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Mini Review

Electrolyte Disturbances as Causative Factors for Generalized Weakness in Emergency Department Patients

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Abstract

Generalized weakness is a common complaint by patients visiting the emergency department. Differential diagnosis of weakness consists of a long list of diseases. In this review we highlight the generalized weakness when linked to electrolyte disturbances. General causes of every electrolyte disturbance are listed. The overall clinical manifestations of each electrolyte disturbance are described with special focus on symptoms and signs related to weakness and muscle affection. The link between the electrolyte concerned and weakness is explained.

Keywords: *Generalized Weakness; Fatigue; Electrolyte Disturbances*

The complain about generalized weakness is frequently encountered in the emergency department. This comes with mostly all age groups but especially with advancing age. The patient describe weakness in different terms. Fatigue, tiredness and exhaustion are examples of patient's terms describing weakness. While frailty, fragility and sickness are the mostly used terms by the patients' relatives. The patient usually relates his/her complain to the ability to perform the usual daily activity including inside home walking and self-care. General causes of generalized weakness are multiple and very diverse. The differential diagnosis of generalized weakness is summarized in table 1. However, weakness usually reflects a combination of effects of age, the overall physical status, the mental health and systemic disorders affecting the patient's wellbeing.

System affected	Examples
Hematological	Anemia
Psychological	Depression, psychosis
Cardiac	Heart failure, myocardial infarction, hypotension, shock
Fever/Sepsis	
Endocrine system	Diabetes mellitus, hypothyroidism, adrenal insufficiency, hypoglycemia, pituitary insufficiency, hyperparathyroidism
Respiratory	Hypoxemia, hypercarbia, tuberculosis
Nutritional	Malnutrition, dehydration, anorexia nervosa
Toxicological	Botulism, organophosphorus poisoning
Neuromuscular	Guillain-Barre syndrome, myasthenia gravis, Eaton-Lambert syndrome, polymyositis, dermatomyositis, steroid induced myopathy
Cerebral/neurological	Cerebrovascular insufficiency
Electrolyte disturbances	Hyperkalemia, hypokalemia, hypernatremia, hyponatremia, hypercalcemia, hypocalcemia
Chronic disease	Malignancy, renal impairment/failure, hepatic insufficiency/failure
Medications	Statins, glucocorticoids, colchicine, chemotherapy
Addiction	Alcohol, drug abuse
Rheumatological disorders	Rheumatoid arthritis, systemic lupus erythematosus

Table 1: *Systemic disorders that may be presented with weakness.*

Hyperkalemia

Causes of hyperkalemia are listed in table 2.

Renal failure
Hemolysis
Acidosis
Trauma with massive muscle destruction
Adrenal insufficiency
Primary hyperaldosteronism
Familial hyperkalemic periodic paralysis
Drug induced: aldosterone antagonist diuretics (e.g. spironolactone or triamterene)

Table 2: *Causes of hyperkalemia.*

Manifestations

Clinically, weakness in hyperkalemia is a late sign and usually preceded with cardiac manifestations that usually push the patient to seek for medical advice and start medical treatment that usually hide the weakness. Cardiac findings are in the form of ECG changes and arrythmias. ECG changes include tall peaked T wave (T wave tenting) especially in precordial leads, wide QRS complex, reduced R wave amplitude, ST segment depression, prolonged PR interval and loss of P wave. Arrythmias include heart block, atrial asystole, ventricular fibrillation and asystole [1].

Vague muscle pain may precede weakness. After serum potassium level exceeds 8 mEq/L, weakness starts to appear in the legs followed by the trunk and then the arms. Face and respiratory muscles are affected late. Patients with periodic paralysis may show symptoms earlier with serum plasma potassium of 5.5 mEq/L due to abnormal membrane function. Muscle weakness is typically reversible after treatment of hyperkalemia [2].

Weakness is produced by changes in neuromuscular conduction. Increased plasma potassium concentration leads to reduction of the ratio between intracellular potassium concentration to extracellular potassium concentration. This leads to a decrease in the magnitude of resting membrane potential. This creates a status of persistent depolarsation that inactivates sodium channels in the cell membrane. The overall membrane excitability decreases and appears in the form of weakness or paralysis [3]. Maury and coworkers explained the hyperkalemic paralysis by a decrease in nerve conduction as was tested by electromyogram that showed profoundly decreased nerve conduction velocities associated with conduction blocks [4].

Hypokalemia

Causes of hypokalemia are listed in table 3.

Diarrhea
Vomiting
Nasogastric suctioning
Medications: diuretics, laxatives, insulin
Mineralocorticoid excess including steroid therapy

Table 3: *Causes of hypokalemia.*

Manifestations

Muscle weakness is the most common manifestation in hypokalemia. With a total body deficit of 300 mEq (serum potassium of 2.0 - 3.0 mEq/L) weakness appears. With total body loss of 500 mEq (serum potassium of < 2.0 mEq/L) areflexia and flaccid paralysis predominate. Pattern of affection is ascending (like hyperkalemia) affecting the lower limbs, then the trunk and upper limbs. Respiratory muscle may be affected with the resultant respiratory failure and death. Muscle weakness is typically reversible after treatment of hyperkalemia [5]. Severe hypokalemia may lead to muscle cramps, rhabdomyolysis and myoglobinuria [6]. Hypokalemic periodic paralysis is a rare disease caused by channelopathy triggered by thyrotoxicosis, heavy exercise, high carbohydrate meal and some drugs. It is caused by an acute transcellular shift of potassium into the cells [7].

Other manifestations of hypokalemia include paralytic ileus (nausea, vomiting and abdominal distension), polydipsia, inability to concentrate urine and cardiac symptoms. Cardiac irritability becomes evident with digitalis toxicity. ECG changes include an initial T-wave fattening. This is followed by ST segment depression and the appearance of U wave (usually appear in lateral pericordial leads V4-V6). Prolongation of PR and QT intervals may occur [8].

Mechanism of hypokalemia to produce weakness include a decrease in extracellular potassium concentration that leads to hyperpolarization of the cell membrane and the resultant muscle weakness [9].

Hypernatremia

Causes of hypernatremia are listed in table 4.

Free water losses from gastrointestinal tract, skin or kidney
Lack of access to or inability to obtain free water
Adrenal hormonal excess
Diabetes insipidus (head trauma or pituitary neurosurgery)
Medications: osmotic diuretics

Table 4: *Causes of hypernatremia.*

Manifestations

Early symptoms may include a strong feeling of thirst, weakness, falls, nausea, and loss of appetite. Severe symptoms include confusion, muscle twitching, hyperreflexia, spasticity and focal neurologic deficit. In hypernatremia the altered mental status usually overwhelms the clinical status. Insomnia, lethargy and coma are mental sequels if hypernatremia passed untreated. Symptoms and signs may be related more to severe volume depletion including weakness, fatigue and lassitude [10].

Hyponatremia

Cause of hyponatremia are listed in table 5.

Dehydration
Congestive heart failure
Cirrhosis
Acute renal failure with oliguria, nephrotic syndrome, chronic renal failure
Adrenal insufficiency.
Hypothyroidism
Inappropriate secretion of antidiuretic hormone
Medications: narcotics, barbiturates, carbamazepine, tolbutamide, cyclophosphamide, vincristine

Table 5: *Cause of hyponatremia.*

Manifestations

Hyponatremia is frequently encountered in patients coming to emergency department. Mostly it starts asymptomatically. Nausea, vomiting, headache and loss of short-term memory, lethargy, fatigue, muscle weakness (worse in legs and arms), spasms or cramps may develop earlier. As serum sodium levels approaches 120 mEq/L changes in the mental status starts to appear as restlessness, irritability and confusion. With serum levels of 110 mEq/L seizures and coma are expected [11]. Rhabdomyolysis is an occasional consequence of hyponatremia and should be considered in patients with muscle pain or tenderness [12].

Hypercalcemia

Cause of hypercalcemia are listed in table 6.

Hyperparathyroidism (primary or secondary)
Neoplasms: multiple myeloma
Adrenal insufficiency
Hyperthyroidism
Immobilization
Sarcoidosis
Vitamin D intoxication
Medications: thiazides

Table 6: *Causes of hypercalcemia.*

Manifestations

Hypercalcemia may be mild (10.5 - 11.9 mg/dL = 2.62 - 2.97 mmol/L), moderate (12.0 - 13.9 mg/dL = 3.0 - 3.47 mmol/L) or severe (14.0 - 16.0 mg/dL = 3.50 - 4 mmol/L). In mild to moderate elevation of serum calcium level, polyuria, polydipsia, nausea, vomiting, constipation and anorexia appear. Mental changes include abnormalities in cognition and memory, depression, changes in personality, emotional lability. Fatigue, malaise and skeletal pains are common. Proximal muscle weakness is usual and muscle fasciculations may be seen. Peptic ulcer and pancreatitis are not uncommon while renal stones are frequent. In severe cases coma follows [13].

ECG shows prolonged PR interval, short QT interval, widened QRS complex and bradycardia in some patients. Other ECG findings include flat or inverted T wave, ST elevation and presence of J (Osborn) wave at the end of QRS complex. Muscle weakness and cardiac complications are due to inhibition of neuromuscular and myocardial depolarization by hypercalcemia as calcium is known to block sodium channels [14].

Hypocalcemia

Cause of hypocalcemia are listed in table 7.

Hypoparathyroidism
Hyperphosphatemia
Hypomagnesemia
Renal tubular acidosis, Chronic renal failure
Malnutrition, malabsorption
Acute pancreatitis
Vitamin D deficiency/resistance

Table 7: *Causes of hypocalcemia.*

Manifestations

Neuromuscular irritability is evident in patients with hypocalcemia in the form of distal extremity paresthesia, numbness and tingling, Chvostek's sign (gentle tapping over the facial nerve induces twitching of the perioral or perinasal muscles), Trousseau's sign (inflating the tourniquet above systolic pressure on the upper arm for 3 minutes induces carpal spasm), muscle cramps and weakness, laryngospasm, tetany and seizures. Muscle cramps can be very painful and progress to carpal spasm or tetany. Neurologically the patient may have personality disturbances, irritability, affected intellectual abilities, confusion, disorientation, psychosis, fatigue and poor memory. ECG may show prolonged PR and QT intervals. Smooth muscle affection may show dysphagia, biliary colic, dyspnea and wheezing. The skin may be dry with coarse hairs and brittle nails, exfoliative dermatitis and psoriasis.

Decreased calcium levels lower the threshold for depolarization which increase the responsiveness of neuromuscular transmission (calcium inhibits depolarization of nerve and muscle fibers and blocks sodium channels) [15,16].

Hypermagnesemia

Cause of hypermagnesemia are listed in table 8.

Renal failure (acute or chronic), enhanced by pump inhibitors, malnourishment, and alcoholism
Pre-eclampsia treated with magnesium sulphate
Magnesium-containing antacids and laxatives
Lithium therapy
Milk-alkali syndrome

Table 8: *Causes of hypermagnesemia.*

Manifestations

Hypermagnesemia may be mild (< 7 mg/dL = 2.88 mmol/L), Moderate (7 - 12 mg/dL = 2.88 - 4.94 mmol/L) or severe (> 12 mg/dL = 4.94 mmol/L). Mild cases of hypermagnesemia show muscle weakness, nausea, dizziness and confusion. Moderate cases show decreased reflexes, drowsiness, sleepiness, dizziness, flushing, headache, constipation and urine retention. Hypotension, bradycardia, blurry vision and ataxia may be also encountered. While in severe cases patient may have flaccid muscle paralysis, hyporeflexia, hypoventilation (bradypnea), more hypotension and bradycardia, prolonged PR interval, atrioventricular block, lethargy. Higher serum magnesium level (> 15 mg/dL = 6.17 mmol/dL) coma, cardiorespiratory arrest may commence [17].

This comes from the effects of magnesium as a physiologic calcium blocker, membrane stabilizer and smooth muscle relaxant. Moreover, increased extracellular magnesium levels inhibits acetylcholine release from the neuromuscular junction [18].

Hypomagnesemia

Cause of hypomagnesemia are listed in table 9.

Starvation
Chronic alcoholism
Patients on total parenteral nutrition
Medications: loop and thiazide diuretics, chemotherapy
Diarrhea
Gastric bypass surgery

Table 9: *Causes of hypomagnesemia.*

Manifestations

Symptoms of low serum magnesium are muscular tremors and fasciculations, ocular nystagmus, tetany (including positive Chvostek's and Trousseau's signs, muscular spasms and cramps), seizures, altered mental state (apathy, delirium and coma) and cardiac arrhythmias such as torsades de pointes (multifocal ventricular tachycardia), atrial and ventricular premature contractions and atrial fibrillation. ECG shows prolonged PR interval, wide QRS complex, peaked t wave. Other possible symptoms are ataxia, vertigo and dysphagia. Hypocalcemia and hypokalemia usually accompany hypomagnesemia.

Magnesium is an essential cofactor in most of the enzymatic actions in the body. Therefore, its deficiency lead to several clinical features. Moreover, magnesium is considered as a membrane stabilizer and important in protein and nucleic acid synthesis and sharing in mitochondrial functions [19].

Hyperphosphatemia

Cause of hyperphosphatemia are listed in table 10.

Renal failure
Medications: phosphate containing laxatives or enemas, Vitamin D intoxication
Hypoparathyroidism
Thyrotoxicosis

Table 10: *Causes of hyperphosphatemia.*

Manifestations

Although mostly asymptomatic, hyperphosphatemia may induce symptomatic hypocalcemia. Therefore, neuromuscular hyperexcitability (positive Chvostek's and Trousseau's signs, hyperreflexia, muscle cramps), tetany, seizures may develop. Hypotension and heart failure are not uncommon [20].

Hypophosphatemia

Cause of hypophosphatemia are listed in table 11.

Poor nutrition
Malabsorption
Medications: antacids

Table 11: *Causes of hypophosphatemia.*

Manifestations

Hypophosphatemia is mostly asymptomatic. Mild hypophosphatemia may induce generalized weakness. Severe cases may show altered mental status, focal neurological symptoms (numbness, reflexive weakness), muscular pain and heart failure [20].

Conclusion

Electrolyte disturbances are considered important factors in developing generalized weakness. Clinical picture and accompanying manifestations are important for primary diagnosis. Most of electrolyte disturbances have muscular and mental elements. ECG changes are very common with electrolyte disturbances and help to identify the disturbance concerned. Generalized weakness due to electrolyte imbalance is largely related to cell membrane depolarization/hyperdepolarization. These electrolyte disturbances may proceed to serious forms of arrhythmias, muscle paralysis and death.

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