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Review Article

Nephrotoxicity and alterations of laboratory tests by drugs: literature review

Nefrotoxicidade e alterações de exames laboratoriais por fármacos: revisão da literatura

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ABSTRACT: Use of nephrotoxic substances, arterial hypertension, diabetes mellitus, among others, may lead to renal injury and compromise their functioning. The presence of kidney damage and kidney function can be assessed by several biochemical markers, such as serum creatinine, serum urea, serum cystatin C, proteinuria, glomerular filtration rate and electrolytes. Several drugs can alter the results of laboratory tests to evaluate the kidney by in vivo or in vitro mechanisms, and it is important to know which drugs cause this type of interference. This review of the literature aimed to present the main drugs that can generate such interferences in the kidney assessment tests and the main mechanisms. Several nephrotoxic drugs can promote increased serum creatinine and urea levels, decreased glomerular filtration rate or proteinuria, and it is important to monitor the renal function of patients who use them. In addition, patients who have chronic kidney disease should avoid the use of some of these drugs or an appropriate dose adjustment should be made if the use of these drugs is essential. Some drugs can inhibit the renal secretion of creatinine, increasing its serum levels, in the absence of changes in renal function. Others may alter the serum electrolyte levels or urinary density, or interfere with the dosage of markers for assessment of renal tubule function. Knowledge of drugs that interfere with the kidney assessment tests by health professionals is essential so that they can correctly interpret laboratory tests, resulting in adequate diagnosis and therapy.

Keywords: Creatinine; Drug-related side effects and adverse reactions; Glomerular filtration rate; Kidney function tests; Proteinuria.

RESUMO: O uso de substâncias nefrotóxicas, hipertensão arterial, diabetes mellitus, dentre outros, podem lesionar os rins e comprometer o seu funcionamento. A presença de lesão nos rins e a função renal podem ser avaliadas por meio de diversos marcadores bioquímicos, tais como creatinina sérica, ureia sérica, cistatina C sérica, proteinúria, taxa de filtração glomerular e eletrólitos. Diversos fármacos podem alterar os resultados dos exames laboratoriais de avaliação dos rins por mecanismos *in vivo* ou *in vitro*, sendo importante o conhecimento de quais medicamentos causam este tipo de interferência. Esta revisão da literatura teve como objetivo apresentar os principais fármacos que podem gerar tais interferências nos exames de avaliação dos rins e seus principais mecanismos. Vários fármacos considerados nefrotóxicos podem promover aumento dos níveis séricos de creatinina e ureia, diminuição da taxa de filtração glomerular ou proteinúria, sendo importante o monitoramento da função renal dos pacientes que os utilizam. Além disso, o uso de alguns destes fármacos deve ser evitado por pacientes que possuem doença renal crônica ou deve ser feito o ajuste adequado da dose caso o seu uso seja imprescindível. Alguns fármacos podem inibir a secreção renal da creatinina, aumentando seus níveis séricos, na ausência de alteração da função renal. Outros podem alterar os níveis séricos de eletrólitos ou a densidade urinária, ou ainda interferir na dosagem de outros marcadores de avaliação da função dos túbulos renais. É fundamental o conhecimento dos fármacos que interferem nos exames de avaliação dos rins pelos profissionais da área da saúde para que estes possam interpretar corretamente os exames laboratoriais, resultando em diagnóstico e terapia adequada.

Palavras-chaves: Creatinina; Efeitos colaterais e reações adversas relacionadas aos medicamentos; Proteinúria; Taxa de filtração glomerular; Testes de função renal.

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INTRODUCTION

The kidneys maintain body homeostasis, since they excrete metabolism products and preserve substances that are essential for the functioning of the organism (proteins, electrolytes and water)[1]. Renal failure occurs when the basic function of the kidneys is compromised due to arterial hypertension, diabetes mellitus, nephrotoxic substances, among others[2]. Kidney function and the presence of kidney damage can be evaluated by various biochemical markers, such as serum creatinine, serum urea, serum cystatin C, proteinuria, glomerular filtration rate and electrolytes, among others[3].

Some drugs are potentially nephrotoxic, and it is important to monitor the renal function of patients who use them. These drugs can induce acute or chronic kidney injury depending on the degree of interference of the drug in the tissue[4]. The acute injury is characterized by sudden and fast loss of kidney function[5], whereas the chronic one is based on the gradual and irreversible loss of kidney function[6]. Other drugs can alter the results of laboratory tests to evaluate the kidneys in vitro, and it is important to know which drugs cause this type of interference[7].

METHOD

This literature review was carried out by surveying national and international scientific publications on the interference of drugs in biochemical laboratory tests for kidney evaluation in the period from March 2018 to July 2020.

Keywords, such as: drug interference, in vivo interferences, in vitro interferences, interfering renal function, drug-induced nephrotoxicity, among others, were used to search for scientific articles in the Scielo, Pubmed and Google Scholar databases. Updated guidelines and books were also used to search for relevant information.

Drugs that interfere with kidney evaluation tests

Table 1 shows the main nephrotoxic drugs and their respective nephrotoxicity mechanisms. Table 2 shows the main drugs that cause interference in vivo in the kidney assessment biomarkers and the mechanisms responsible for the interference, while Table 3 shows the main drugs that cause interference in vitro in these biomarkers.

Table 1 - Main nephrotoxic drugs and their respective mechanisms of nephrotoxicity

Mechanism of nephrotoxicity	Therapeutic class and drugs
Acute interstitial nephritis	Antihypertensives (hydrochlorothiazide, chlortalidone, indapamide, furosemide, bumetanide, pyretamide)
	Antibacterials (sulfadiazine, sulfamethoxazole, cephalosporins, penicillins, quinolones, rifampicin)
	Antivirals (acyclovir, indinavir)
	Hypouricemiant (allopurinol)
	Non-steroidal anti-inflammatory drugs
	Radiological contrasts
	Drugs that act on the gastrointestinal tract (ranitidine, omeprazole, pantoprazole, lansoprazole)
	Antineoplastic (cisplatin)
Chronic interstitial nephritis	Mood stabilizer (lithium)
	Immunosuppressants (cyclosporine, tacrolimus)
	Antineoplastics (carmustite, semustite)
Glomerulonephritis	Antibacterials (penicillins)
	Mood stabilizer (lithium)
	Non-steroidal anti-inflammatory drugs
	Antineoplastic (interferon alfa)
Renal tubular toxicity	Antibacterials (aminoglycosides, rifampicin)
	Antivirals (cidofovir, tenofovir)
	Antifungal (amphotericin B)
	Radiological contrasts
	Antineoplastics (cyclophosphamide, cisplatin, lenalidomide, methotrexate)
Thrombotic microangiopathy	Immunosuppressants (cyclosporine, tacrolimus)
	Antineoplastics (bortezomib, vincristine)
	Platelet antiaggregants (clopidogrel, ticlopidine)
Alteration of intraglomerular hemodynamics	Non-steroidal anti-inflammatory drugs
	Radiological contrasts
	Immunosuppressants (cyclosporine, tacrolimus)
Nephrolithiasis	Antiepileptics (topiramate, zonisamide)
Unknown mechanism	Antivirals (atazanavir)

Table 2 - Main drugs that cause in vivo interference in the kidney assessment markers and the mechanisms responsible for the interference

Response	Mechanism	Drugs
Increased serum uric acid	Reduction in the volume of extracellular fluid	Diuretics
Increased serum cystatin C	Increased transcription of the Cystatin C gene	Dexamethasone, methylprednisolone
Increased serum creatinine	Reduction of creatinine secretion	Spironolactone, triamterene, amiloride, trimethoprim, fibrates, probenecid, cimetidine
Increased urinary density	Dehydration	Atropine
	Unknown	Cimetidine, ciprofloxacin
Increased urinary pH	Reduction of aldosterone secretion	Lithium
	Reduced bicarbonate reabsorption	Topiramate, zonisamide
	Unknown	Cimetidine
Decreased urinary density	Reduction of aldosterone secretion	Lithium
Decreased urinary pH	Desconhecido Unknown	Ciprofloxacin
Hyperkalaemia	Decreased potassium secretion	Spironolactone, triamterene, amiloride, heparin
	Decreased aldosterone secretion	Captopril, enalapril, losartan
Hypokalemia	Increased potassium secretion	Hydrochlorothiazide, chlortalidone, indapamide, furosemide, bumetanide, pyretamide, prednisolone, prednisone
	Unknown	Salbutamol, itraconazole
Hyponatremia	Potentiates the action of the antidiuretic hormone in the kidneys	Carbamazepine
	Decreased aldosterone secretion	Captopril, enalapril
	Decreased sodium reabsorption	Hydrochlorothiazide, chlortalidone, indapamide, furosemide, bumetanide, pyretamide, oxcarbamazepine
Proteinuria	Increased permeability of kidney tissue	Polymyxins

Table 3 - Main drugs that cause in vitro interference in kidney assessment biomarkers

Response	Drugs
False increase in serum creatinine	Sulfamethoxazole + trimethoprim, cephalosporins, ascorbic acid
False increase in serum uric acid	Paracetamol
False increase in urinary sodium	Lithium
False negative for bilirubin in urine	Ascorbic acid
False negative for glucose in urine	Levodopa
False positive for ketones ia urine	Levodopa, captopril, valproic acid
False positive for glucose in urine	Acetylsalicylic acid, cephalosporins, benzylpenicillin, amoxicillin, nitrofurantoin
False positive for proteinuria	Ranitidine, penicillins

Antihypertensive drugs

The continuous use of diuretics can cause an increase of about 50% in serum uric acid levels, which is the result of a reduction in the volume of extracellular fluid[8]. Thiazide diuretics, such as hydrochlorothiazide, chlortalidone and indapamide, and loop diuretics, such as furosemide, bumetanide and pyretamide, are potentially nephrotoxic and can cause acute interstitial nephritis[4]. In addition, these drugs promote increased renal potassium secretion, resulting in hypokalemia, and may even cause hyponatremia due to decreased sodium reabsorption[8].

On the other hand, potassium-sparing diuretics, such as spironolactone, triamterene and amiloride, can cause hyperkalaemia as an adverse reaction[9]. These drugs also competitively inhibit creatinine secretion due to their cationic nature, leading to an increase in serum creatinine levels in the absence of changes in renal function[10].

Captopril is an antihypertensive that inhibits the angiotensin-converting enzyme (ACE). The decrease in aldosterone due to the use of the drug leads to increased serum potassium levels and reduced serum sodium levels. This medication also reduces the glomerular filtration pressure, resulting in a transient increase in serum urea and creatinine levels[8]. Another effect of the drug is the interference in tests for the detection of ketones in urine through an unknown mechanism, resulting in false positive[11]. Enalapril maleate, another drug of the same therapeutic class, also causes increased serum potassium levels and reduced serum sodium levels[8].

Losartan, in turn, blocks angiotensin II AT1 receptors, which results in increased sérum potassium levels. This hyperkalaemia occurs due to the reduction of aldosterone, a mechanism similar to that of ACE inhibitors. This drug can also cause a transient increase in serum urea and creatinine levels[8].

Antibacterials

The combination of sulfamethoxazole and trimethoprim provides increased levels of serum creatinine due to the interference of drugs in the Jaffé colorimetric reaction[12]. Trimethoprim, because of its cationic nature, competes with creatinine tubular secretion, resulting in increased creatinine serum levels, in the absence of impaired renal function[13,14]. Crystals derived from the metabolism of sulfadiazine, an antimicrobial of the sulfonamide class, as well as sulfamethoxazole, precipitate in the renal tubules resulting in acute interstitial nephritis[15].

Aminoglycosides are a class of antibacterials that cause renal tubular toxicity. They accumulate in the renal tissue due to the presence of specific receptors in the proximal tubule, where occurs the endocytosis of the aminoglycosides mainly in the mesangial cells that are present in the fenestrated capillaries of the glomerulus, impairing the renal filtration mechanism and, consequently, elevating the serum levels of creatinine. In addition, aminoglycosides can cause kidney damage due to inhibition of sodium-dependent glucose transporters. Aminoglycosides gradually accumulate in lysosomes and stimulate morphological changes. In addition to reducing glomerular filtration, they can cause enzymuria, proteinuria, aminoaciduria, glycosuria and various electrolyte changes, such as hypokalemia, hypomagnesemia, which can cause Fanconi syndrome or Bartter-like syndrome[16]. Gentamicin is an aminoglycoside which can disrupt lysosomes in nephrotic cells by releasing acid hydrolases and cytochrome C enzymes to the cytoplasm, thus stimulating the cell apoptosis signaling cascade[17].

Cephalosporins, which belong to beta-lactams group, interfere with the Jaffé method in the determination of serum creatinine, providing falsely increased results[18]. In addition, this class of antimicrobials can interfere with glycosuria tests, inducing false-positive results[19]. Some examples are cephalexin, cefaclor and cefuroxime, which alter reactions with Benedict's reagent and Fehling's solution that detect glucose in the urine, making the result positive. In addition, cephalosporins are potentially nephrotoxic, and can cause acute interstitial nephritis[4].

Penicillins, also from the beta-lactam group, can cause acute interstitial nephritis and glomerulonephritis[4]. In addition, they may interfere with the immersion reagent strip test, resulting in false positive for proteinuria, through an unknown mechanism[21]. Benzylpenicillin also induces false positive for glucose, which occurs in methods based on copper reduction, such as in reactions using Benedict's reagent and Fehling's solution[11]. Kidney excretion of amoxicillin also interferes with tests based on the reduction of copper for the measurement of glucose in the urine, promoting false positive results[11].

Ciprofloxacin, a drug of the quinolone class, leads a decrease in pH, an increase in proteinuria and urinary density[22]. The quinolones still trigger an inflammatory process in the renal tissue that, consequently, can result in acute interstitial nephritis[9].

The use of rifampicin can cause acute tubular necrosis, increased serum levels of creatinine and urea, and the development of acute interstitial nephritis[5,23]. The accumulation of vancomycin in lysosomes in the proximal tubular cells, in turn, results in kidney damage due to inhibition of the sphingomyelinase enzyme causing cell necrosis and acute interstitial nephritis[24].

The administration of polymyxins can result in proteinuria, and the mechanism of the effect is similar to its action on the bacterial membrane, where the drug increases the permeability of renal tissue promoting the flow of ions,

water and molecules[25,26].

The use of nitrofurantoin can interfere in laboratory tests of glucose oxidase and reduction of copper to determine glycosuria, resulting in false positive[27].

Antivirals

Acyclovir, an antiviral inhibitor of viral DNA polymerase, is excreted by kidney in its original form. Thus, there is precipitation of drug crystals in the renal tubules, obstructing them, which can cause acute interstitial nephritis[9,28].

Among the protease inhibitor antivirals, atazanavir has a cumulative nephrotoxic effect by an unknown mechanism[29]. Indinavir, on the other hand, has well-defined nephrotoxicity, with precipitation of indinavir sulphate crystals in the renal tubules and the development of acute interstitial nephritis[28]. Cidofovir, like acyclovir, is excreted by kidney almost entirely in its original form. Its use can result in proximal tubular injury, since the fraction of the drug absorbed by the renal cells is converted into cidofovir-phosphocholine, impairing the synthesis and degradation of cell membrane phospholipids[28,30,31].

The use of tenofovir, an antiviral reverse transcriptase inhibitor, is related to the onset of Fanconi syndrome. The drug is absorbed by the proximal tubular cells through an ion transport mechanism, however the percentage of tenofovir that is captured by the cells is greater than that excreted, resulting in its intracellular accumulation. This imbalance occurs due to changes in the expression of renal tubular transporters and mitochondrial metabolism[29,32].

Antifungals

The nephrotoxicity of amphotericin B is due to the vasoconstrictor effect on afferent arteriole and stimulation of the tubulo-glomerular feedback system, which consequently decreases blood flow in the kidneys, reducing the glomerular filtration rate and increasing serum levels of creatinine and urea. The lack of oxygen in the kidney cells activates the production of inflammation mediators. The accumulation of these mediators reduces the cellular antioxidant activity favoring the oxidation of DNA, thus generating an oxidative lesion in the kidney tissue, cellular apoptosis and renal tubular toxicity[32]. Itraconazole, on the other hand, has hypokalemia as one of its most common adverse effects, but its mechanism is unknown[33].

Antiparkinsonian

Levodopa can cause false positive result in the reagent strip technique for the detection of ketones in urine. In the glucose oxidase method for detecting glucose in the urine, the drug can cause false negative result. The interference mechanism for the two tests is unknown[34].

Alkaloid

Atropine, a muscarinic antagonist, is used as an antidote in organophosphate poisoning and in the treatment of bradycardia. Its use can result in increased urine density, since the drug can promote dehydration in the patient[35].

Mood stabilizer

Lithium carbonate is used in the therapy of acute manic episodes, bipolar disorder and in addition to antidepressants. Lithium is almost entirely excreted by the renal system, promoting an increase in pH and a decrease in density in urine samples[36]. This drug decreases the expression of water channels in the collecting duct, as well as reduces the activity of arginine-vasopressin in the urinary concentration. The accumulation of the drug inside the cell compromises the response of the kidney cells to vasopressin and aldosterone, resulting in tubular dysfunction and, consequently, nephrogenic diabetes insipidus and renal tubular acidosis. Another manifestation is nephropathy due to the use of lithium because of its modulating action in the inositol monophosphate pathway, decreasing the concentration of inositol and compromising the cellular metabolism with the accumulation of the drug in the distal nephron of the kidneys[37]. The nephrotoxic effect of lithium on the kidneys can manifest in the form of chronic interstitial nephritis or glomerulonephritis[4]. Lithium is also capable of interfering with the results of electrolyte analyzers, providing falsely high levels of sodium in the urine[34].

Hypouricemiante drugs

Allopurinol alters the physiological synthesis mechanism of nitric oxide due to its ability to induce the production of reactive oxygen species and, consequently, interfere with kidney function. Nitric oxide participates in kidney homeostasis through the regulation of renal blood flow and the excretion of salts and water, resulting in reduced glomerular filtration rate and the development of acute interstitial nephritis[38].

Probenecid prevents gout attacks by acting on the renal elimination of excess uric acid. However, because it is a cation, it competitively inhibits the tubular secretion of creatinine, resulting in increased serum levels of creatinine, although there is no change in renal function[39].

Hypolipidemic

Fibrates interfere with laboratory tests to assess kidney function, as they reduce tubular creatinine secretion, resulting in increased serum creatinine levels independent of glomerular filtration rate[10].

Non-steroidal anti-inflammatory drugs

The use of non-steroidal anti-inflammatory drugs (NSAIDs), such as salicylates, causes an increase in serum creatinine during the first seven days of therapy due to reduced secretion. The effect occurs until the drug reaches stable plasma concentration and, consequently, inhibits the production of prostaglandins[40]. NSAIDs are potentially nephrotoxic, and can cause changes in intraglomerular hemodynamics, glomerulonephritis and acute and chronic interstitial nephritis[41].

The use of acetylsalicylic acid can interfere with the reagent strip for glucose in the urine and the result is falsely increased. Paracetamol, in turn, interacts with the chemical test of phosphotungstic acid for serum detection of uric acid, falsely increasing dosage values[34].

Glucocorticoids

High doses of glucocorticoids result in increased synthesis and plasma concentration of cystatin C, which is a biomarker that can be used to evaluate the glomerular filtration rate. There are reports that the effect is observed with the use of methylprednisolone and dexamethasone, as these drugs stimulate the transcription of the cystatin C gene[42]. In addition, drugs such as prednisolone and prednisone can trigger hypokalemia, especially in patients who have mutations in the genes responsible for the expression of glucocorticoid receptors[43,44].

Vitamin

Ascorbic acid (vitamin C) interferes with the Jaffé method for the determination of creatinine, providing falsely increased results, since ascorbic acid reacts with alkaline picrate. In addition, ascorbic acid can cause false negative results in bilirubin dosage by interfering in vitro in the diazotation reaction and also in vivo in bilirubin metabolism, since supplementation with ascorbic acid can decrease messenger RNA levels of hemeoxygenase-1, a bilirubin biosynthesis limiting enzyme[34].

Radiological contrast

Radiological contrasts can alter renal hemodynamics through a vasodilatory effect interspersed with the vasoconstrictor, compromising blood flow in the kidneys, resulting in acute tubular necrosis or acute interstitial nephritis. In acute tubular necrosis there are cellular lesions in the renal tubules that block renal blood flow and impair oxygenation of renal medulla. The acute interstitial nephritis manifests milder[45].

Drugs that act on the gastrointestinal tract

Because it is a type 2 histamine receptor antagonist, cimetidine reduces the release of gastric juice in the stomach. It is excreted largely in its original form by the kidneys. Its use promotes an increase in the density and pH of urine. In addition, it competitively inhibits tubular secretion of creatinine due to its cationic nature. Ranitidine, a drug of the same class, promotes false positive result for proteinuria. However, the mechanism is unknown. Meanwhile, it is known that the effect is apparent when using the reagent strip test[46]. Ranitidine still has a nephrotoxic effect, which can cause acute interstitial nephritis[4].

Omeprazole, pantoprazole and lansoprazole are proton pump inhibiting drugs. Among its adverse effects related to kidney injury, what stands out is acute interstitial nephritis. This inflammation is associated with the accumulation of the drug in the interstitial tubules, which leads to an immune response[47].

Immunosuppressants

Nephrotoxicity of cyclosporine is manifested by interstitial fibrosis, hyaline degeneration of afferent arterioles and tubular atrophy, a clinical condition associated with kidney ischemia. The factors that cause kidney damage are glomerular vasoconstriction, decreasing blood flow and glomerular filtration rate, and stimulation of pro-fibrogenic molecules in kidney tissue. The continuous use of cyclosporine causes a permanent endothelial disorder with cell proliferation and activation of an inflammatory process in the kidneys, resulting in dysfunction of production and degeneration of the extracellular matrix components and, consequently, alteration of the original kidney structure[48]. Cyclosporine can cause changes in intraglomerular hemodynamics, the development of chronic interstitial nephritis and thrombotic microangiopathy in the kidneys[4].

Tacrolimus, like cyclosporine, reduces the glomerular filtration rate by modifying the intraglomerular hemodynamics. The drug stimulates tubular vacuolization, interstitial fibrosis and hyaline degeneration of renal arterioles[49].

Antineoplastic agents

Cyclophosphamide is an alkylating agent that produces toxic metabolites during its process of metabolism in the kidneys, injuring the bladder epithelium and proximal tubule cells, in addition to reducing the glomerular filtration rate[50]. The use of carmustite and semustite, other alkylating agents, can lead to the development of chronic interstitial nephritis[4].

Cisplatin, an platinum-derived antineoplastic agent, is associated with the development of acute interstitial nephritis and renal tubular toxicity[4]. This drug can stimulate the apoptotic and necrotic process of kidney cells due to the ability to compromise nuclear and mitochondrial DNA, originating reactive oxygen species and activating cell death pathways. The kidney damage that the drug induces stimulates the synthesis of cytokines responsible for the activation of adhesion molecules and attraction of immune cells, resulting in the development of the inflammatory process. These kidney lesions are also associated with the impairment of antioxidant mechanisms by the formation of free radicals induced by cisplatin[51].

Proteasome inhibitors (bortezomib), as well as antimicrotubule agents (vincristine), can cause thrombotic microangiopathy due to an autoimmune process or drug accumulation in kidney tissue[52]. Lenalidomide, an immunomodulatory agent, is related to the occurrence of Fanconi syndrome, whereas interferon alfa can cause glomerulonephritis[4,50].

The use of methotrexate, which is an antimetabolic antineoplastic agent, leads to appearance of acute renal failure through the formation of crystals that are deposited in the distal tubule of the kidneys. The drug also stimulates the synthesis of free radicals causing tubular necrosis[50].

Platelet antiaggregants and anticoagulants

The use of clopidogrel, a platelet antiaggregant, is associated with thrombotic microangiopathy, as well as ticlopidine. The thrombocytopenia caused by ticlopidine is more severe than that caused by clopidogrel. Sometimes, the acute kidney injury resulting from the use of clopidogrel is associated with a reduction in the activity of ADAMTS13, which is an enzyme involved in the blood clotting process, thus suggesting a mechanism for the nephrotoxicity of the drug. Other times there is no change in the enzyme. Therefore, the mechanism is not completely elucidated[52]. Heparin, on the other hand, compromises renal tubular secretion of potassium, causing hyperkalaemia[53].

Antiepileptics

Topiramate and zonisamide inhibit renal reabsorption of bicarbonate and calcium, promoting metabolic acidosis and increasing the urine pH. Metabolic impairment resulting from the use of these drugs induces nephrolithiasis associated with a reduction in urinary citrate rate and renal tubular acidosis due to the inability to acidify urine by the kidneys[54].

Carbamazepine stimulates the action of the antidiuretic hormone in the kidneys, favoring hyponatremia[55]. The use of oxcarbazepine, in turn, can result in hyponatremia, due to the direct action of the drug in the renal tubules, promoting a reduction in sodium reabsorption[56].

In the case of valproic acid, there is interference in the reagent strip method for detecting ketonuria. The effect is due to the renal excretion of the drug in the form of a keto-metabolite, resulting in false positive for ketone in urine[57].

Bronchodilator

One of the adverse effects of salbutamol, an agonist of beta 2 adrenergic receptors, is hypokalemia. This drug activates the sodium-potassium ATPase pump in cell membranes, resulting in intracellular translocation of potassium[58].

FINAL CONSIDERATIONS

It is essential to know the drugs that interfere in the kidney evaluation exams by health professionals so that they can correctly interpret the laboratory exams, resulting in an adequate diagnosis and therapy. Several drugs are potentially nephrotoxic, and it is important to monitor the kidney function of patients who use them. In addition, the use of some of these drugs is not recommended by patients who have chronic kidney disease or the appropriate dose adjustment should be made if the use of these drugs by these patients is essential.

Authors' participation: *Palloma Aline de Melo*: Contextualização, Desenvolvimento, Revisão, Formatação; *Bruna Gabriela Rocha: Revisão; William Neves Oliveira*: Revisão; *Thays Santos Mendonça*: Revisão; *Caroline Pereira Domingueti*: Contextualização, Desenvolvimento, Revisão, Orientação.

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