium uptake by stimulating catecholamine release. Overdosage of barium chloride in a suicide attempt can lead to severe hypokalemia and fatal ventricular arrhythmias. There have also been reports of incidental hypokalemia following widespread food poisoning due to industrial barium contamination of table salt. In addition to its hypokalaemic effect, chloroquine potentiates cardiac arrhythmias by

inhibiting atrioventricular conduction. Penicillins cause a dose-dependent hypokalaemic side effect. A nonabsorbable anion, penicillin, promotes the exchange of potassium for Na+ in the distal convoluted tubule (DCT).[22-24]

Type 1 and type 2 Bartter syndrome

Type 1 and type 2 Bartter syndrome (BS) is a rare genetic disorder that affects the kidneys. Children with this condition can develop hypokalemia because the kidneys excrete too much potassium. BS type I occurs due to a mutation of the gene that encodes NKCC2, while BS type II is due to a mutation of the gene that produces the ROMK channel. Types I and II are the most severe forms of BS and are characterized by polyhydramnios, newborn hypotension, and hypokalemic alkalosis.[25]

Liddle syndrome

Liddle syndrome is a rare genetic disorder that affects the kidneys. Children with this condition can develop hypokalemia because the kidneys excrete too much potassium. Liddle syndrome causes hypertension and hypokalemic alkalosis, but plasma renin and serum aldosterone levels decrease. This condition is caused by an autosomal dominant (AD) mutation of ENaC in DCT.[25]

Diagnosis of hypokalemia in children

Hypokalemia is a condition where there is a low level of potassium in the blood. It can be caused by a variety of factors, including certain medications, vomiting, diarrhea, and kidney problems. The diagnosis of hypokalemia can be established by detailed anamnesis regarding the child's disease history. Clinical symptoms such as weakness, fatigue, muscle cramps, and irregular heartbeat, as well as any recent illnesses or medications, can help clinicians establish a diagnosis of hypokalemia. Physical examination related to hypokalemia symptoms in the form of limb reflex examination and irregular heartbeat.[9]

Laboratory evaluation in the form of routine blood tests (blood potassium levels), urine tests, and electrocardiograms (ECG). A normal range of potassium in the blood for children is typically between 3.4 to 4.7 millimoles per liter (mmol/L). A low level of potassium in the blood may indicate hypokalemia. Urine tests may also be done to check the levels of potassium in the urine. This can help determine whether hypokalemia is caused by a problem with the kidneys. An ECG check is aimed at evaluating the heart's rhythm and looking for signs of irregular heartbeat, which can be a symptom of hypokalemia.[9,10]

Management of hypokalemia in children

Treatment typically of hypokalemia involves addressing the underlying cause of the condition and replenishing potassium levels through dietary changes or supplements. Treatment of hypokalemia has four objectives; reduction of potassium loss, replenishment of potassium reserves, evaluation of potential toxicity, and determination of the cause in order to prevent future episodes. Discontinuation of laxatives, the use of potassium-neutral or potassium-sparing diuretics (if diuretic therapy is required, as in heart failure), treatment of diarrhea or vomiting, the use of H2 blockers in patients with nasogastric suction and effective control of hyperglycemia (if glycosuria is present) are measures that can be performed in patients with hypokalemia. The treatment options may vary depending on the severity of the condition, the underlying cause, and the patient's overall health.[10,12]

Some options for hypokalemia treatment are potassium supplements, a potassium-rich diet, intravenous potassium, and treating underlying conditions. Oral supplementation is administered to patients with serum potassium levels between 2.5 and 3.5 mmol/L. Oral administration of potassium should be accompanied by much fluid (between 100 and 250 mL of water, depending on the form of potassium tablets) and is better administered with or after meals. Increasing the intake of potassium-rich foods can help to restore normal potassium levels in the blood. Foods

that are high in potassium include bananas, oranges, apricots, tomatoes, potatoes, sweet potatoes, spinach, beans, and lentils.[16-18]

Urgent intravenous potassium is administered if potassium levels are less than 2.5 mEq/L, with strict follow-up, continuous ECG monitoring, and serial potassium level measurement. Intravenous potassium is also selected for the management of hypokalemia patients accompanied by nausea, vomiting, or severe stomach disorders. Frequent serum K assessments during and after therapy may be necessary to avoid exceeding the target of 4-5 mmol/L. Hypokalemia can be caused by several underlying conditions, such as chronic kidney disease, excessive sweating, and certain medications. Treating the underlying condition can help to improve potassium levels in the blood.[17]

Complications of hypokalemia

Hypokalemia, or low blood potassium levels, can have several complications depending on the severity and duration of the condition. Some of the common complications of hypokalemia are cardiac arrhythmia, muscle weakness, renal impairment, gastrointestinal disturbances, respiratory failures, increased risk of falls, and worsening of other medical conditions. Hypokalemia can cause various cardiac arrhythmias, including ventricular tachycardia, ventricular fibrillation, and atrial fibrillation. These arrhythmias can lead to life-threatening complications such as sudden cardiac arrest. Potassium is essential for proper nerve and muscle function. Hypokalemia can lead to muscle weakness, cramping, and even paralysis in severe cases. Hypokalemia can affect the function of the kidneys, leading to impaired urine concentration and a reduced ability to excrete waste products from the body. Low potassium levels can cause gastrointestinal disturbances such as constipation, bloating, and abdominal cramping. Severe hypokalemia can lead to respiratory failure, as the respiratory muscles may become too weak to function correctly. Hypokalemia can cause weakness, dizziness, and impaired balance, increasing the risk of falls and injuries. Hypokalemia can worsen other medical conditions such as hypertension, heart failure, and diabetes.[1,9]

2. Conclusion

Hypokalemia is an overview of underlying diseases and requires immediate management. Understanding the pathophysiology of hypokalemia will improve the accuracy of diagnosis and accelerate hypokalemia interventions in children, as well as prevent complications due to hypokalemia.

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