CE 1.5 Pharmacology and 1.5 ANCC Contact Hours

Looking "Fit and Thin" to Win

Diuretic Drug Abuse In and Outside the Arena

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I am a clinical nurse specialist in a large city with multiple universities. Twice this past quarter, we have observed students admitted to the emergency department for complaints of weakness, arrhythmias, and life-threatening hypokalemia. One student nearly died. Assessment of 1 student revealed chronic lasix use to control weight for gymnastic competitions. Another student obtained hydrochlorothiazide online to reduce weight before a wrestling tournament. Are these cases rare events, or do they represent a larger problem? Are there any resources available regarding diuretic abuse?

Diuretics increase the rate of urine flow and sodium excretion, which modifies the volume as well as composition of body fluids. Although life-saving in the treatment of hypertension, as well as liver, kidney, and heart failure, diuretics are also used to rapidly lose weight or mask drug use. Diuretics mask drug use by decreasing drug concentration or metabolites available for testing through increasing urine volume or by modulating urinary pH to inhibit passive excretion of the drug in urine.[1]

Diuretic abuse is more common than you might think. Despite being banned in and out of competition in 1988, abuse continues, requiring further expansion and development of drug testing methods to capture diuretic abuse as well as the drugs the user is trying to hide, such as anabolic androgenic steroids, hormones, stimulants, narcotics, cannabinoids, $\beta 2$ agonists, and β-blockers to name a few.[1,2] All classes of diuretics have taken their place on the prohibited list of the International Olympic Committee and World Anti-doping Agency (WADA), which is updated yearly.[2,3]

As a class of drugs, diuretics differ significantly in structure, renal activity, chemical identity, and behavior and can be classified by mechanism of action. The Table provides a summary of sample of diuretics available in and outside the United States. Apart from obtaining a therapeutic use exemption, diuretic use is prohibited in sports.[1,3]

THE TEMPTATION OF DIURETICS

Diuretics provide rapid weight loss, which can confer an advantage in wrestling, boxing, gymnastics, and dance. Abuse can range from a single dose before a competition to chronic use. Diuretics with a short half-life such as furosemide and hydrochlorothiazide are preferred and the most commonly abused.[1,3] Besides the risks associated with electrolyte and fluid imbalances, alteration of the thermoregulatory system remains a silent and major risk. Skeletal muscle temperature can exceed core temperature quickly with sport activities. Add concomitant dehydration and the road to victory may end in exhaustion, muscle cramps, impaired vasodilation for cooling, gout, arrhythmias, myocardial infarction, and even death.[1,3] Diuretics used with androgenic-anabolic steroids enhance muscle definition and tone for body builders. Models, flight attendants, and flight crews have also succumbed to the rapid weight loss option with diuretics.[3]

ASSESSMENT OF DIURETIC ABUSE

Diagnosis of diuretic abuse is a challenge related to patient denial and pharmacokinetic properties of diuretics. Most abused diuretics have a short half-life and after 12 to 24 hours are essentially undetectable. Furthermore, with sustained exercise, decreases in renal and hepatic blood flow further mask drug expression in urine.[3]

The lack of provider education in diuretic abuse, coupled with a clinical presentation of hypokalemic metabolic

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Table. Diuretics by Class Summary Table[1,3]

Class	Actions	Agent Examples	Uses	Adverse Effects	Risk for Abuse
Carbonic anhydrase (CA) inhibitors	Inhibit CA (carbonate dehydratase, carbonate hydrolase) in the proximal tubule cells of the nephron Reduces the ability to exchange Na^+ with H^+; weak diuretic activity Generally prescribed for nondiuretic indications; decrease rate of aqueous humour formation, production of metabolic acidosis	Dorzolamide (Trusopt)—a sulfonamide and topical CA inhibitor for ocular hypertension or open angle glaucoma Brinzolamide (Azopt)—for ocular hypertension or open angle glaucoma Acetazolamide (Diamox)—increases bicarbonate excretion in urine making blood more acidic to increase ventilation and helps individuals acclimatize to high altitude	Open angle glaucoma High-altitude motion sickness Premenstrual fluid retention Epilepsy Gout	Metabolic acidosis Kidney stones	Low
Loop diuretics	Short-acting diuretic class that blocks $Na^+/K^+/Cl^-$ symporter in the ascending loop of Henle Significantly reduces the ability of the kidney to concentrate urine with significant excretion of Na^+ and Cl^-, Ca^{2+}, Mg^{2+}, and K^+ After rapid absorption from the GI tract, all but a small percentage of the drugs bind with plasma proteins Short life averaging 1 to 3.5 h Increases venous capacity and decreases left ventricular filling pressure	Furosemide (Lasix) Bumetanide (Bumex, Burinex) Ethacrynic acid (Edecrin) Torsemide (Demadex)	Pulmonary edema and heart failure Hypertension Ascites associated with cirrhosis Hyponatremia May lead to activation of the rennin-angiotensin-aldosterone and secondary hyperaldosteronism, resulting in hypokalemia and metabolic alkalosis	Fluid imbalance Electrolyte imbalance Hypotension Hypokalemia Arrhythmias Ototoxicity ↑LDL/triglycerides ↓ HDL Gout Significant potential for drug-drug interactions particularly with Aminoglycoside anticoagulants Digitalis Lithium Propranolol Probenecide	High, particularly for furosemide

(continues)

Table. Diuretics by Class Summary Table[1,3], Continued

Class	Actions	Agent Examples	Uses	Adverse Effects	Risk for Abuse
Thiazide and thiazide-like diuretics	Inhibit Na^+/Cl^- symporter Diuretic action in the early distal convoluted tubule with a lesser effect in the proximal tubule Reduce Na^+ reabsorbtion in the distal renal tubule	Chlorothiazide (Diuril) Hydrochlorothiazide (Esidrix, Microzide) Metolazone (Zaroxolyn)	Most widely used particularly for treatment of hypertension Low cost Good tolerance Good compliance	Similar to loop diuretics Hyperlipidemia ↑ incidence erectile dysfunction Drug-drug interactions: ↓ effectiveness of anticoagulants, uricosuric drugs, insulin, and sulfonylureas	Very high, particularly for hydrochlorothiazide
Osmotic diuretics	Low-molecular- compounds Acts in the proximal tubule and loop of Henle Enhances the osmolality of the plasma and urine with reduction of water reabsorbtion in the distal nephron With expansion of the extracellular fluid volume, blood viscosity decreased and rennin release inhibited All electrolytes are excreted	Glycerin (Glycerol) Isosorbide (Imdur, Ismo, Monoket) Mannitol (Osmitrol)	Specific uses Reduction of cerebral edema Acute tubular necrosis Acute glaucoma Ocular surgery	Hypernatremia Dehydration	Low
Mineralocorticoid receptor antagonists	Competitive inhibitors of aldosterone Potassium sparing Drug efficacy a function of endogenous levels of aldosterone; the higher the level, the greater the drug effect For treatment of edema or HTN, often combined with thiazide or loop diuretics or other K^+-sparing agents	Spironolactone (Aldactone) Eplerenone (Inspra) Amiloride (Midamor) Triamterene (Dyrenium)	An alternative to potassium replacement therapy Often coprescribed with thiazide or loop diuretics	Spironolactone has affinity for progesterone and androgen receptors; may result in Gynecomastia Impotence Menstrual irregularity May foster development of malignant tumors	Low

Abbreviations: GI, gastrointestinal; HDL, high-density lipoprotein; HTN, hypertension; LDL, low-density lipoprotein

alkalosis, makes diagnosis of diuretic abuse difficult. Symptoms could be the function of vomiting, diuretic abuse, or Bartter syndrome. Urine chloride concentration can help in diagnosis. Urinary chloride level less than 15 mEq/L is associated with vomiting. Urinary chloride between 20 and 70 mEq/L suggests use of loop diuretics.[3]

Diuretic abuse outside the sports arena can present as severe hypokalemia in an underweight person. In 1 case study, a 22-year-old woman with a body mass index of 18 kg/m^2 presented with a potassium level of 1.1 mmol/L. The patient revealed that she took 250 mg of furosemide a day to improve the "shape of her muscles."[4] Diuretic abuse in persons with bulimia nervosa can also result in pseudo-Bartter syndrome. Symptoms may include hypokalemia, hypochloremia, alkalosis, hyperaldosteronism without kidney pathology, and a normal urinary chloride level. Symptoms resolve as soon as the diuretic use and/or purging behavior ceases.[5,6]

Anecdotal evidence suggests suspect diuretic abuse in young women with suspected eating disorder and hypokalemia without hypertension and to obtain urine sample for chloride concentrations. Again, if chloride levels are high, more than likely, the urine assay will test positive for thiazides or furosemide.[7]

THE FUTURE

A new tool is under development for antidoping. The athlete biological passport has recently been implemented, which provides individual within-subject longitudinal monitoring of blood and urine markers. Rather than comparisons of results between individuals, intraindividual comparisons are used, which may be more accurate and more resilient in the face of increasing legal challenges. With the steroid module completed, other modules are planned for the future to detect misuse of hormones or modulators taken to enhance performance.[8]

RESOURCES

A prohibited drug list in print and PDF format, as well as iPhone and iPad applications, is provided by WADA (wada-ama.org). The WADA site is very helpful for athlete and student education. For young women, the Web site "Weighing the Facts—Eating Disorders: Information, Resources and Recovery" (http:www.weighingthefacts.blogspot.com) has exceptional information presented in a caring and hopeful way. Using nonmedical and understandable language, life-saving information is presented in a visually appealing way with dedicated pages exploring risks of diuretic abuse. This site would be appropriate to use in the education of young women and even teenagers in situations that the clinical nurse specialist is concerned about diuretic abuse and/or eating disorders. In addition, the Web site offers multiple language translations as well as links to other important resources for persons with image problems and eating disorders.

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