International Journal of Web of Multidisciplinary Studies
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
website: https://ijwos.com OPEN ACCESS E-ISSN : 3049-2424
Volume 3 Issue 7 , July 2026 DOI: https://doi.org/10.71366/ijwos

Medication-Related Electrolyte Abnormalities in Hospitalized Patients: Risk Factors and Monitoring Strategies

Dr. M. Anusha[1], V. Niveditha Reddy[2], K. Swapna[3], V. Priyanka[4], A. Revanth[5], V. Pandu Ranga Reddy[6]
[1] *Assistant Professor - Department of Pharmacy Practice, Malla Reddy college of pharmacy, Dhulapally, Secunderabad, Telangana, 500100 (Affiliated to Osmania University).*
[2,3] *pharm-D(PB) 1st year, Students, Malla Reddy college of pharmacy, Dhulapally, Secunderabad, Telangana, 500100 (Affiliated to Osmania University)*
[4,5,6] *pharm-D 4th year, Students, Malla Reddy college of pharmacy, Dhulapally, Secunderabad, Telangana, 500100 (Affiliated to Osmania University)*

Article Info

Article History:

Published: 26 July 2026

Publication Issue:
Volume 3, Issue 7
July-2026

Page Number:
561-575

Corresponding Author:
V. Niveditha Reddy

Abstract:

Electrolyte abnormalities are common in hospitalized patients and may be associated with significant morbidity, prolonged hospitalization, and adverse clinical outcomes. Electrolyte disturbances are an important and potentially preventable cause of morbidity especially in patients on multiple drugs or with underlying co-morbidities. Many commonly prescribed drugs, such as diuretics, renin-angiotensin-aldosterone system inhibitors, proton pump inhibitors, corticosteroids, antidepressants and some antimicrobial agents, have been associated with changes in the levels of sodium, potassium, magnesium, calcium and phosphate. Other factors that might further increase the risk of medication-related electrolyte abnormalities include advanced age, renal dysfunction, cardiovascular disease, gastrointestinal losses, polypharmacy, and concomitant use of multiple medications that affect electrolyte levels. Thus, early recognition of susceptible patients and proper laboratory monitoring are important to prevent serious complications. This review summarizes major medication-related electrolyte abnormalities seen in hospitalized patients, their mechanisms and risk factors, and current approaches to electrolyte monitoring. It also discusses prevention and management strategies, and the role of clinical pharmacists in medication review, identification of high-risk patients, and optimization of electrolyte monitoring. Increased awareness and risk-based monitoring may help detect and manage medication-related electrolyte disturbances early and contribute to safer pharmacotherapy in hospitalized patients.

Keywords: Drug-induced electrolyte disorders; Electrolyte disturbances; Medication-related electrolyte abnormalities; Risk factors; Electrolyte monitoring; Medication safety; Clinical pharmacy; Hospitalized patients

1.Introduction

Electrolytes are important components of body fluids, taking part in several physiological processes, including fluid balance, acid-base homeostasis, neuromuscular activity, cardiac conduction, and cell function. The major electrolytes required for normal physiological function are sodium, potassium, calcium, magnesium, chloride and phosphate. Alterations in their serum concentrations may be mild and asymptomatic or may be severe with neurological manifestations, cardiac arrhythmias, organ dysfunction and other potentially life-threatening complications.

Electrolyte abnormalities are especially pertinent in hospitalized patients due to the presence of acute illness, multiple comorbidities, impaired renal function, alterations in fluid and nutritional status and exposure to several medications . Recent studies in critically ill and hospitalized populations demonstrate the high prevalence of electrolyte

Copyright © 2025 The Author(s) : This is an open access article under the CC BY license (http://creativecommons.org/licenses/by-nc/4.0/)

disturbances and the occurrence of multiple abnormalities at the same time. Early recognition and appropriate management are important as multiple electrolyte disturbances have been associated with poorer clinical outcomes.

Electrolyte abnormalities are an important and potentially modifiable contributor to medication use. Drugs may disrupt electrolyte homeostasis by various mechanisms such as altered renal electrolyte excretion, changes in gastrointestinal absorption, interference with hormonal regulation, redistribution of electrolytes between the intra- and extracelluar compartments, and direct effects on renal tubular function. Commonly used medications, including diuretics, renin–angiotensin–aldosterone system inhibitors, antidepressants, antiepileptic drugs, proton pump inhibitors, corticosteroids and some antimicrobial agents, have been associated with electrolyte imbalances of sodium, potassium, magnesium, calcium or other electrolytes .

The diagnosis of medication-induced electrolyte derangements in hospitalized patients may be difficult since the cause is often multifactorial. The same abnormality may be due to underlying diseases, renal dysfunction, gastrointestinal losses, intravenous fluid administration, nutritional status and concurrent drugs. Assessment is complicated by polypharmacy, as several medications with the potential to affect electrolyte homeostasis may be administered simultaneously. Therefore, any electrolyte derangement that occurs during pharmacotherapy should be considered in the context of the patient's medications and other clinical risk factors.

Thus, proper monitoring of serum electrolytes is an important element of medication safety, particularly in patients receiving drugs that are known to affect electrolyte balance. Identification of high risk patients, baseline evaluation when appropriate, periodic follow-up and early intervention in the presence of abnormal laboratory findings, may reduce the risk of serious complications. This review article highlights the medication-induced electrolyte abnormalities in hospitalized patients, with an emphasis on the offending medications, mechanisms involved, risk factors, and the approach to effective electrolyte monitoring and prevention [1,2].

2.Electrolyte Homeostasis: An Overview

Electrolyte homeostasis is the coordinated regulation of intake, absorption, distribution and excretion to maintain electrolyte concentrations within physiological ranges. The kidneys are the main organs of this process due to the regulation of the excretion of electrolytes and water in accordance with the physiological needs of the body. The gastrointestinal tract , the endocrine system , and the movement of fluid between the intracellular and extracellular compartments also are involved in the maintenance of the electrolyte balance .

Sodium is the principal extracellular cation and is a major determinant of extracellular fluid volume and plasma osmolality. Renal function and hormonal mechanisms, such as antidiuretic hormone, the renin–angiotensin–aldosterone system, and natriuretic peptides, tightly regulate sodium and water balance. For example , sodium concentrations can change leading to hyponatremia or hypernatremia . Severe or rapid onset of these can have significant neurological consequences .

Potassium is primarily intracellular and is important in maintaining the resting membrane potential of excitable tissues. Normal potassium homeostasis is important for the function of skeletal muscle, nerve and especially the heart. Serum potassium concentration is influenced by dietary intake, renal excretion, gastrointestinal losses, acid–base status, insulin, catecholamines and aldosterone. Low and high potassium levels can alter the heart's electrical activity and lead to clinically important arrhythmias.

Calcium has important roles in bone mineralization, muscle contraction, neuronal transmission, blood coagulation and intracellular signalling. Calcium homeostasis is largely regulated by the interplay of parathyroid hormone, vitamin D, the kidneys, the gastrointestinal tract and bone. Disruptions in these regulatory mechanisms, or medication side effects, may cause hypocalcemia or hypercalcemia.

Magnesium is an intracellular electrolyte for the most part and is a cofactor for many enzyme reactions. It is involved in neuromuscular function, energy metabolism, cardiac electrophysiology and regulation of other electrolytes, in

particular potassium and calcium. Magnesium homeostasis is primarily regulated by intestinal absorption and renal excretion. Hypomagnesemia can also be a cause of persistent hypokalemia or abnormalities in calcium regulation.

Chloride is the major anion in the extracellular fluid and plays a role in fluid balance, electroneutrality and acid-base regulation. It correlates closely with sodium and bicarbonate concentrations. Hypochloremia and hyperchloremia are both common in hospitalized patients, owing to an underlying illness, gastrointestinal losses, renal disturbances, or the administration of intravenous fluids and medications.

Phosphate is mainly intracellular and in bone and is important for energy generation in cells, bone mineralization, cell membrane structure, and acid-base buffering. Gastrointestinal absorption, renal handling, bone storage and hormonal regulation determine the net phosphate balance. Hypophosphatemia and hyperphosphatemia may occur in hospitalized and critically ill patients and may have important clinical implications.

These electrolytes are physiologically interrelated and alteration of one electrolyte may affect concentration or regulation of another. Acute disease, renal impairment, fluid therapy, nutritional changes, gastrointestinal losses and pharmacological treatment, all contribute to disruption of this balance in hospitalized patients. Mechanisms of normal electrolyte homeostasis thus provide the basis for understanding how pharmacologic agents can disrupt these homeostatic mechanisms and result in clinically important electrolyte disorders [2,3].

3.Electrolyte Abnormalities Related to Medication

Many drugs can upset the balance of electrolytes in different ways. Certain drugs increase the loss of electrolytes in the urine or gastrointestinal tract, whereas others decrease electrolyte excretion, interfere with hormonal regulation, alter intestinal absorption, or shift electrolytes between the intracellular and extracellular compartments. These effects are of particular importance in hospitalized patients, who are often receiving multiple medications and may have renal dysfunction, acute illness, fluid disturbances, or other conditions that affect electrolyte homeostasis.

Medications are not always the only cause of an electrolyte abnormality. For example, a patient on a diuretic may also be vomiting, eating less, or have renal impairment. Therefore, drug-induced electrolyte abnormalities should be considered as an interaction between the drug and the patient's underlying condition and other risk factors. Recognition of common offending medications may help clinicians recognize abnormalities earlier and when closer laboratory monitoring is indicated.

A.DRUG INDUCED HYPONATREMIA

Hyponatremia, which is low concentration of sodium in the blood, is one of the most common electrolyte abnormalities seen in hospitalized patients. Medications that cause hyponatremia are often those that cause the body to lose sodium or cause the body to retain more water than sodium.

Thiazide diuretics are some of the better known drugs that have been associated with hyponatremia. They promote renal sodium loss and decrease the kidney's ability to dilute urine appropriately. Another important category is psychotropic medications. Hyponatremia has been associated with selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), some antipsychotics, and anticonvulsants such as carbamazepine. Many of these agents produce inappropriate antidiuretic activity with resultant excessive water retention and dilution of serum sodium. Desmopressin and some anti-cancer drugs can also cause similar disturbances in water regulation.

The clinical presentation depends on both the degree and the speed of sodium fall. Mild cases may be asymptomatic or have nausea, headache or fatigue. A rapid or severe drop may lead to confusion, seizures, reduced consciousness and other serious neurological complications. Elderly patients and those on a number of drugs that affect sodium and water balance require special care.

Drug-induced hyponatremia usually occurs due to increased sodium loss in urine or excess water retention leading to dilution effect on serum sodium.

Drug Induced Hypernatremia

Hypernatremia is an increased concentration of sodium in the blood. It is usually a sign of a water deficit relative to sodium, rather than an excess of sodium in the body. As a result, drug-induced hypernatremia typically occurs when a drug either increases water loss, inhibits renal water conservation or, occasionally, provides an excess sodium load.

Lithium is a classic drug used for this condition. Prolonged lithium therapy can modify the renal response to antidiuretic hormone and lead to nephrogenic diabetes insipidus. This causes the kidneys to produce large volumes of dilute urine. If the water lost is not adequately replaced, the serum sodium may rise. Urinary water loss can also be promoted by osmotic agents (e.g., mannitol). Osmotic cathartics such as lactulose and others may contribute to the effect by loss of water through the gastrointestinal tract. Hypertonic sodium bicarbonate or sodium chloride may contribute sodium directly if given in sufficient amounts.

Patients who cannot independently obtain water, such as some critically ill, debilitated or elderly hospitalized patients, are especially vulnerable.

Core concept: The basic problem in drug-induced hypernatremia is loss of too much free water relative to sodium, or, less commonly, excess sodium [4].

B.Drug-Induced Hypokalemia

Potassium is essential for the normal electrical activity of both skeletal and cardiac muscle. Some drugs cause the body to lose more potassium than usual, and others temporarily move potassium from the blood into cells. Hypokalemia can result from either.

Loop diuretics e.g. furosemide and thiazide diuretics are common causes as they increase renal potassium loss. Corticosteroids and mineralocorticoids can also increase potassium excretion in the correct clinical context. Some antimicrobial agents can cause renal potassium wasting, including high-dose beta-lactams and drugs that cause renal tubular injury.

Insulin and beta-2 adrenergic agonists such as salbutamol/albuterol have a different mechanism of action. These drugs do not necessarily remove potassium from the body, but rather stimulate the movement of potassium from the extracellular fluid into the cells. Total-body potassium may not be depleted initially, but the serum potassium concentration can fall.

Mild hypokalemia may be asymptomatic, but greater decreases may lead to weakness, muscle cramps, gastrointestinal dysfunction and cardiac electrical abnormalities. This risk is especially relevant in patients with cardiovascular disease or on other drugs predisposing to arrhythmias.

Key concept: Medications cause hypokalemia mainly due to renal/GI potassium loss or potassium shift from blood to cells [2,6].

C.Drug-induced hyperkalemia

Hyperkalemia is defined as a serum potassium level above the normal range. This is in contrast to hypokalemia . The most important drug - related mechanism is usually reduced renal elimination of potassium .

Drugs affecting the renin-angiotensin-aldosterone system are especially important. ACE inhibitors and angiotensin receptor blockers inhibit aldosterone activity and may thereby decrease renal potassium excretion. Potassium sparing diuretics such as spironolactone, eplerenone and amiloride act via different mechanisms to achieve a similar effect. Potassium supplementation can further increase the risk when potassium excretion is already compromised. Some

other drugs , such as some beta-blockers and other agents , might work by changing how potassium moves between cells and the extracellular fluid .

The importance of these drugs clinically really depends on the patient. A drug that causes minimal changes in potassium in a patient with normal renal function may cause marked hyperkalemia in a patient with chronic kidney disease or when several potassium-raising drugs are present.

High potassium levels are problematic because they can interfere with the electrical conduction of the heart and lead to fatal arrhythmias.

Core concept: drug-induced hyperkalemia is most often due to decreased urinary potassium excretion, particularly when drugs interfere with aldosterone-mediated potassium excretion[6,7].

D.Drug-Induced Hypomagnesemia

Magnesium is sometimes called a “forgotten” electrolyte, as it might not get as much attention as sodium or potassium. However, magnesium deficiency may impact neuromuscular and cardiac function and may be associated with other electrolyte disturbances, particularly hypokalemia and hypocalcemia.

There are two main ways many drugs can lower magnesium: gastrointestinal or renal. Proton pump inhibitors (PPIs) have been linked to hypomagnesemia, especially when used for long periods of time, and impaired intestinal absorption of magnesium has been suggested as the main mechanism . Evidence from observational studies supports an association; however, estimates are heterogeneous across studies and populations.

Loop diuretics and thiazide diuretics can increase urinary loss of magnesium. Renal magnesium wasting can also be caused by aminoglycosides, amphotericin B, cisplatin, calcineurin inhibitors and some other drugs.

A major clinical clue is the presence of refractory hypokalemia. If there is also magnesium deficiency, potassium replacement alone may not be sufficient to correct the potassium abnormality.

Core concept: Drug-induced hypomagnesemia is mainly due to reduced magnesium absorption in the gut or increased renal magnesium loss [3].

E.Calcium Disturbances Induced by Drugs

Drugs can disrupt calcium balance by altering bone turnover, vitamin D activity, parathyroid hormone regulation, renal handling of calcium, or magnesium balance, causing hypocalcemia or hypercalcemia.

Hypocalcemia associated with drug therapy has been reported with bisphosphonates and some other antiresorptive therapies, as suppression of bone resorption reduces calcium release from bone into the circulation. Cisplatin. Aminoglycosides and some other drugs can also contribute directly or indirectly. Some antiepileptic drugs when used for a long time may interfere with vitamin D metabolism and consequently calcium homeostasis. Further, drugs that cause severe hypomagnesemia can interfere with normal calcium regulation and contribute to hypocalcemia.

Alternatively, drugs or supplements that increase calcium availability or alter its renal or hormonal regulation may be responsible for drug-associated hypercalcemia. Thiazide diuretics decrease urinary calcium loss and may raise serum calcium in susceptible patients. Lithium may affect the regulation of parathyroid hormone and has also been associated with hypercalcemia in some patients. High calcium concentrations may also arise from excess calcium or vitamin D.

Clinically significant disturbances of calcium may affect the nervous system, muscles, gastrointestinal tract, kidneys, bones and cardiovascular system.

Core concept: Medication-related calcium abnormalities are due to disruption of normal relationships between bone, kidney, gastrointestinal absorption, vitamin D and parathyroid hormone [2,3].

F.Phosphate Drug-Related Abnormalities

Phosphate is important for cellular energy production, bone mineralization, cell membranes and several metabolic processes . Phosphate abnormalities may not be routinely checked, but drugs can cause clinically significant changes, especially in patients with other risk factors.

Drug-related hypophosphatemia may occur due to decreased gastrointestinal absorption, increased urinary phosphate loss, or phosphate shift into cells. Antacids containing aluminum can bind phosphate in the gastrointestinal tract and reduce its absorption. Insulin can drive phosphate into cells, particularly in the setting of disorders with marked metabolic derangements. Renal tubular dysfunction and increased urinary loss of phosphate may occur with tenofovir disoproxil fumarate. Another important example is ferric carboxymaltose. This can increase biologically active fibroblast growth factor 23 (FGF23), which promotes renal phosphate wasting.

Severe or prolonged hypophosphatemia may cause muscle weakness and impaired cellular energy metabolism and persistent medication-associated phosphate loss may adversely affect bone health.

Drug-induced hyperphosphatemia is less commonly attributed to routine drug therapy. This may be due to an excess administration of phosphate-containing preparations or administration of phosphate to a patient with insufficient renal phosphate excretion. Renal function and the amount of phosphate administered are important considerations.

Key concept: drug-induced phosphate disorders are usually caused by altered intestinal absorption, renal phosphate handling, intracellular redistribution or phosphate overload.

Generally these abnormalities indicate that the same drug can act on electrolytes by very different mechanisms. So for hospitalized patients it is important to review the medication chart along with electrolyte results. Rather than seeing an abnormal laboratory value in isolation, the clinician should consider whether a recently begun drug, a change in dose of a drug, a combination of drugs, renal impairment or some other clinical factor may be involved in the disturbance[8].

4. Major Drug Classes and Associated Electrolyte Abnormalities

Numerous drugs used in hospitalized patients can modify the concentration of electrolytes. The pattern of disturbance depends upon the pharmacological action of the drug, its site of action, duration of treatment, dose, renal function and the presence of other drugs or disease. Certain drug classes require special attention because they are frequently used and have known effects on electrolyte homeostasis.

Diuretics

Diuretics are among the most important drug groups associated with electrolyte disturbances. Thiazide diuretics act on the distal convoluted tubule to increase sodium and chloride excretion and are particularly associated with hyponatraemia. Both thiazide and loop diuretics may lead to increased urinary losses of potassium and magnesium, resulting in hypokalemia and hypomagnesemia. Conversely, potassium-sparing diuretics (eg, spironolactone, eplerenone, and amiloride) reduce potassium excretion and may cause hyperkalemia, particularly in patients with impaired renal function or in patients receiving other medications that increase serum potassium levels.

Renin-angiotensin-aldosterone system blockers

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are widely used in the treatment of hypertension, heart failure and some renal diseases. These drugs reduce renal potassium excretion by blocking aldosterone production or action. Therefore, hyperkalemia is a significant potential adverse event, especially in patients with chronic kidney disease, diabetes, or concomitant use of potassium-sparing diuretics or potassium supplements.

Proton pump inhibitor

Proton pump inhibitors (PPIs) are commonly used in hospitalized patients for stress-ulcer prophylaxis in selected patients and for acid-related gastrointestinal disorders. Hypomagnesemia is mostly related to long-term use of PPI due to impaired gastrointestinal magnesium absorption. Magnesium deficiency is clinically important because it may play a role in secondary hypokalemia and hypocalcemia.

Psychotropic drugs

Hyponatremia has been reported with several antidepressants, antipsychotics and anticonvulsants. Selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors are particularly relevant especially in the older adults. Some antipsychotic drugs and carbamazepine also interfere with water regulation. In many cases the abnormality resembles the syndrome of inappropriate antidiuresis, in which too much water retention leads to a low serum sodium concentration.

Mineralocorticoid-Active Drugs and Corticosteroids

Corticosteroids may influence sodium and potassium homeostasis depending on their glucocorticoid and mineralocorticoid effects. Some of the drugs with strong mineralocorticoid activity may cause sodium retention and renal potassium loss. Thus, prolonged exposure may cause hypokalemia especially in the presence of other potassium-lowering factors.

Anti-Microbial Agents

Some antimicrobial agents may have renal tubular effects that lead to electrolyte abnormalities. Aminoglycosides and amphotericin B can increase renal losses of magnesium and potassium. Other antimicrobial agents may have an indirect contribution via nephrotoxicity or gastrointestinal adverse effects such as diarrhea.

Antineoplastic and Immunosuppressive Agents

Electrolyte disturbances in cancer therapy are of clinical importance. Platinum-based agents (especially cisplatin) are associated with renal magnesium wasting and severe hypomagnesemia. Epidermal growth factor receptor inhibitors may also disrupt renal magnesium conservation. Calcineurin inhibitors, such as tacrolimus and cyclosporine, may interfere with the kidney's handling of electrolytes. Thus, depending on the agent and the clinical setting, antineoplastic therapy may affect magnesium, potassium, sodium, calcium and phosphate homeostasis.

Drugs That Affect Bone and Mineral Metabolism

Bisphosphonates, denosumab, vitamin D preparations, calcium supplements, lithium and some anticonvulsants can affect calcium metabolism in a variety of ways. Antiresorptive therapies may cause hypocalcemia, with susceptible patients at greatest risk, while hypercalcemia can result from excessive supplementation with calcium or vitamin D. Lithium may affect regulation of parathyroid hormone and has been associated with increased concentrations of calcium.

In summary, the medication list of a hospitalized patient should be considered an important part of the evaluation whenever a new electrolyte abnormality is seen. When more than one drug affecting electrolytes is prescribed together, care should be exercised[2–4,6,8].

5. Mechanisms of Drug-Induced Electrolyte Disturbances

There are multiple ways to develop medication related electrolyte abnormalities. Drugs may interfere with electrolyte homeostasis at the level of the kidney, the gastrointestinal tract, the endocrine system or at the cellular level. Knowledge of these mechanisms helps explain why the same electrolyte abnormality may be seen with drugs that are pharmacologically unrelated.

a. Renal Electrolyte Loss Increased

The kidneys control the final amount of many electrolytes that are excreted from the body. Therefore drugs that interfere with tubular reabsorption may increase electrolytes loss in urine.

The most obvious example is that of diuretics. They block sodium transport in different nephron sites, thus increasing sodium delivery to more distal tubular segments, and possibly increasing potassium excretion. Loop and thiazide diuretics also can cause increased loss of magnesium. Nephrotoxic drugs, such as cisplatin, aminoglycosides, and amphotericin B, may impair tubular function and lead to renal wasting of one or more electrolytes.

b. Decreased renal electrolyte loss

Also possible is the reverse mechanism. Some medications can make the kidney less able to get rid of an electrolyte, and this can lead to the electrolyte building up in the blood.

A classic example is hyperkalemia associated with ACE inhibitors, ARBs and potassium-sparing diuretics. Decreased aldosterone production or action leads to decreased potassium secretion in the distal nephron. The effect is considerably more important in patients with impaired renal function.

c. Altered GI absorption or loss

Certain drugs may interfere with the absorption of electrolytes from the gastrointestinal tract. For instance, long term use of PPIs may result in reduced magnesium absorption from the intestine. There are some phosphate-binding agents that can reduce phosphate absorption.

Drugs that induce persistent vomiting or diarrhoea may also cause indirect electrolyte losses. In these cases the drug does not necessarily directly affect an electrolyte transporter. Rather the GI adverse effect causes electrolyte and fluid loss.

d. Intra-Extracellular Redistribution

Presence of an abnormal serum electrolyte concentration does not necessarily mean that the electrolyte has been lost from the body. Some drugs cause movement of electrolytes from the extracellular to the intracellular compartments.

Insulin and beta-2 adrenergic agonists may lower serum potassium concentrations by promoting the movement of potassium into cells. Similarly, insulin can promote an intracellular shift of phosphate. Such redistribution effects may lead to rapid changes in measured serum concentrations.

e. Change of hormonal regulation

A number of hormones regulate electrolyte and water balance, particularly antidiuretic hormone, aldosterone, parathyroid hormone, and vitamin D. Drugs that interfere with these pathways can therefore cause abnormalities in electrolytes.

Psychotropic drugs, anticonvulsants and certain antineoplastic agents can induce water retention and hyponatremia due to inappropriate antidiuretic activity. ACE inhibitors and ARBs affect potassium regulation by aldosterone, while lithium can affect both renal handling of water and parathyroid regulation.

f. Drug-Associated Renal Dysfunction

Some drugs change electrolyte levels indirectly by affecting the function of the kidney. If glomerular filtration or tubular function declines, the kidney may not be able to excrete or retain electrolytes appropriately. This is particularly important for potassium, magnesium and phosphate.

As such, drug-induced electrolyte disturbances can result from actual electrolyte loss or gain, changes in water balance, movement of electrolytes between compartments, impaired absorption, hormonaleffects, or renal dysfunction. In hospitalized patients more than one mechanism may be occurring simultaneously[2–4,8].

6. Risk factors for drug-induced electrolyte abnormalities

Not all patients on an electrolyte altering medication develop an abnormality. Clinical vulnerability is defined as the interplay between drug exposure and patient-specific factors.

Elderly Age: Older hospitalized patients are particularly vulnerable because aging is associated with changes in renal function, body-water composition, thirst response, and physiological reserve. Older adults also tend to have multiple chronic diseases and take multiple medications at the same time. These can potentiate the electrolyte effects of the individual drugs.

Renal failure Kidney failure: Renal function largely determines the risk of electrolytes. Impaired renal function may alter the excretion of potassium and phosphate and the handling of sodium, magnesium, calcium and water. It can also increase the exposure to drugs that are cleared renally.

Taking many drugs (polypharmacy): Patients in hospital are often given a variety of different drugs. The more medicines that are taken, the greater the chance that two or more will affect the same electrolyte, either by adding to each other's effect or by interacting. For example, the combination of an ACE inhibitor and a potassium-sparing diuretic can increase the risk of hyperkalemia.

Several Comorbidities: Heart failure, chronic kidney disease, diabetes mellitus, liver disease, endocrine disorders and malignancy can independently influence fluid and electrolyte homeostasis. The addition of medications that can alter electrolytes may decrease the patient's ability to compensate.

Gastrointestinal Losses and Inadequate Nutritional Intake: Vomiting, diarrhea, decreased oral intake, and malnutrition are common in hospitalized patients and may deplete total body stores of potassium, magnesium, phosphate, and other electrolytes. Then drugs that cause additional losses can more easily produce clinically significant abnormalities.

Acute & Critical Illness: Serious illnesses such as sepsis, major surgery, trauma, acute kidney injury, and others can cause rapid changes in fluid distribution, renal perfusion, hormonal responses, and cellular electrolyte movement. Critically ill patients are therefore prone to large fluctuations in electrolyte values over short periods.

Treatment Dose and Length: For some medications, the risk of an electrolyte imbalance may be greater with higher doses, longer duration of treatment, or cumulative exposure. Duration is particularly relevant for abnormalities such as PPI-associated hypomagnesemia while some redistribution effects may develop rapidly.

Co-Administration of Drugs That Alter Electrolytes: The risk is increased with concomitant use of several drugs affecting the same electrolyte. Therefore, the whole regimen should be considered in a medication review, rather than looking at individual medicines.

These risks underline the need for an individualised approach. The presence of a high risk medication alone is not determinative of whether an abnormality will occur, the patient's renal function, age, comorbidities, concurrent medications, nutritional status and clinical condition collectively determine the actual risk[1,4,6].

7. Clinical presentation and complications:

The clinical presentation of electrolyte disturbances caused by drugs is very variable. Mild abnormalities may be asymptomatic and only detected on routine laboratory testing. The more severe or rapid the development of the abnormality, the more likely neurological, muscular, cardiovascular, gastrointestinal and metabolic manifestations will occur.

Sodium disorders: Mild hyponatremia can cause nonspecific symptoms such as nausea, headache, dizziness, fatigue or difficulty concentrating. More severe or fast developing hyponatremia can lead to confusion, altered consciousness, seizures, and cerebral edema.

Hypernatremia affects mainly the nervous system as the increase in extracellular osmolality causes water to move out of the cells. In severe cases patients may develop intense thirst, weakness, irritability, confusion, neuromuscular abnormalities, seizures, or coma.

Potassium Disorders: Potassium plays a major role in cardiac electrophysiology and both low and high concentrations are of particular importance.

Low potassium can make you feel tired and cause muscle weakness, cramping, constipation, and in severe cases, paralysis or irregular heart rhythms. Hyperkalemia can lead to serious conduction defects and life-threatening arrhythmias. Characteristic electrocardiographic changes and muscle weakness may be observed.

Disorders of Magnesium: Low magnesium levels can cause tremor, muscle cramps, muscle weakness, tetany, seizures, and neuropsychiatric manifestations. Complications include ventricular and supraventricular arrhythmias. Magnesium deficiency can also make hypokalemia difficult to treat and can also contribute to hypocalcemia.

Calcium Abnormalities : Hypocalcemia may cause increased neuromuscular excitability, which may manifest as perioral or peripheral paresthesia, muscle cramps, carpopedal spasm, tetany, or seizures. Severe abnormalities may also affect heart function.

Hypercalcemia can cause nausea, constipation, weakness, lethargy, polyuria, dehydration, confusion and renal complications. Severe hypercalcemia can result in neurologic and cardiac manifestations.

Abnormalities of Phosphate: Mild hypophosphataemia may be asymptomatic. Severe phosphate deficiency may lead to defective cellular energy generation, generalized muscle weakness, neurologic impairment, respiratory muscle weakness, cardiac impairment, and in severe cases, serious systemic complications.

Hyperphosphatemia is a frequent finding in patients with renal impairment. Prolonged elevation may lead to abnormalities in calcium balance and to soft-tissue or vascular calcification, especially in patients with chronic kidney disease.

Thus, the clinical relevance of medication-induced electrolyte disturbances goes beyond an abnormal lab result. Severe disturbances may affect cardiac conduction, neurological function, muscle activity, renal function and clinical stability. Early identification is especially important since mild abnormalities may be silent initially and become clinically significant when the offending medication is continued or additional risk factors develop[1,3–6,8].

8.Diagnosis and evaluation

The assessment of a suspected medication-related electrolyte abnormality should extend beyond the identification of an abnormal laboratory value. Electrolyte disturbances in hospitalized patients are often multifactorial. In addition to renal dysfunction, gastrointestinal losses, acute illness, intravenous fluids, nutritional changes and endocrine disorders, medications may also contribute. Thus, identifying medication involvement requires a systematic review of the patient's clinical condition and medication exposure.

The first step is to confirm the electrolyte abnormality and assess its severity. Interpret serum concentrations of sodium, potassium, magnesium, calcium, phosphate and chloride in the context of laboratory reference ranges and the clinical condition of the patient. Unexpected results may need to be repeated, particularly where laboratory or sampling error is possible. For example, an unexpectedly high potassium value should be assessed for pseudohyperkalemia before starting unnecessary treatment.

The assessment is based on a comprehensive medication history. Take into account all prescription drugs, recent discontinued drugs, over-the-counter products, supplements, intravenous medications and fluids. Special attention should be paid to new medications initiated, recent dose escalations, and combinations of drugs known to affect the same electrolyte. The temporal association of exposure to the drug and the development of the abnormality may increase the suspicion of a drug-related etiology.

We also need to check renal function because the kidneys are responsible for the excretion of many electrolytes. Serum creatinine and estimated glomerular filtration rate may help to assess if reduced elimination is contributing to the abnormality. Depending on the electrolyte under investigation, further tests may include glucose, acid–base parameters, serum or urine osmolality, urinary electrolyte concentrations, albumin, vitamin D, parathyroid hormone and other relevant laboratory tests.

Clinical assessment must include the presence of symptoms and complications. Electrocardiography is particularly useful when a significant potassium, calcium or magnesium abnormality is suspected, as these disturbances may have an effect on cardiac conduction.

The ultimate goal is not only to classify an abnormality as "drug induced", but to estimate the relative contribution of the drug in the context of all possible causes." In many hospitalized patients, it is more appropriate to describe an abnormality as possibly medication related until other contributing factors have been evaluated[3–6,8].

9. Strategies for Electrolyte Monitoring in Hospitalized Patients

Efficient monitoring requires more than simply duplicating laboratory orders for electrolytes. Monitoring should be individualized according to the drug being administered, the electrolyte most likely to be affected, the baseline risk of the patient, renal function, severity of illness and changes in clinical status.

Baseline Evaluation: Whenever clinically appropriate, before starting any medications known to have a major effect on electrolyte homeostasis, electrolyte concentrations and renal function should be assessed. Baseline values are used to determine if an abnormality existed before treatment and as a reference for subsequent changes.

Baseline potassium and renal function are especially important when initiating or switching therapies that can increase potassium including renin-angiotensin-aldosterone system inhibitors and potassium-sparing agents. Similarly, magnesium assessment may be appropriate in patients at increased risk who are requiring prolonged therapy with medications known to be associated with magnesium depletion[3,7,9].

10. Treatment Monitoring

After starting a medication that alters electrolytes, laboratory monitoring should be guided by expected pharmacologic effects and the patient's specific risk. Fewer risk factors and stable renal function might imply less frequent monitoring than in older, critically ill or renally impaired patients receiving multiple interacting medications.

The frequency of monitoring should be increased following major clinical changes such as acute kidney injury, large gastrointestinal losses, large changes in fluid balance, initiation or discontinuation of interacting medications, or major dose adjustments.

It is important that monitoring is not focused on a single electrolyte. The electrolytes are physiologically related. For example, hypomagnesemia may be present with and contribute to hypokalemia and hypocalcemia. Thus, the presence of one abnormality should raise the possibility of associated electrolyte disturbances when clinically indicated.

Follow Up on an Abnormal Result: An abnormal value should not be the end of the monitoring process but a stimulus for re-evaluation. Clinicians should review the medication regimen, determine whether the suspected medication is still needed, identify other causes, take appropriate corrective measures and repeat laboratory testing as dictated by the severity and clinical situation.Therefore, a risk based approach would be favored to a single monitoring schedule for each patient.

Prevention and Management Strategies : Many medication-related electrolyte disturbances are potentially preventable or minimized by early recognition of patients at high risk, appropriate drug selection and dosing, and timely laboratory monitoring.

Medication review and reduction of risk: Prevention starts with knowing which medications can alter the electrolyte status. Before starting therapy, clinicians should assess renal function, baseline electrolytes, comorbidities, fluid status, nutritional status and concomitant medications.Potentially harmful combinations should be identified. For example, the concurrent use of multiple potassium-raising drugs may increase the risk of hyperkalemia several-fold, especially in patients with impaired renal function .

Corrective Actions to Address Contributing Factors: If an abnormality develops, reversible contributing factors should be addressed. These include vomiting, diarrhea, dehydration, inadequate intake, inappropriate supplementation, renal dysfunction, or inappropriate intravenous fluid administration.

Possible Medicine Change: Management of a medication with a significant contribution may include dose reduction, temporary withholding, discontinuation, or substitution with an alternative medication. But discontinuation should not be automatic. The benefits of the medication in the clinical setting should be balanced against the severity of the electrolyte disturbance and availability of alternative management strategies .

This is especially true of the renin-angiotensin-aldosterone system inhibitors. For patients who are benefiting from these therapies in terms of cardiovascular or renal benefits, current guidance emphasizes addressing reversible causes and managing hyperkalemia when possible rather than unnecessarily stopping beneficial therapy.

Electrolyte Loss or Replacement: Electrolyte deficiencies can be replaced orally or intravenously, depending on severity of deficiency, symptoms, gastrointestinal function and urgency of correction. Methods to counteract high concentrations of an electrolyte may include those that reduce intake, increase excretion, cause redistribution of the electrolyte, or antagonize its immediate physiological effects.

Correction should be carefully controlled, as too rapid correction of certain abnormalities may be harmful. Management therefore has to be individualized depending on the electrolyte involved, severity, duration, symptoms and underlying aetiology.

Next steps: After treatment, electrolyte concentrations should be rechecked to ensure that the intervention has been successful. If abnormalities remain, the original diagnosis, continued exposure to drugs, renal function and associated electrolyte abnormalities should be reassessed [3,5,7,9].

11. Clinical Pharmacist Role

As medication assessment is a vital element of the clinical pharmacist's role, they are well positioned to support the prevention, recognition and management of medication related electrolyte abnormalities.One key responsibility is medication reconciliation and review.

Pharmacists can recognize drugs known to affect sodium, potassium, magnesium, calcium, phosphate, or other electrolytes and can determine if multiple drugs with similar effects are being given concurrently.

Pharmacists can also help to identify patients at risk. Patients on polypharmacy, patients with renal impairment, patients with multiple comorbidities and older adults may require closer laboratory surveillance when administered electrolyte-altering medications.

Another important contribution is the assessment of drug-laboratory relationships. In cases of electrolyte derangement, the pharmacist can evaluate the dates of initiation or adjustment of medications, identify possible pharmacological associations, consider other causes, and communicate suspected medication-related problems to the health care team.

Where appropriate, clinical pharmacists can recommend appropriate interventions such as laboratory monitoring, dose adjustment, electrolyte replacement, reconsideration of interacting medications or alternative therapies. Pharmacists can also provide guidance on appropriate intravenous fluid and electrolyte replacement strategies and surveillance for complications of treatment

In a multicenter observational study on drug-related electrolyte disorders in intensive care units, the assessment of drugs and the involvement of clinical pharmacists in identifying drug-related electrolyte problems were important. This supports the integration of medication-focused evaluation into the multidisciplinary management of electrolyte abnormalities.

The pharmacist's role can therefore be summarized as a continuous process of risk identification,

medication review, laboratory monitoring, intervention and follow-up with the aim to improve medication safety [1].

12. Challenges and gaps in current monitoring practice

Electrolyte abnormalities are clinically important, but there are challenges in detecting and monitoring them.The absence of a global monitoring strategy is a major challenge. Monitoring guidelines vary widely depending on the drug, underlying disease, patient characteristics, and the guideline being followed. Therefore, determining the ideal frequency of electrolyte testing for individual hospitalized patients can be challenging.

Another problem is polypharmacy. A patient may be on multiple drugs that increase or decrease the same electrolyte at the same time. Thus, the risk of a full course of medications may be underestimated when each medication is evaluated separately.

The fact that electrolyte abnormalities have multiple causes adds another diagnostic problem. At the same time, renal disease, acute illness, gastrointestinal losses, fluid administration, nutritional deficiencies and medications may all be present. Thus, definitive medication causality is difficult to establish, especially in critically ill patients.

Some electrolytes are also monitored more frequently and routinely than others. Laboratory panels often ordered include sodium and potassium but magnesium and phosphate may require individual testing. Thus, clinically relevant abnormalities of these electrolytes may be missed if testing is not specifically considered.

The second important issue is the time lag between detecting an abnormality and acting on it. Lab results do not make patients safer by themselves. Identify the abnormality, evaluate its possible causes, take appropriate action and do follow-up testing. A study of hospitalized patients with potassium abnormalities showed that a significant proportion had dyskalemia on discharge, suggesting that recognition and full correction are not always concordant

Current evidence also generally focuses on individual electrolytes or specific classes of medications. More research assessing the combined effects of polypharmacy and multiple simultaneous electrolyte abnormalities would be more representative of real-world hospitalized populations.

13. Future Perspectives

Medication-related electrolyte abnormalities: future directions. 1. Avoid the "one size fits all" approach to laboratory testing intervals, which are currently applied to all patients. 2. Move towards risk-based laboratory testing.

Incorporation of information on medication, laboratory findings, renal function, comorbidities and other risk factors in electronic health records could facilitate automatic detection of patients at increased risk. Clinical decision-support systems may be able to notify clinicians of the initiation of a high-risk medication in a patient with pre-existing electrolyte abnormalities or of the administration of potentially dangerous drug combinations.

In time, predictive models may help identify patients who require more intensive monitoring. These models may include age, renal function, previous electrolyte values, comorbidities, number of drugs, specific combinations of drugs and change in clinical condition.

Other electrolytes, which are not routinely monitored, e.g. magnesium and phosphate, should also be given more consideration in suitable high risk populations. Future studies should evaluate whether targeted monitoring of these electrolytes improves clinically meaningful outcomes.

Collaboratively developed standardized hospital protocols among physicians, pharmacists, nurses, and laboratory professionals may improve consistency in monitoring and management. Further prospective studies are needed to determine optimal monitoring intervals for specific medications and patient populations and whether pharmacist-led or electronic monitoring interventions reduce serious electrolyte-related complications[1,7,9].

14. Conclusion

Medication-related electrolyte abnormalities are an important medication safety concern in the hospitalized patient. Drugs commonly used may disturb electrolyte homeostasis by renal, gastrointestinal, hormonal and intracellular mechanisms. These include diuretics, renin–angiotensin–aldosterone system inhibitors, proton pump inhibitors, psychotropic drugs, corticosteroids, antimicrobial agents and antineoplastic therapies.

An electrolyte disturbance rarely develops solely on the basis of medication exposure. Advanced age, reduced kidney function, acute illness, gastrointestinal losses, other diseases, polypharmacy and concurrent use of several electrolyte-altering drugs can significantly change the individual risk.

Effective management therefore requires a systematic approach including baseline risk assessment, recognition of potentially responsible medications, appropriate laboratory monitoring, evaluation of alternative causes, correction of abnormalities and follow-up. Monitoring strategies should be tailored to the medication, electrolyte, renal function, clinical condition, and overall risk profile.

Clinical pharmacists can play an important role in medication review, identifying high risk combinations, interpreting medication–electrolyte relationships, making monitoring recommendations and working with the multidisciplinary healthcare team. Standardized monitoring protocols and electronic decision-support systems, developed in the future, may further improve early detection and prevention.

Ultimately, medication-related electrolyte abnormalities should not be considered in isolation as laboratory abnormalities, but rather as potentially preventable medication-related problems. Increased awareness, individualised monitoring and timely multidisciplinary intervention can all help to make pharmacotherapy safer and more effective for inpatients.

References

1. Ayhan YE, İlerler EE, Sosyal D, Bektay MY, Karakurt S, Daşkaya H, et al. Assessment of drug-induced electrolyte disorders in intensive care units: a multicenter observational study. Front Med (Lausanne). 2024;11:1343483. doi:10.3389/fmed.2024.1343483.

2. Liamis G, Milionis HJ, Elisaf M. A review of drug-induced hyponatremia. Am J Kidney Dis. 2008;52(1):144-153. doi:10.1053/j.ajkd.2008.03.004.

3. Capinha M, Lavrador M, Liberato J, Pinheiro A, Aveiro A, Figueiredo IV, et al. Drug-induced hyponatremia: insights into pharmacological mechanisms and clinical practice management. J Clin Med. 2025;14(18):6584. doi:10.3390/jcm14186584.

4. Liamis G, Milionis HJ, Elisaf M. A review of drug-induced hypernatraemia. NDT Plus. 2009;2(5):339-346. doi:10.1093/ndtplus/sfp085.

5. Yun G, Baek SH, Kim S. Evaluation and management of hypernatremia in adults: clinical perspectives. Korean J Intern Med. 2023;38(3):290-302. doi:10.3904/kjim.2022.346.

6. Liamis G, Hoorn EJ, Florentin M, Milionis H. An overview of diagnosis and management of drug-induced hypomagnesemia. Pharmacol Res Perspect. 2021;9(4):e00829. doi:10.1002/prp2.829.

7. Liamis G, Milionis HJ, Elisaf M. Medication-induced hypophosphatemia: a review. QJM. 2010;103(7):449-459. doi:10.1093/qjmed/hcq039.

8. De Nicola L, Ferraro PM, Montagnani A, Pontremoli R, Dentali F, Sesti G. Recommendations for the management of hyperkalemia in patients receiving renin-angiotensin-aldosterone system inhibitors. Intern Emerg Med. 2024;19(2):295-306. doi:10.1007/s11739-023-03427-0.

9. Weinstein J, Girard LP, Lepage S, McKelvie RS, Tennankore K. Prevention and management of hyperkalemia in patients treated with renin-angiotensin-aldosterone system inhibitors. CMAJ. 2021;193(48):E1836-E1841. doi:10.1503/cmaj.210831.