# A Review: Diuretics Mechanism, Clinical Application, Side Effects, Monitoring and Management of Diuretics

Souraj N. Deshmukh <sup>\*</sup>, Sanjay K. Bais Fabtech College of Pharmacy, Sangola, Solapur, Maharashtra, India <sup>\*</sup>Corresponding Author: sourajdeshmukh10@gmail.com

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## Abstract

Diuretics are a class of drugs that encourage the body to excrete more water and electrolytes by increasing the production of urine. They are frequently used to treat ailments like oedema, heart failure, hypertension, and several kidney problems.

Diuretics function by concentrating on various kidney regions, mainly influencing the reabsorption of sodium, which causes water loss. With different modes of action and therapeutic uses, diuretics come in a variety of forms, such as potassium sparing diuretics, thiazides, and loop diuretics.

Diuretics are beneficial, but they can have negative effects as well, like electrolyte imbalances, dehydration, and kidney failure in certain circumstances. For this reason, careful monitoring is required while taking diuretics. They are essential in the management of cardiovascular and renal diseases because of their function in controlling blood pressure and fluid balance.

Keywords – Diuretics, electrolyte, urine, therapeutic uses, public health.

# INTRODUCTION

Diuretics, also known as "water pills," are a class of drugs that work by encouraging the body to excrete more water and electrolytes especially salt and chloride which in turn increases the output of urine.

These medications are commonly used in the medical industry to treat a wide range of illnesses, mostly those related to fluid retention, like heart failure, chronic renal disease, hypertension, and several liver diseases.

Diuretics can lower blood pressure and lessen the strain on the heart by decreasing the amount of fluid in the blood vessels.

Different diuretics work at different places in the kidneys and have varied effects on fluid clearance and electrolyte balance. The three most popular kinds are potassium-sparing diuretics, thiazide diuretics, and loop diuretics.

Diuretics are essential for treating a wide range of illnesses, but because they can cause dehydration, electrolyte imbalances, and kidney dysfunction, it is important to closely manage their use.

In order to give readers a thorough understanding of the many kinds of diuretics and their roles in contemporary medicine, this article will examine their methods of action, therapeutic applications, and possible adverse effects.<sup>[1]</sup>

# **Medical Uses**

# Hypertension (High Blood Pressure)

Diuretics help lower blood pressure by reducing the volume of fluid in the blood vessels, which decreases the overall pressure on vessel walls.

# **Heart Failure**

In patients with heart failure, diuretics help reduce fluid buildup in the lungs and other parts of the body, easing symptoms like shortness of breath and swelling.

# Edema

Diuretics are used to treat swelling caused by fluid retention in conditions such as liver cirrhosis, kidney disease, and certain types of vascular disorders.

# **Kidney Disorders**

They assist in managing conditions like chronic kidney disease and nephrotic syndrome by helping control fluid balance and reduce swelling.

# Glaucoma

Certain diuretics (e.g., carbonic anhydrase inhibitors) are used to lower the pressure inside the eye, helping treat glaucoma.

# Hypercalcemia

Diuretics, particularly loop diuretics, can help reduce high calcium levels in the blood.

# **Preventing Kidney Stones**

Thiazide diuretics reduce calcium excretion in urine, lowering the risk of forming calcium-based kidney stones.

These uses demonstrate the versatility of diuretics in managing various fluid related health conditions **Types of diuretics** 



# Figure1: Types of Diuretics

There are actually five primary categories of diuretics, each of which targets a different area of the kidney and is prescribed for a distinct set of ailments:

# **Thiazide Diuretics**

# Examples

Indapamide, chlorthalidone, and hydrochlorothiazide (HCTZ).

# Mechanism

They cause an increase in the excretion of water and sodium by blocking the distal convoluted tubule's ability to reabsorb sodium.

# Uses

Frequently used to treat mild episodes of heart failure and excessive blood pressure.

# **Loop Diuretics**

# Examples

Ethacrynic acid, bumetanide, torsemide, and furosemide.

# Mechanism

These cause more significant fluid excretion by blocking the reabsorption of water, salt, and chloride in the loop of Henle.

## Uses

For more severe conditions such as pulmonary oedema, renal or liver disease-related oedema, and heart failure.

## **Diuretics that Spare Potassium**

## Examples

Include triamterene, amiloride, eplerenone, and spironolactone.

## Mechanism

By acting in the distal tubule and collecting duct, these diuretics promote the excretion of sodium and water while preventing potassium loss.

## Uses

For the maintenance of potassium levels and in the treatment of hyperaldosteronism, it is frequently coupled with thiazide or loop diuretics.

## **Inhibitors of Carbonic Anhydrase**

## Example

Methazolamide and acetazolamide.

## Mechanism

They increase the excretion of bicarbonate, salt, and water by inhibiting the proximal tubule's carbonic anhydrase enzyme.

## Uses

Although less common as diuretics, these medications can be beneficial for glaucoma, altitude sickness, and some forms of metabolic alkalosis.

## **Diuretics Osmotic**

## Example

Mannitol

## Mechanism

They cause the kidneys' osmotic pressure to rise, which draws water into the urine and stops the renal tubules from reabsorbing it.

Uses

Usually used to treat acute kidney injury or lower intracranial pressure, which causes brain swelling. The selection of diuretics is contingent upon the patient's state and the intended treatment outcome, with each having a unique mechanism of action.<sup>[2]</sup>

## Mechanism of action

# **Thiazide Diuretics' Mode of Action**

By preventing the kidneys from reabsorbing salt, thiazide diuretics especially affect the distal convoluted tubule (DCT), a portion of the nephron. A thorough description of their mechanism may be found below:

# Distal Convoluted Tubule (DCT) is the site of action

The kidney's functional unit is called the nephron, and it is made up of the glomerulus, proximal tubule, distal convoluted tubule, loop of Henle, and collecting duct.

The distal convoluted tubule's early section is affected by thiazide diuretics.

# Sodium-Chloride Symporter (NCC) Inhibition

In the distal convoluted tubule, thiazides block the sodium-chloride symporter (NCC) on the luminal (apical) membrane of the epithelial cells.

Normally, this symporter helps the circulation to reabsorb sodium (Na+) and chloride (Cl-) ions from urine (or tubular fluid). Thiazide diuretics lessen the reabsorption of sodium and chloride ions by inhibiting this symporter.

# **Elevation of Chloride and Sodium Excretion**

Urine sodium concentration rises as a result of reduced sodium reabsorption, which leaves more sodium in the tubular lumen.

Osmotic balance causes water to follow sodium, which increases the excretion of both water and chloride.

In the end, this mechanism produces more urine, which contributes to the reduction of fluid accumulation in diseases like oedema and hypertension (high blood pressure).

# Impacts on Ions of Hydrogen and Potassium

Potassium (K+) levels may be indirectly impacted by thiazides. The body increases sodium reabsorption in the collecting ducts to make up for sodium reabsorption that is blocked in the DCT. Potassium secretion is substituted for the increased sodium reabsorption in the collecting ducts, increasing potassium output.

Thus, hypokalaemia, or low potassium, is a possible adverse reaction to thiazide diuretics.

Furthermore, greater hydrogen ion secretion may result from increased sodium flow in the collecting ducts, which could cause metabolic alkalosis, a disease in which the blood becomes more alkaline.

## **Prolonged Hypotensive Impact**

Long-term usage of thiazides produces a vasodilatory impact in addition to their diuretic action, which helps to decrease blood pressure.

In spite of their diuretic effects, thiazides are thought to eventually lower peripheral vascular resistance, which lowers blood pressure.

## Effect on the Uptake of Calcium

An additional special effect of thiazide diuretics is that they promote calcium reabsorption in the DCT. Thiazides increase the activity of the sodium-calcium exchanger on the basolateral membrane of DCT cells, which results in more calcium being reabsorbed into the bloodstream by decreasing sodium reabsorption through the sodium-chloride symporter.

Because of this property, thiazides can be used to treat disorders such as hypercalciuria, or elevated calcium levels in the urine, and they can also help prevent some forms of kidney stones from forming.<sup>[3]</sup>

# Loop diuretics ' Mode of Action

Furosemide, bumetanide, and torsemide are examples of loop diuretics that function by blocking the  $Na^+-K^+-2Cl^-$  cotransporter (NKCC2) in the kidneys' thick ascending limb of the loop of Henle. This is a detailed synopsis of their mode of operation:

## Inhibition of Na<sup>+</sup>-K<sup>+</sup>-2Cl<sup>-</sup> Cotransport

Diuretics that block the NKCC2 transporter prevent sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), and chloride (Cl<sup>-</sup>) from being reabsorbed into the renal cells from the tubular lumen.

## **Reduced Sodium Reabsorption**

Loop diuretics raise the amounts of sodium and chloride in the urine by preventing the reabsorption of sodium, chloride, and potassium ions through inhibiting this transporter.

## **Enhanced Water Excretion**

Water reabsorption and sodium reabsorption are related. Osmotic forces cause water to follow sodium into the urine when it is not reabsorbed, increasing the amount of urine produced (diuresis).

# Disruption of Counter current Multiplier System

Water reabsorption from the collecting ducts is reduced as a result of the kidney's inability to establish a concentration gradient in the medulla due to the inhibition of ion reabsorption. This improves water excretion even more.

## **Other Electrolyte Changes**

Because loop diuretics affect ion transport systems, they also increase the excretion of magnesium  $(Mg^{2+})$  and calcium  $(Ca^{2+})$ , in addition to sodium, chloride, and potassium.

# Vasodilation

Although less pronounced than their diuretic activity, loop diuretics can also have vasodilatory effects that lower blood pressure.

To sum up, loop diuretics increase the outflow of water and electrolytes by preventing the reabsorption of sodium, potassium, and chloride in the loop of Henle.<sup>[4]</sup>

## **Potassium-Sparing Diuretic**

Unlike other diuretics like loop and thiazide diuretics, which can result in considerable potassium loss during diuresis, potassium-sparing diuretics assist prevent potassium loss during diuresis. They mainly affect the exchange of sodium and potassium in the kidneys by acting on the distal tubule and collecting duct of the nephron.

## **Potassium-Sparing Diuretic Types**

Based on how they work, potassium-sparing diuretics can be roughly divided into two categories:

## **Aldosterone Antagonists**

Contains eplerenone and spironolactone.

## **Sodium Channel Blockers**

Amiloride, triamterene, and others.

## **Method of Action**

# Eplerenone and spironolactone, which are aldosterone antagonists

**Target Site** 

The collecting duct and distal convoluted tubule's aldosterone-sensitive areas.

## Mechanism

By attaching to mineralocorticoid receptors, these medications inhibit the effects of aldosterone.

## **Aldosterone's Typical Function**

A hormone called aldosterone stimulates the nephron's mineralocorticoid receptors, allowing potassium to be expelled while sodium and water are reabsorbed.

More sodium reabsorption results from an increase in the activity of ENaC (epithelial sodium channels) in the collecting duct.

Potassium channels in the tubular lumen are activated by the negative charge created by sodium reabsorption, which causes potassium to be secreted into the urine.

## Aldosterone Antagonist Effects

Spironolactone and eplerenone inhibit sodium reabsorption through the ENaC channels by blocking aldosterone, which lowers the electrical gradient that promotes potassium release.

As a result, the body excretes less potassium, which aids in potassium conservation.

Due to the increased excretion of sodium, there is also a slight diuretic effect since less sodium is reabsorbed.<sup>[5]</sup>

# Triamterene and amiloride, which block sodium channels

ENaC in the collecting duct and distal convoluted tubule is the target site.

## Mechanism

In the apical membrane of the main cells in the distal nephron, these medications directly block the epithelial sodium channels (ENaC).

## **Common Function of ENaC**

ENaC creates a negative charge in the tubule lumen by facilitating the reabsorption of sodium from the lumen into the cells. Through potassium channels, this negative charge encourages the production of potassium into the urine.

## Sodium channel blockers' effects

These medications lower salt reabsorption and the lumen's negative potential by blocking ENaC. Consequently, the motivation for potassium release into the urine is diminished.

As a result, the body excretes sodium while retaining potassium.

Increased water excretion as a result of ENaC suppression has a modest diuretic impact. Synopsis of Activities

Potassium-sparing diuretics provide an effective means of preventing hypokalaemia while generating mild diuresis by inhibiting potassium release and preventing sodium reabsorption. They are frequently employed as supplemental treatment in ailments were keeping potassium levels stable is essential.

# Carbonic anhydrase inhibitors

A class of diuretics known as carbonic anhydrase inhibitors (CAIs) inhibits the carbonic anhydrase enzyme, mainly in the kidney's proximal tubule. The reabsorption of bicarbonate, salt, and water depends on this enzyme. CAIs cause diuresis (increased urine output) by blocking this enzyme.

## Action Mechanism

## **Carbonic Anhydrase Inhibition**

The process of turning carbon dioxide (CO<sub>2</sub>) and water (H<sub>2</sub>O) into carbonic acid (H<sub>2</sub>CO<sub>3</sub>), which then splits into bicarbonate (HCO<sub>3</sub><sup>-</sup>) and hydrogen ions (H<sup>+</sup>), is catalysed by carbonic anhydrase.

Carbonic anhydrase in the kidneys promotes the production of carbonic acid and its subsequent breakdown into water and carbon dioxide, which diffuse back into the cell, facilitating the reabsorption of bicarbonate.

## **Elevated Excretion of Bicarbonate**

In the proximal tubule, less bicarbonate is reabsorbed when carbonic anhydrase is blocked. This causes the urine's outflow of bicarbonate to rise, making the urine more alkaline.

## **Excretion of Water and Sodium**

Since sodium and bicarbonate are often reabsorbed together, sodium reabsorption is decreased when bicarbonate reabsorption is inhibited. This causes water and sodium to be excreted in the urine, which has a mild diuretic effect.

## **Equilibrium Acid-Base**

Reduced serum bicarbonate levels as a result of increased bicarbonate excretion can result in a metabolic acidosis, or a drop in blood ph.

## **Impact on Additional Tissues**

## Eyes

CAIs are used to treat glaucoma by lowering intraocular pressure because they inhibit carbonic anhydrase in the ciliary body, which reduces the generation of aqueous humour.

## Brain

Inhibiting carbonic anhydrase decreases the production of cerebrospinal fluid in the central nervous system, and CAIs such as acetazolamide are occasionally used to treat disorders such as acute mountain sickness and pseudotumor cerebri.

## **Typical Inhibitors of Carbonic Anhydrase**

Acetazolamide

Dorzolamide

Brinzolamide

In conclusion, bicarbonate reabsorption in the kidneys is decreased by carbonic anhydrase inhibitors, which increases salt and bicarbonate excretion in the urine and has a mild diuretic effect. They are also helpful in the treatment of mountain sickness and glaucoma.<sup>[6]</sup>

## **Osmotic diuretics**

Which include mannitol and urea, are a type of diuretics that promote water excretion by generating an osmotic gradient in the renal tubules. They mostly affect the descending limb of the loop of Henle and the proximal convoluted tubule (PCT), which are the areas of the nephron that are most permeable to water. This is a thorough description of how they work:

## The Nephron's Osmotic Mechanism

When given into the bloodstream, osmotic diuretics are tiny, non-absorbable molecules that raise the osmolality of plasma.

These materials are not reabsorbed by the nephron; thus, they stay in the tubular lumen after being filtered by the glomerulus and into the renal tubules. As a result, the tubular fluid's osmotic pressure rises, which prevents water from being passively reabsorption in the proximal tubule and the loop of Henle's descending limb.<sup>[7]</sup>

## Water Reabsorption Inhibition

Water cannot be reabsorbed into the peritubular capillaries due to the elevated osmotic pressure inside the tubular lumen.

Diuresis, or an increase in urine volume, is the result of water remaining in the lumen.

The concentration of electrolytes (such as sodium, potassium, and chloride) in the tubular fluid rises as a result of the decreased water reabsorption.

## **Electrolyte Impact**

Solvent drag is the term for the phenomenon where electrolytes such as sodium, potassium, and chloride are pulled along by a large amount of water in the tubular lumen.

Osmotic diuretics are not primarily employed to change electrolyte levels, but as a result, there is a slight increase in the excretion of these electrolytes.

## **Nephron Action Sites**

Proximal Convoluted Tubule (PCT): Osmotic diuretics significantly affect this area by preventing water reabsorption, as this is where most of it takes place.

Descending Limb of the Loop of Henle: Because of its high-water permeability, the descending limb is another important location where osmotic diuretics work to stop the absorption of water.

## Impact on the Distal Nephron and Collecting Duct

Osmotic diuretics have less of an impact in the distal nephron and collecting ducts because hormones such antidiuretic hormone (ADH) more closely control water reabsorption in these areas.

The distal nephron's activity can be modestly changed by the increased flow of sodium and water in the early segments, though, as this lowers the concentration gradient needed for water reabsorption.

## **Excretion in pharmacokinetics**

Since osmotic diuretics, such as mannitol, are poorly absorbed from the gastrointestinal tract, they are usually given intravenously.

They stay in the renal tubules after passing through the glomerulus and are eliminated in the urine without being broken down.

## **Clinical uses**

Diuretics are drugs that cause the body to excrete more water and electrolytes (mostly sodium) in the urine, which lowers the body's fluid content. They are extensively employed in clinical practice to treat a wide range of illnesses, especially those related to cardiovascular problems or fluid retention. An extensive summary of diuretics' medical applications is provided below:<sup>[9]</sup>

## Elevated blood pressure, or hypertension

## Mechanism

By excreting water and sodium from the blood, diuretics help reduce blood pressure by decreasing blood volume. As a result, blood vessel walls are under less pressure, which lowers blood pressure.

### **Diuretics Used Types**

For mild to severe hypertension, thiazide diuretics (such as hydrochlorothiazide and chlorthalidone) are frequently the first line of treatment. They are employed at the kidney's distal convoluted tubule. When a more forceful diuresis is required, such as in individuals with severe hypertension or kidney disease, loop diuretics (such as furosemide and bumetanide) are used.

## Justification

Reducing blood pressure lowers the chance of cardiovascular events such as renal damage, heart attacks, and strokes.

# **Heart Illness**

# Mechanism

The inability of the heart to pump blood effectively results in oedema, or fluid accumulation in the tissues, and pulmonary oedema, or accumulation of fluid in the lungs. Diuretics lessen this fluid overload, reducing swelling and breathlessness among other effects.

## **Diuretics Used Types**

Due to their potent diuretic action, loop diuretics (such as furosemide and torsemide) are recommended for the treatment of acute heart failure or severe instances.

Thiazide Diuretics: For long-term care to preserve fluid balance, thiazide diuretics are occasionally used with loop diuretics. Potassium-Sparing Diuretics (e.g., spironolactone, eplerenone): These diuretics have the extra benefit of preventing hypokalaemia, or low potassium levels, which is caused by other diuretics. They also prevent aldosterone, a hormone that exacerbates heart failure.

Justification: Lowering fluid overload contributes to symptom relief, increased exercise tolerance, and a decrease in heart failure-related hospital admissions.<sup>[10]</sup>

# **Oedema Linked to Hepatic Cirrhosis**

## Mechanism

Because liver cirrhosis reduces albumin production, it can cause fluid retention that can result in ascites, or an accumulation of fluid in the belly, and peripheral oedema. Diuretics assist in controlling this fluid retention.

## **Diuretics Used Types**

Since spironolactone can inhibit aldosterone, which is frequently elevated in cirrhosis, it is the primary option.

In cases where spironolactone is not enough to control the fluid overload, loop diuretics are given. Justification: Diuretics help patients live better lives by minimizing oedema and reducing abdominal distension and discomfort brought on by ascites.

## **Diabetic Syndrome**

# Mechanism

The kidney disease known as nephrotic syndrome causes a large loss of protein in the urine, which exacerbates oedema. Diuretics aid in controlling the fluid overload brought on by this illness.

## **Diuretics Used Types**

Because of the severity of the oedema, loop diuretics are the most effective in this situation. Thiazide Diuretics: For a synergistic effect, thiazide diuretics can be administered with loop diuretics.

Justification: Reducing fluid excess in nephrotic syndrome helps to avoid problems such as pleural effusions, which are accumulations of fluid in the lungs, by reducing swelling.<sup>[7]</sup>

## <sup>I</sup>llness of the kidneys (CKD)

## Mechanism

Due to compromised kidney function, patients with chronic kidney disease (CKD) frequently have fluid retention and hypertension. Diuretics aid in the treatment of these signs.

## **Diuretics Used Types**

Due to its potency and efficiency even in cases of impaired kidney function, loop diuretics are frequently necessary. When renal function is still largely intact in the early stages of CKD, thiazide diuretics may be administered.

Justification: Diuretics lower cardiovascular risks and assist delay the course of kidney damage in patients with chronic kidney disease (CKD) by controlling fluid retention and hypertension.<sup>[11]</sup>

# Severe Bronchial Oedema

# Mechanism

The accumulation of fluid in the lungs due to acute pulmonary oedema, which is frequently brought on by left-sided heart failure, causes significant respiratory distress. Diuretics aid to increase oxygenation by quickly lowering the fluid load.

# **Diuretics Used Types**

The cornerstone of treatment, loop diuretics (such as intravenous furosemide) are known for their quick onset of effect.

Justification: Quickly clearing the patient's lungs of fluid is essential for maintaining breathing, preventing respiratory failure, and stabilizing the patient.<sup>[12]</sup>

# High blood calcium levels, or hypercalcemia

# Mechanism

Certain malignancies and hyperparathyroidism are two disorders that can cause hypercalcemia. In order to reduce blood calcium levels, loop diuretics promote the excretion of calcium in the urine.

# **Diuretics Used Types**

In order to increase calcium excretion, loop diuretics, such as furosemide, are administered in combination with intravenous saline.

Justification: Controlling hypercalcemia helps avoid problems like cardiac arrhythmias, kidney stones, and bone discomfort.

# **Increased Intraocular Pressure and Glaucoma**

## Mechanism

By decreasing the amount of aqueous humour produced in the eye, diuretics—more especially, carbonic anhydrase inhibitors—lower intraocular pressure.

# **Diuretics Used Types**

Carbonic anhydrase inhibitors: These include acetazolamide, and they are used to treat acute altitude sickness as well as disorders like glaucoma.

Justification: In glaucoma patients, lowering intraocular pressure helps avoid optic nerve damage and visual loss.<sup>[13]</sup>

## Severe Altitude Illness

# Mechanism

Rapid ascent at high altitudes can cause acute mountain sickness (AMS), which can result in fluid retention and brain oedema. Carbonic anhydrase inhibitors change the acid-base balance and encourage diuresis, which helps minimize fluid accumulation.

# **Diuretics Used Types**

# Acetazolamide

It promotes breathing and reduces fluid retention to aid in the body's adaptation to high altitudes.

Justification: Climbers who manage their AMS symptoms, such as headache and fluid retention, are better able to acclimatize to high elevations and are at lower risk of serious problems including highaltitude pulmonary oedema (HAPE).

# Nephrogenic and Central Diabetes Insipidus

## Mechanism

Patients with diabetes insipidus, a disorder marked by increased thirst and urination as a result of abnormalities with antidiuretic hormone (ADH) function, may paradoxically produce less pee when using thiazide diuretics.<sup>[14</sup>

# **Diuretics Used Types**

Thiazide diuretics: They lessen the amount of urine produced by lowering the glomerular filtration rate (GFR) in the distal tubule by the reduction of sodium reabsorption.

# Justification

For individuals with diabetes insipidus, this use helps lessen the burden of frequent urination and dehydration.

# Synopsis of Diuretic Types and Typical Applications

Thiazide diuretics: Mostly used as adjuncts in heart failure and for hypertension.

Loop diuretics: Good in treating severe fluid retention in pulmonary oedema, congestive heart failure, and chronic kidney disease.

Potassium-Sparing Diuretics: Included in the treatment of liver cirrhosis and heart failure, as well as used to prevent hypokalaemia.

Inhibitors of carbonic anhydrase: Beneficial for glaucoma, AMS, and several metabolic conditions. Diuretics are essential in treating these illnesses, but their use needs to be closely watched to prevent

negative effects such electrolyte imbalances, dehydration, and kidney failure.

# Side effects

Diuretics, sometimes referred to as "water pills," are drugs that aid the body in getting rid of extra salt and water. They are frequently used to treat illnesses like high blood pressure, heart failure, and some renal problems. Diuretics have several adverse effects even though they can be quite beneficial. Depending on the kind of diuretic (such as thiazide, loop, or potassium-sparing diuretics) being used, these adverse effects can differ. The following are a few typical possible adverse effects:<sup>[15]</sup>



Figure 2: Side Effects of Diuretics

# **Typical Adverse Reactions**

# Imbalance of Electrolytes:

Particularly with thiazide and loop diuretics, low potassium levels (hypokalaemia) or low salt levels (hyponatremia) are prevalent.

Hyperkalaemia is a condition caused by potassium-sparing diuretics (high potassium levels).

# Lack of fluids

Dehydration, which results in symptoms including dry mouth, thirst, and decreased urine production, can be brought on by excessive water loss.

# Light-headedness or dizziness

Dizziness or fainting can be brought on by a drop in blood pressure, particularly when standing up fast (orthostatic hypotension).

# **Higher Urine Output**

Especially during the first few days of treatment, diuretics increase urine production, which may result in more frequent trips to the loo.

## Spasms in the muscles

Electrolyte abnormalities, especially low potassium, can cause weakness or cramping in the muscles. Less Frequent Adverse Effects

## **Elevated Blood Sugar**

People with diabetes may need to be concerned about certain diuretics since they can raise blood sugar levels, especially thiazide diuretics.

## **Increased Triglycerides and Cholesterol**

Particularly thiazide diuretics occasionally cause an increase in triglyceride and cholesterol levels. **Gout** 

Certain diuretics raise uric acid levels, which may lead to the painful condition known as gout, which is characterized by inflammation of the joints.

## **Dysfunctional Kidney**

Due to alterations in fluid and electrolyte balance, diuretics can occasionally lower kidney function, particularly if they are not well managed.

## **Allergic Reactions**

Sulfonamide-derived diuretics may cause allergic reactions in certain individuals, such as rashes or more serious allergy symptoms.

## Handling Adverse Effects

#### Frequent blood tests

Keeping an eye on kidney function and electrolyte levels can help identify abnormalities early.

Dietary Adjustments: For people using non-potassium-sparing diuretics, eating foods high in potassium, such as oranges or bananas, may be advised.

#### Fluid Intake

It may be crucial to modify fluid intake while managing the condition in order to prevent dehydration. If you encounter any of these adverse effects or have questions about diuretics, it's advisable to speak with a healthcare professional for advice specific to your circumstances.<sup>[16]</sup>

## Contraindications

Diuretics assist the body get rid of extra fluid, which is why they are frequently used to treat illnesses like heart failure, hypertension, and oedema. However, depending on the kind of diuretic, there are a number of contraindications related to their use:

#### **Thiazide Diuretics**

## Example

Hydrochlorothiazide

## Severe renal impairment

Patients with severe renal insufficiency may not benefit from thiazides.

Hypokalaemia

These medications may make the low potassium levels worse.

Thiazides may make hyponatremia low sodium even worse.

Hypercalcemia

Thiazides exacerbate diseases with elevated calcium levels by increasing the reabsorption of calcium. **Gout** 

Thiazides can exacerbate gout by raising uric acid levels.

## Sulpha allergy

Patients who have sulpha allergies should use thiazides with caution as some of them contain sulpha.

# **Loop Diuretics**

# Examples

Bumetanide and Furosemide

Severe electrolyte abnormalities: Loop diuretics can exacerbate hypokalaemia, hyponatremia, and other imbalances.

Dehydration

Excessive fluid loss and dehydration may result with certain medications.

# Kidney failure

Loop diuretics could exacerbate recent kidney damage.

# **Risk of ototoxicity**

Excessive dosages may harm hearing, especially when taken with other ototoxic medications.

# Sulpha allergy

As with thiazides, persons with sulpha allergies should use cautiously.

# Diuretics that spare potassium

# Examples

Amiloride, Spironolactone

Hyperkalaemia

In individuals who are already at risk of excessive potassium levels, these diuretics exacerbate potassium retention and pose a concern.

# **Renal dysfunction**

Hyperkalaemia and other adverse consequences may become more severe due to impaired renal function.

Low levels of aldosterone are already present in Addison's disease; potassium-sparing diuretics may exacerbate the imbalance.

Concurrent use of supplements or other potassium-sparing medications raises the possibility of hyperkalaemia.<sup>[17]</sup>

# Inhibitors of Carbonic Anhydrase

# Example

Acetazolamide

# Severe liver disease

By lowering ammonia clearance, it can exacerbate hepatic encephalopathy.

Acidosis, hypokalaemia, and other imbalances can result from electrolyte abnormalities.

Electrolyte imbalances may become worse due to adrenal insufficiency.

# Sulpha allergy

Because these medications also include sulpha, people who are allergic to sulpha should use them with caution.

# **General Warnings Against All Diuretics**

Low amounts of potassium, sodium, calcium, or magnesium indicate severe electrolyte imbalances.

# **Pregnancy and nursing**

The foetus or newborn may be at risk from some diuretics.

# Severe dehydration

Diuretics may make the loss of fluid worse.

# **Reactions allergic**

Proven hypersensitivity to any of the diuretic's ingredients.

In order to ascertain whether diuretics are safe for their particular situation, patients should always speak with their healthcare professional.

## Monitoring and management



Figure 3: Monitoring and Management

In order to ensure the safe and efficient use of diuretics while minimizing potential side effects, monitoring and management are crucial. Depending on the type of diuretic, underlying medical issues, and intended course of therapy, different restrictions may app<sup>[18]</sup>

# Keeping an eye on parameters

Important variables to keep an eye on in people using diuretics are

#### Electrolytes

# Potassium (K<sup>+</sup>)

Potassium-sparing diuretics can result in hyperkalemia, whereas thiazide and loop diuretics can produce hypokalaemia. It's crucial to regularly test for potassium.

## Sodium (Na<sup>+</sup>)

Diuretics, particularly thiazides, can result in hyponatremia. Check salt levels on a regular basis. Magnesium  $(Mg^{2+})$ 

It's important to evaluate magnesium levels because loop diuretics might cause hypomagnesaemia.

## Calcium (Ca2+)

Loop diuretics lower calcium levels, while thiazide diuretics raise them.

## The Function of the Renal

# Blood urea nitrogen (BUN) and serum creatinine

Diuretics can have an impact on kidney function, especially in individuals who already have renal impairment. In order to stop renal insufficiency from getting worse, kidney function must be closely monitored.

## **Glomerular filtration rate (GFR)**

To identify any deterioration in renal function, routine GFR evaluations are advised.<sup>[19]</sup>

## The level of blood pressure

Since diuretics are frequently used to treat hypertension, blood pressure should be checked frequently to confirm that the medication is working as intended and to prevent hypotension.

## Static Equilibrium

## **Everyday weight**

Tracking weight fluctuations aids in determining fluid balance and early detection of dehydration or excessive fluid retention.

## Urine output

To guarantee proper diuresis and prevent fluid excess or depletion, monitoring urine output is essential for hospitalized patients or those using high-dose diuretics.

# Levels of Uric Acid

Uric acid levels should be checked, especially in patients with a history of gout, as thiazides can raise uric acid levels and raise the risk of gout.

# **Blood Sugar Amounts**

It is crucial to monitor blood glucose levels, especially in diabetic patients, as diuretics, especially thiazides, might reduce glucose tolerance.

# Auditory Function (In Case of Loop Diuretics)

Due to the potential for ototoxicity from high dosages of loop diuretics (such as furosemide), hearing evaluations may be necessary for high-risk patients or those on high-dose therapy.

# **Techniques for Management**

# **Dose Modification**

# Titration

To reduce adverse effects, start with a low dose and raise it gradually, especially in elderly patients or those with renal impairment.

Reducing the frequency of administration after diuresis is achieved is a possible strategy, particularly in cases of chronic diseases such as heart failure or hypertension.<sup>[20]</sup>

# **Control of Potassium**

# Potassium supplementation

To avoid hypokalaemia, patients on thiazides or loop diuretics may need to consume potassium-rich foods, such as bananas and oranges, or take potassium supplements.

## **Potassium-sparing combos**

To control potassium levels, potassium-sparing diuretics (such spironolactone) can be taken with thiazides or loop diuretics.

Avoiding too much potassium

In order to prevent hyperkalaemia in patients on potassium-sparing diuretics, it's critical to stay away from potassium supplements and meals high in potassium.

# **Managing Hydration**

Fluid restriction: In order to prevent worsening fluid overload, individuals with heart failure or certain kidney illnesses may need to limit their consumption of fluids.

# Sufficient hydration

To prevent negative outcomes like hypotension and renal damage, individuals who are susceptible to dehydration or excessive fluid loss (such as the elderly, in hot weather) should maintain their current level of hydration.

# Watching for Adverse Reactions

Dizziness, low blood pressure, decreased urine production, dry mucous membranes, and increased thirst are some of the symptoms of dehydration.

# **Ototoxicity (in relation to loop diuretics)**

Individuals taking large dosages should be closely watched for any tinnitus, hearing loss, or imbalance issues.

## **Guarding Against Gout Attacks**

Patients with gout may be administered febuxostat or allopurinol to avoid attacks since thiazide diuretics have the tendency to raise uric acid levels.

## **Instruction for Patients**

## **Dietary advice**

Patients on potassium-losing diuretics should be encouraged to avoid foods high in potassium, while those on potassium-sparing diuretics should be told about meals rich in potassium.

# **Self-monitoring**

Patients can be trained to keep an eve on their daily weight and blood pressure levels, as these measurements can provide early warning signs of fluid imbalance or blood pressure fluctuations.

Patients should be informed about typical adverse effects, such as cramping in the muscles, lightheadedness, and increased thirst, and should be counselled when to seek medical assistance. Confirmation

Frequency of routine blood tests varies based on the diuretic type and patient's condition. For instance, individuals with renal problems or those using potassium-sparing diuretics might need more regular monitoring. Routine clinical evaluation: Follow-up appointments are necessary on a regular basis to evaluate blood pressure, kidney function, and fluid balance, particularly in high-risk groups such as the elderly and heart failure patients.

Diuretics must be properly managed with both routine monitoring and individual changes based on the patient's condition and therapeutic response.

## **Efficacy and outcomes**

A class of drugs known as diuretics aids the body in excreting extra water and salt (sodium) through the urine. They are frequently used to treat illnesses such renal problems, oedema (swelling), heart failure, and hypertension (high blood pressure). This is a synopsis of their effectiveness and results:<sup>[21]</sup>

## **Diuretic Types**

## **Diuretics thiazide**

Examples include chlorthalidone and hydrochlorothiazide.

## Uses

Mostly for the treatment of hypertension.

## Efficacy

By lowering blood volume and the heart's workload, it is effective in lowering blood pressure. Results

When used for the treatment of hypertension, they have been demonstrated to lower the risk of cardiovascular events (such as stroke and heart attack).

## **Diuretics Loop**

Examples are bumetanide, torsemide, and furosemide.

Uses

Frequently administered to patients with severe fluid overload and cardiac failure.

## Effectiveness

By affecting the kidney's Henle loop and causing a large fluid leak, this medication is quite successful in treating fluid retention, or oedema.

## **Results**

Patients' quality of life is improved by reducing heart failure symptoms including oedema and dyspnoea. To avoid electrolyte abnormalities and dehydration, they might need to be closely watched.<sup>[22]</sup>

## **Diuretics that Spare Potassium**

Examples include amiloride, eplerenone, and spironolactone.

Uses

To stop potassium loss, it is frequently taken in conjunction with other diuretics.

## Efficacy

Beneficial in hyperaldosteronism and heart failure (especially in more severe situations).

## **Results**

It has been demonstrated that spironolactone increases the survival rate of individuals with severe heart failure. By keeping potassium levels stable, it lowers the chance of arrhythmias.

# **Diuretics Osmotic**

Mannitol is one example.

# Uses

Mostly in emergency situations, such as treating acute renal injury or lowering intracranial pressure. Effective in lowering intracranial or intraocular pressure quickly.

# Results

Although its usage is restricted to particular clinical conditions, it has the potential to save lives in emergency situations.

# **Overall Results**

Blood Pressure Control: The first line of treatment for hypertension is usually diuretics, particularly thiazides. Because of their capacity to lower peripheral resistance and blood volume, they are useful in lowering both the diastolic and systolic blood pressure, which lowers the risk of cardiovascular events.

Heart Failure Management: In order to lessen the symptoms of heart failure, potassium-sparing diuretics and loop diuretics are essential. They lessen the accumulation of fluid in the lungs and other tissues, which can enhance general function and exercise tolerance.

Electrolyte Balance: Although diuretics are useful, they can lead to electrolyte imbalances such as low sodium or potassium), which need to be watched. Options that spare potassium can lessen the chance of hypokalaemia, or low potassium.

Kidney Protection: Diuretics should be used carefully to control oedema in circumstances such as chronic kidney disease. However, significant fluid loss from misuse or overuse might worsen renal impairment.<sup>[23]</sup>

# **Important Things to Think About**

Adverse effects: Dehydration, orthostatic hypotension, and electrolyte imbalances (hypokalaemia or hyperkalaemia) are common adverse effects. To reduce these hazards, dosage adjustments and monitoring are essential.

# **Combination Therapy**

To improve blood pressure control, diuretics are frequently used in conjunction with other antihypertensive medications such as beta-blockers or ACE inhibitors.

# **Long-term Results**

When taken properly, diuretics can lower mortality and enhance quality of life for people with chronic diseases such as heart failure and hypertension.

When taken as directed, diuretics have been shown to help reduce symptoms and improve long-term outcomes in the treatment of cardiovascular and renal diseases.

# **Combination therapy**

Diuretic-based combination therapy is a popular treatment strategy for diseases like hypertension, heart failure, and several renal illnesses. Diuretics lessen fluid retention and blood pressure by assisting the body in getting rid of extra salt and water. They can provide complimentary modes of action and be more effective when taken in combination with other medications than when taken alone. These are a few typical diuretic combinations:<sup>[24]</sup>

# **ARBs/ACE Inhibitors and Diuretics**

Example: Hydrochlorothiazide combined

# **Beta-Blockers and Diuretics**

Metoprolol with hydrochlorothiazide, for instance.

Use

Frequently administered for chronic heart failure and hypertension.

# Mechanism

Beta-blockers and diuretics both lower heart rate and contraction force, which can aid in the management of blood pressure and cardiac disorders. Diuretics also reduce blood volume.

## Calcium channel blockers (CCBs) with diuretics

Amlodipine with hydrochlorothiazide, for instance.

Use

Excellent for controlling hypertension, particularly in older persons and other specific populations.

#### Mechanism

CCBs relax blood arteries while diuretics reduce fluid retention, giving blood pressure a two-pronged reduction with either Losartan (ARB) or Lisinopril (ACE inhibitor).

#### Use

Often used to treat heart failure and hypertension.

#### Mechanism

While ACE inhibitors or ARBs block the renin-angiotensin-aldosterone pathway, further lowering blood pressure and lessening the workload on the heart, diuretics aid in reducing fluid content.

## **Mixing Diuretics from Various Classes**

Example

Combining thiazide diuretics (such as hydrochlorothiazide) with loop diuretics (such as furosemide). Use

Beneficial in cases of heart failure, resistant hypertension, and severe oedema.

Mechanism

Thiazide diuretics can have a longer-lasting effect than loop diuretics, which are far more effective in removing fluid. When using a single diuretic, compensatory salt reabsorption may occur. This combination can avoid this.

#### Aldosterone antagonists combined with diuretics

Example

Using a thiazide diuretic together with spironolactone.

Use

Beneficial in resistant hypertension, heart failure, and disorders such as hyperaldosteronism.

#### Mechanism

While other diuretics aid in the evacuation of fluid, aldosterone antagonists such as spironolactone prevent salt and water retention brought on by high levels of aldosterone.

## Advantages of Diuretic Combination Therapy

#### **Enhanced Effectiveness**

When diuretics are used in conjunction with other antihypertensives, blood pressure is frequently lowered more significantly and fluid excess is avoided more than when diuretics are taken alone.

#### **Decreased negative Effects**

As opposed to using large dosages of a single prescription, using smaller amounts of each treatment helps reduce negative effects.

#### Managing Drug Resistance

It may be more efficient to employ several modes of action when treating patients with resistant oedema or hypertension.

Dangers and Things to Think About:<sup>[25]</sup>

Electrolyte Imbalances: Depending on the medications taken, combination therapy may raise the risk of problems such as low potassium (hypokalemia) or high potassium (hyperkalemia).

# **Renal Function**

It's critical to carefully check kidney function, particularly when utilizing combinations that may affect the flow of blood to the kidneys.

# Hypotension

When taking medications with potent antihypertensive effects together, there is a chance that blood pressure will fall too low. The patient's unique situation, underlying medical conditions, and reaction to first therapies all play a role in selecting the best combination.

# **Patient Education**

For patients taking diuretics, patient education is essential since it minimises risks, guarantees the medication's safe and effective usage, and aids in the patient's achievement of the intended health outcomes. Here's why it's essential:

## **Recognizing Appropriate Use**

Diuretics may result in frequent urination, particularly at first. It is important for patients to know when and how to take them, which is usually in the morning, to prevent problems with their sleep and everyday activities.

For a medication to be effective, the schedule and dosage must be followed exactly, and patient education helps to guarantee that these guidelines are followed.

# Avoiding Electrolyte Imbalance and Dehydration

Diuretics may result in electrolyte imbalances, including potassium, sodium, and magnesium, or dehydration. Symptoms like weakness, dizziness, cramping in the muscles, or even more serious diseases like irregular heartbeats can be brought on by these imbalances. By educating patients, you may possibly avoid major issues by helping them spot early indicators of dehydration or imbalances and seek medical assistance when needed.<sup>[26]</sup>

# **Encouraging Treatment Plan Adherence**

Patients are more likely to follow their treatment plan if they comprehend the purpose of the diuretic and how it helps manage their illness (e.g., decreasing blood pressure, minimizing oedema in heart failure).<sup>[26]</sup>

For the long-term management of chronic illnesses such as heart failure and hypertension, adherence is essential because skipping doses might result in uncontrollable symptoms or complications.

# Modifications to Diet and Lifestyle

Depending on the type of diuretic, dietary changes may be necessary, such as ingesting foods high in potassium or reducing salt intake. Patients can make decisions that will promote the efficacy of their medication if they are informed about these adjustments.

# Handling Interactions and Side Effects

Diabetics may cause adverse effects, which patients should be aware of and learn how to treat. For instance, they ought to know that while increased urination is common, they ought to get medical attention if they suffer from severe vertigo or fainting.

Since diuretics may interfere with other medications a patient is taking, education also aids in preventing drug interactions. By being aware of possible interactions, negative consequences might be avoided.

# **Giving Patients Power**

Patients feel more equipped to take control of their health and make wise decisions when they are informed about the medications they are taking. Better self-care and self-assurance in managing any problems that may come up throughout therapy result from this. Better health outcomes and more individualized care can result from educated patients' increased ability to communicate with their healthcare professionals.

# **Enhancing General Health Results**

In the end, patients with greater knowledge who know how to take diuretics effectively and safely will probably be able to better manage their condition whether it be oedema, heart failure, or high blood pressure.

As a result, there are fewer issues, fewer hospital stays, and an overall higher standard of living.

# Cost and availability

Diuretics, sometimes referred to as "water pills," are generally readily available and reasonably priced in the US. They are available in several forms, such as potassium-sparing diuretics, loop diuretics, thiazide diuretics, and carbonic anhydrase inhibitors. An outline of their price and accessibility is provided below:<sup>[27]</sup>

## Price

Diuretics like spironolactone, furosemide (Lasix), and hydrochlorothiazide (HCTZ) have generic equivalents that are reasonably priced. Without insurance, monthly costs can range from \$10 to \$50, depending on the medication and dosage.Versions with brand names may cost up to \$100 or more a month. On the other hand, using generic substitutes can drastically save expenses.Prescription savings plans such as Mira or Single Care can reduce these costs by as much as 80%.

## Accessibility

Most pharmacies, including small drugstores and big pharmacies like CVS and Walgreens, carry insurance and diuretics. Most private plans Medicare typically cover them. Generic versions are available even without insurance, and many pharmacies provide savings plans or lowered prices to patients who pay cash.Since diuretics are frequently used to treat ailments like oedema, heart failure, and hypertension, they are typically accessible and reasonably priced for the majority of people. To get the greatest deals, it's wise to check costs across pharmacies and look into any relevant discount schemes.<sup>[28]</sup>

## CONCLUSION

Diuretics are vital drugs that aid in the treatment of illnesses including high blood pressure, heart failure, and some kidney problems that are caused by excessive fluid retention. They aid in lowering blood pressure, decreasing blood volume, and reducing swelling (oedema) by encouraging the excretion of water and salt through urine. Depending on the individual patient's demands and the particular medical condition, different types of diuretics, such as thiazide loop, and potassium-sparing, are utilized.Diuretics are useful for regulating fluid balance and alleviating symptoms, but because they can cause electrolyte imbalances and dehydration, they should be used with caution. To guarantee its safe usage, appropriate dosage changes and routine monitoring are essential. In the end, diuretics are still a useful tool for treating a variety of cardiovascular and renal diseases, providing notable advantages when used appropriately.

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