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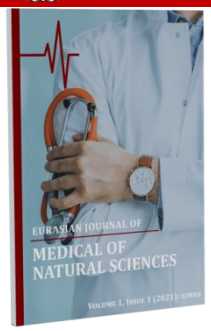

ANALYSIS OF THE SPECTRUM OF DIURETIC USE, GENERAL AND PRIVATE PHARMACOLOGY

Sokhib Rashidov Zamon o'g'li
Khilola Musaeva Usmonqul qizi
Madina Shakhmurova Aladdin qizi
Avazbek Abdurazzoqov Abduvakhob o'g'li
Shakhnoza Shodmonova Feruz qizi
Department of pharmacology, Tashkent medical academy
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ABSTRACT

Drugs called diuretics are used to treat and control edematous and non-edematous medical disorders. One class of medications is diuretics. This exercise examines the uses, side effects, and indications of diuretics as a useful treatment for heart failure, hypertension, ascites, and other conditions as appropriate. In order to help members of the interprofessional team treat patients with heart failure and related conditions, this activity will highlight the mechanism of action, adverse event profile, and other important factors (such as off-label uses, dosing, pharmacodynamics, pharmacokinetics, monitoring, and pertinent interactions). Since diuretics are among the most widely given medications and, despite their effectiveness, are frequently used to treat patients who are at a significant risk of problems, it is crucial to comprehend and value their pharmacokinetics and pharmacodynamics (see Keller and Hann's recent review). Despite the unique pharmacokinetic and pharmacodynamic characteristics of the available diuretic medications that influence response and the possibility of side effects, many clinicians use them in a stereotypical way, which decreases effectiveness and may increase side effects (a list of common diuretic side effects is provided). Although there are many applications for diuretics, this review will concentrate on their usage to treat edema and extracellular fluid (ECF) volume expansion; readers interested in learning more about how diuretics are used to treat kidney stones, hypertension, and other disorders are directed elsewhere.

Introduction. Water makes up to 60% of the normal adult's body weight and is essential to numerous bodily physiological functions. Thus, as demonstrated by the potentially disastrous effects of fluid imbalance, fluid and electrolyte homeostasis is essential for human survival. Through a variety of physiological mechanisms, including hormonal regulation (vasopressin and natriuretic peptides), skin management, hemodynamic changes, renal control of salt and water excretion, and neural regulation of thirst, the balance of total body fluid is a highly regulated process that guarantees the maintenance of a balance between

fluid gain and loss. Specifically, renal excretion of urine guarantees the removal of excess electrolytes and products of metabolic activity in addition to water, preserving fluid balance [1-7]. Electrolyte balance and fluid balance are so closely related in both the extracellular (rich in Na+ & Cl- ions) and intracellular (rich in K+ ions) compartments that it should come as no surprise that the main tactic of renal fluid management is electrolyte trading. When it comes to fluid control and, consequently, water homeostasis, medications that impact renal regulation of electrolyte excretion have the biggest impact. Diuretics are medications that pharmacologically shift the control of renal fluids in favor of water and electrolyte excretion. Therefore, diuretics are drugs that raise urine production and volume [8,9,10]. The main way that this family of medications accomplishes this goal is by inhibiting receptors that let the renal tubules reabsorb Na+, the most prevalent extracellular cation. This raises the osmolality of the renal tubules, which in turn inhibits water reabsorption. While aquaretics function directly by just altering the excretion of water, osmotic diuretics directly enhance luminal hyperosmolarity in the renal tubules without influencing electrolyte balance. This thorough analysis covers every pertinent facet of diuretic therapy, with a focus on understanding the fundamental pharmacophysiological mechanisms of medication action and adverse effects, as well as more practical issues of dosage [11,12,13]. Depending on their mode of action and location throughout the nephron, diuretics can be divided into a number of groups and subcategories. All of the available individual medications in all of the various classes are listed, together with information about their chemical makeup, unique properties, primary site of action along the nephron, diuretic target molecule, and the percentage of inhibited Na+ reabsorption. Additionally, also gives information (to put things in a broader perspective) about miscellaneous agents that do not have a conspicuous diuretic action and are not used for diuresis, but they do have some diuretic effect which is noticeable which must be taken into account during therapy with these agents [14,15,16,17].

The main purpose of the presented analytical manuscript is to provide a brief overview of scientific research devoted to the analysis of the spectrum of application, general and private pharmacology of drugs with diuretic activity.

Classification and Action Mechanisms. Usually, the mechanism by which diuretic medications block transport is categorized second, followed by the primary site of action along the nephron. The Na-K-2Cl cotransporter (NKCC2, encoded by SLC12A1) along the thick ascending limb and macula densa is inhibited by the loop diuretics furosemide, bumetanide, and torsemide acting from the lumen. As organic anions, they interact with the chloride-binding site (2) to bind within the translocation pocket on the transport protein (see below for clinical implications). They inhibit the transporter because they are too big to pass through the pocket like chloride does [1-4]. Thiazides and thiazide-like medications, commonly known as distal convoluted tubule diuretics, are organic anions that function similarly but attach to the thiazide-sensitive NaCl cotransporter (NCC, which is encoded by SLC12A3) along the distal convoluted tubule. Both loop and distal convoluted tubule diuretics work from the luminal side of the tubule, and this mechanism of action explains a significant part of their actions [3,7,8] (Tab 1.).

Table 1. Classification and Action Mechanisms of diuretics.

№	Types of diuretics	Agents of diuretics	Common side effects of diuretics
1.	**Loop diuretics**	**Furosemide, bumetanide, torsemide**	Hypersensitivity reactions Extracellular fluid volume depletion Hypokalemic alkalosis Hypomagnesemia Ototoxicity
2.	**Distal convoluted tubule diuretics**	**Hydrochlorothiazide, Chlorthalidone**	Hypersensitivity reactions Hyponatremia Hypokalemic alkalosis hyperglycemia/diabetes Hyperuricemia/gout Hypomagnesemia Hypokalemia and prerenal azotemia, when combined with loop diuretics
3.	**Potassium-sparing diuretics**	**Amiloride and triamterene**	Hypersensitivity Hyperkalemia Metabolic acidosis Azotemia Gynecomastia, vaginal bleeding (spironolactone)

Effective Treatment of ECF Volume Expansion with Diuretics. Verifying that the dosage produces a tubule concentration over the threshold is crucial when starting diuretics to treat edema in patients with normal or aberrant kidney function. Moss ambulatory individuals should observe an increase in urine volume within 2–4 hours of an oral dose, indicating that this threshold has been achieved. Outpatients who experience a discrepancy between diuresis and weight loss may be experiencing limited effectiveness due to excessive sodium chloride consumption. In this situation, measuring 24-hour urine sodium excretion and using creatinine to verify collection adequacy may confirm excessive sodium chloride intake, though single urine [Na+] collections may not provide completely accurate results [11-15]. Urine volume should rise in the six hours after a dosage for hospitalized patients if the dose reaches the threshold. Diuresis should happen more quickly following an intravenous dose, according to the connection between plasma diuretic concentration and time displayed in Figure 2B. If furosemide is selected as the diuretic, this difference can be particularly noticeable. Based on the dose-response curve, it is common practice to double the dosage if no impact is seen during this time, for instance, from 20 to 40 mg of furosemide or from 80 to 160 mg of furosemide. As explained below, the dosage is then increased to the highest safe amount [7-11].

Diuretic Dosage Based on Evidence for ECF Volume Expansion. While pharmacological characteristics have historically been used to guide loop diuretic dosage recommendations, more recent research on acute decompensated heart failure has placed an emphasis on patient-centered outcomes. The higher dose (2.5 times the usual daily dose) of loop diuretics is well tolerated and effective for treating acute decompensated heart failure,

according to the Diuretic Strategies in Patients with Acute Decompensated Heart Failure trial, which compared high and low doses of the medication [3-8]. Worsening renal function, which was employed as a hazard signal in this investigation, is one issue with intensive diuretic therapies in this case. However, a higher creatinine level in this research, which indicates poor renal function, is actually linked to a better prognosis rather than a worse one. A tiered care approach has been suggested in cases where appropriate diuresis is not achieved. This methodology was effectively applied in randomized trials and shown at least as much efficacy as invasive methods like ultrafiltration, despite not being directly compared with other ways [9-14].

For AKI, diuretics. There have been many different recommendations for and against the use of diuretics in AKI. Extremely high dosages of diuretics, which can turn oliguric AKI into nonoliguric AKI, were frequently used at the end of the 20th century. However, controlled trials showed no change in mortality and were linked to deafness. According to a subsequent retrospective trial, "the widespread use of diuretics in critically ill patients with acute renal failure should be discouraged" because it is linked to an increased risk of death in patients with AKI. However, the inherent limitations of such retrospective investigations cannot be resolved by statistical methods [14-20]. Patients with adult respiratory distress syndrome were randomly assigned to either a liberal or restrictive fluid policy in this trial; diuretics were used extensively for those assigned to the restricted fluid policy. According to the trial's findings, individuals with AKI who were randomly assigned to a diuretic-administration technique had a decreased adjusted odds ratio for mortality. This trial indicated that previous reported unfavorable outcomes from diuretic therapy in AKI probably did represent confounding by indication, even though it is not conclusive. In order to maintain euvolemia in AKI, it now seems reasonable to employ diuretics as an adjuvant. However, it's usually preferable to stay away from really high dosages and to avoid taking diuretics to postpone more permanent treatments like dialysis [5-11].

Discussion. A class of drugs called diuretics is used to treat and control edematous and non-edematous diseases. Drugs in the diuretic class. In this exercise, the benefits, side effects, and contraindications of diuretics as a treatment for heart failure, hypertension, ascites, and other conditions are reviewed (and other disorders when relevant). The mechanism of action, adverse event profile, and other important elements (such as off-label uses, dosage, pharmacodynamics, pharmacokinetics, monitoring, and pertinent interactions) that are relevant for members of the interprofessional team in the treatment of patients with heart failure and related conditions will be highlighted in this activity [1, 3, 4, 7,8]. Diuretic medications, which target the transport of solutes via the nephron, are frequently prescribed to people with normal or diminished kidney function. Although every diuretic medication has a distinct pharmacokinetic profile, these variations might not be given enough thought when the medications are being utilized therapeutically. The use of diuretics to treat heart failure is now supported by recent large-scale clinical trials. However, even in the presence of such data, a thorough comprehension of the pharmacokinetics and pharmacodynamics of diuretics improves the clinical management of diuresis. Since the medications can significantly reduce dyspnea and edema, they should be used as efficiently as possible to enhance patient-centered clinical results. Since ECF volume abnormalities exist into the twenty-first century, the

creation of diuretic medications—one of scientific medicine's greatest achievements—will likely remain essential to medical practice for some time to come [3-11]. As the patient's primary caregiver, nurses should be aware of the negative effects of diuretics and be able to notify the treating physician if a patient's health deteriorates. This is especially true for hospitalized patients in intensive care units, where patient safety is guaranteed by regular arterial blood gas analysis, daily body weight checks, and updated urine output records. In an outpatient scenario, pharmacists are crucial, and they should be on the lookout for any drug interactions or prescriptions with inappropriate dosages. Diuretics are prescription-only medications, and any requests for them made over-the-counter should be denied and, if necessary, reported to prevent potential health harm from suspected diuretic abusers [12-20]. The interprofessional team consists of a number of medical professionals, including specialists and physicians such as cardiologists and otorhinolaryngologists, as well as clinical pharmacists, nurses, and other healthcare workers, who work together to prevent any negative effects from diuretic medication [5-11].

Conclusions. People with normal or diminished kidney function frequently use diuretic medications, which are substances that target solute transport throughout the nephron. Every diuretic medication has a distinct pharmacokinetic profile, but when the medications are administered therapeutically, these variations might not be given enough thought.

There is now evidence to support the use of diuretics to treat heart failure according to recent large-scale clinical trials. However, a thorough grasp of diuretic pharmacokinetics and pharmacodynamics improves the clinical approach to diuresis even in the presence of such data. Since the medications can significantly reduce dyspnea and edema, maximizing their use should enhance patient-centered clinical results.

One of the biggest achievements of scientific medicine has been the creation of diuretic medications, which will remain essential to medical practice for the foreseeable future due to the prevalence of ECF volume problems into the twenty-first century.

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