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Interference of medicines in laboratory exams

Interferência dos medicamentos nos exames laboratoriais

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ABSTRACT

Objective: Conduct a survey on the interference of drugs in laboratory tests. **Methodology:** To identify the interference of each medication in laboratory tests, the Municipal List of Essential Medicines (Remume) of a medium-sized municipality in the state of Minas Gerais was used along with the following sources of information: Dynamed, Micromedex® and Nursing Reference Center. **Results:** We observed that the majority (67.7%) of Remume drugs can interfere in one or more laboratory tests; among them, the main classes of drugs are diuretics, beta blockers, ß-lactams, sulfonamides, macrolides, tricyclic antidepressants and selective serotonin reuptake inhibitors antidepressants. **Conclusion:** It is extremely important to disseminate knowledge about these interferences so that health professionals are alert and know how to identify the possible changes, reducing analytical errors and subsequently misdiagnosis and erroneous monitoring. Continued education on drug interference in laboratory tests is equally important.

Key words: generic drugs; clinical laboratory techniques; diagnostic errors.

RESUMO

Objetivo: *Realizar um levantamento sobre a interferência dos medicamentos nos exames laboratoriais.* ***Métodos:*** *Utilizamos a Relação Municipal dos Medicamentos Essenciais (Remune) de um município de médio porte do estado de Minas Gerais e as seguintes fontes de informações: Dynamed, Micromedex® e Nursing Reference Center.* ***Resultados:*** *Observamos que a maioria (67,7%) dos medicamentos da Remune pode interferir em um ou mais exames laboratoriais; entre eles, as principais classes de medicamentos são os diuréticos, betabloqueadores, betalactâmicos, sulfonamidas, macrolídeos, antidepressivos tricíclicos e antidepressivos inibidores seletivos da recaptação de serotonina.* ***Conclusão:*** *É muito importante divulgar o conhecimento a respeito dessas interferências para que os profissionais da área da saúde possam identificar as possíveis alterações nos exames, reduzindo erros analíticos e diagnósticos e monitoramentos equivocados. Portanto, faz-se necessária a educação continuada sobre as interferências de medicamentos nos exames laboratoriais.*

Unitermos: *medicamentos genéricos; técnicas de laboratório clínico; erros de diagnóstico.*

RESUMEN

Objetivo: *Llevar a cabo una encuesta acerca de la interferencia de los medicamentos en las pruebas de laboratorio.* ***Métodos:*** *Usamos la Relación Municipal de Medicamentos Esenciales (Remume) de una municipalidad mediana en el estado de Minas Gerais y las siguientes fuentes de información: Dynamed, Micromedex® y Nursing Reference Center.* ***Resultados:*** *Observamos que la mayor parte (67,7%) de los medicamentos de Remume puede interferir en una o más pruebas de laboratorio; entre ellos, las principales clases son los diuréticos, beta bloqueadores, betalactámicos, sulfonamidas, macrólidos, antidepresivos tricíclicos y*

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antidepresivos inhibidores selectivos de la recaptación de serotonina. ***Conclusión:*** *Es muy importante divulgar el conocimiento respecto a esas interferencias para que los profesionales de la salud puedan identificar las posibles alteraciones en las pruebas, reduciendo errores analíticos y diagnósticos y monitoreos equivocados. Por lo tanto, es necesaria una educación continuada acerca de las interferencias de medicamentos en las pruebas de laboratorio.*

Palabras clave: *medicamentos genéricos; técnicas de laboratório clínico; errores diagnósticos.*

INTRODUCTION

Medicines are major sources of variation in laboratory test results, and not always they can be discontinued for the conduction of those tests[1]. Some drugs can produce false-negative or false-positive results; having access to this item of information is very important in laboratory routine, as well as in clinical practice and pharmaceutical care, because it deals with change in the clinical laboratory diagnosis and interference in the monitoring and evaluation of patient prognosis[2].

Thus, it is essential to obtain data about medications and their time of use by the patient for the last 10 days before collecting biological material for the conduction of a laboratory test. Commonly, patients forget reporting some medicines they use to the laboratory personnel, therefore it is necessary to be attentive to any abnormality in the tests[3].

Numerous medicines can cause biological (*in vivo*) and analytical (*in vitro*) interferences that affect laboratory tests. When a medication produces the change of a biological marker by means of a physiological or pharmacological mechanism, there is the *in vivo* interference or adverse drug reaction. For example, the changes in serum uric acid, which can be caused by the use of enalapril and hydrochlorothiazide[2]. On the other hand, *in vitro* interference of a drug or its biotransformation product can happen at an analytical step in which those tests can interact with the substances of the employed chemical reagents, producing a false result of the analysis[2]. As an example, the reduction that the ascorbic acid can cause in plasma levels of glucose when measured by the method of glucose oxidase[3].

Given the above, it is important that both professionals working in clinical laboratories and those involved in the care of patients know how to recognize the types of interference drugs can cause on laboratory tests, as they can alter some markers and interfere in the conduct of health professionals. Besides, care must be greater with patients treated with several medicines concomitantly for a prolonged time, because the chances of interference are higher.

The objective of this work was to conduct a survey on the interference on laboratory tests by the medicines present at the Municipal List of Essential Medicines (Remume) of a medium-sized municipality of the state of Minas Gerais, in order to warn and spread this knowledge to the population and health professionals.

METHODS

The present study used the last version of Remume (130 medicines belonging to different classes) of a medium-sized municipality of the state of Minas Gerais (234,937 inhabitants[4]), made available by the Municipal Office of Health (Semusa) in 2019. From the obtained data, we carried out a search about the interference each medication can cause in laboratory tests, by means of the site Saúde Baseada em Evidências (Evidence-Based Health), using the databases Dynamed, Micromedex® and Nursing Reference Center. The names of medicines in English were searched as key words. Later, medicines were classified according to the Anatomical Therapeutic Chemical Code (ATC), which distributes the active substances in different groups, pursuant to the organ or system in which they act and their therapeutical, chemical and pharmacological properties[5]. From this search, a table was built to be used as a material for rapid consultation by all health professionals involved in patient care.

RESULTS

The medications present at Remume used in basic attention were distributed according to ATC classification regarding the treatment of: disorders of the digestive system and metabolism and food supplements; diseases of the blood and blood-forming organs; cardiovascular diseases; skin conditions; genitourinary tract disorders, sex hormones and immunoglobulins; inflammatory processes and hypothyroidism; systemic infectious diseases; musculoskeletal disorders; nervous system diseases and sleep disorders; parasitic diseases; respiratory diseases. The interference of those medicines in laboratory tests is represented in the **Table** according to the group they belong to.

TABLE – Interferences in laboratory testing caused by medications

Treatment of disorders of the digestive system and metabolism and food supplements		
Indication	**Medicine**	**Laboratory change**
Food supplement	Folinic acid	-
Antiemetic	Bromopride	-
Oral rehydration salts	Sodium chloride, anhydrous glucose, potassium chloride, sodium citrate dihydrate	-
Food supplement	B-complex vitamins	-
Hypoglycemic agent	Glibenclamide	-
Hypoglycemic agent	Glicazide	-
Antiacid	Aluminum hydroxide + magnesium hydroxide	↑ serum calcium levels ↓ serum phosphate levels
Hypoglycemic agent	NPH human insulin	↓ serum potassium levels ↓ serum magnesium levels
Hypoglycemic agent	Regular human insulin	↓ serum potassium levels ↓ serum magnesium levels
Hypoglycemic agent	Linagliptin	↑ serum uric acid levels
Hypoglycemic agent	Metformin	False-positive urine ketones ↓ serum folic acid levels ↓ serum vitamin B12 levels
Antifungal drug	Nystatin	-
Antiulcer medication	Omeprazole	False-positive urine THC ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↓ serum magnesium levels
Food supplement	Pyridoxine	False-positive urine methadone False-positive urine opiates ↑ serum AST levels ↓ serum folic acid levels ↑ serum urobilinogen levels
Treatment of diseases of the blood and blood-forming organs		
Indication	**Medicine**	**Laboratory change**
Antiplatelet agent	Acetylsalicylic acid	↑ serum glucose levels Larger doses (1.3 g four times a day): ↑ urinary excretion and ↓ serum uric acid levels Smaller doses (< 325 mg three times a day): ↓ urinary excretion and ↑ serum uric acid levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ urinary VMA levels ↓ serum TSH levels High doses: ↑ prothrombin time
Food supplement	Folic acid	High continuous doses: ↓ serum levels of B-complex vitamins (B1, B2, B3, B5, B6, B7, and B12)
Antiplatelet agent	Clopidogrel	↑ serum bilirubin levels ↑ serum AST and ALT levels ↑ serum LDH levels ↑ serum GGT levels ↑ serum total cholesterol levels ↑ serum urea levels ↑ serum uric levels
Anticoagulant	Dabigatran	↓ hemoglobin levels
Anticoagulant	Enoxaparin	↓ hematocrit ↑ serum AST and ALT levels ↑ serum potassium levels

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Anticoagulant	Heparin	Thrombocytopenia ↑ serum AST and ALT levels ↑ serum potassium levels ↓ hematocrit
Antianemic drug	Iron sulfate	Fecal occult blood can be obscured by the black color of iron in feces
Anticoagulant	Sodium warfarin	Macroscopic or microscopic hematuria
Treatment of cardiovascular diseases		
Indication	**Medicine**	**Laboratory change**
Antiarrhythmic	Amiodarone	↓ serum T4 levels ↓ serum T3 levels
Antihypertensive medication Antianginal drug	Amlodipine	-
Antihypertensive medication Antianginal drug Antiarrhythmic	Atenolol	↑ serum urea levels ↑ serum LDL-c levels ↓ serum HDL-c levels ↑ serum potassium levels ↑ serum triglyceride levels ↑ serum uric acid levels ↑ ANA titers ↑ serum glucose levels
Antihypertensive medication	Captopril	↑ false-positive urine acetone Neutropenia Agranulocytosis Proteinuria ↑ serum potassium levels ↑ serum urea levels ↑ serum creatinine levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels False-positive ANA
Antihypertensive medication Antianginal drug	Carvedilol	↑ serum urea levels ↑ serum LDL-c levels ↓ serum HDL-c levels ↑ serum potassium levels ↑ serum triglycerides levels ↑ serum uric acid levels ↑ serum glucose levels ↑ ANA titers
Antihypertensive medication	Clonidine	↑ serum glucose levels ↓ concentrations of urinary catecholamines and VMA False-positive Coombs test
Antiarrhythmic Cardiotonic drug	Digoxin	-
Antihypertensive medication	Enalapril	Neutropenia Agranulocytosis ↑ serum potassium levels
Antihypertensive medication Diuretic	Spironolactone	False increase in digoxin levels ↑ serum potassium levels ↓ serum sodium levels ↑ serum magnesium levels ↑ serum uric acid levels ↑ serum urea levels ↑ serum creatinine levels ↑ plasma renin activity ↑ urinary calcium excretion ↑ serum cortisol levels

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Antihypertensive medication Diuretic	Furosemide	↑ serum uric acid levels ↑ serum glucose levels ↓ serum potassium levels ↓ serum sodium levels ↓ serum calcium levels ↓ serum magnesium levels ↑ serum urea levels ↑ serum creatinine levels
Antihypertensive medication	Hydralazine	↓ hemoglobin levels Leukopenia Agranulocytosis Thrombocytopenia False-positive direct Coombs test
Antihypertensive medication Diuretic	Hydrochlorothiazide	↓ serum potassium levels ↓ serum chlorine levels ↑ serum calcium levels ↓ serum magnesium levels ↑ serum uric acid levels ↑ serum glucose levels ↑ serum cholesterol levels ↑ serum HDL-c levels ↑ serum triglyceride levels ↑ serum bilirubin levels ↑ serum creatinine levels ↓ serum sodium levels
Antianginal drug Vasodilator	Isosorbide dinitrate	-
Antianginal drug Vasodilator	Isosorbide mononitrate	-
Antihypertensive medication	Losartan	↑ serum urea levels ↑ serum creatinine levels ↑ serum AST and ALT levels ↑ serum bilirubin levels ↑ serum potassium levels
Antihypertensive medication	Methyldopa	False increase in catecholamine levels ↑ serum urea levels ↑ serum creatinine levels ↑ serum potassium levels ↑ serum sodium levels ↑ serum prolactin levels ↑ serum uric acid levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↑ prothrombin time False-positive direct Coombs test
Antihypertensive medication Antianginal drug	Nifedipine retard	False-positive ANA and direct Coombs test
Antihypertensive medication Antianginal drug Antiarrhythmic	Propranolol	↑ serum urea levels ↑ serum LDL-c levels ↓ serum HDL-c levels ↑ serum potassium levels ↑ serum triglyceride levels ↑ serum uric acid levels ↑ ANA titers ↓ or ↑ serum glucose levels

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Antilipemic	Simvastatin	↑ glycated hemoglobin ↑ serum glucose levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum GGT levels ↑ serum bilirubin levels ↑ serum creatine phosphokinase levels
Treatment of skin conditions		
Indication	**Medicine**	**Laboratory change**
Antifungal agent	Ketoconazole	↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↓ serum testosterone levels
Antifungal agent	Clotrimazole	↑ serum AST levels
Wound cleaning	Collagenase + chloramphenicol	-
Anti-inflammatory	Dexamethasone	-
Painkiller	Lidocaine	-
Antibiotic	Neomycin + Bacitracin	-
Antibiotic	Potassium permanganate	-
Antibiotic	Silver sulfadiazine	Agranulocytosis Aplastic anemia Thrombocytopenia Leukopenia Hemolytic anemia
Treatment of genitourinary tract disorders, sex hormones and immunoglobulins		
Indication	**Medicine**	**Laboratory change**
Contraceptive	Algestone + estradiol	-
	Anti-RH immunoglobulin	-
Contraceptive	Levonorgestrel	-
Contraceptive	Levonorgestrel + ethinylestradiol	-
Contraceptive	Medroxyprogesterone	↑ serum alkaline phosphatase levels ↑ serum LDL-c levels ↓ serum HDL-c levels ↑ serum T4 levels ↑ serum T3 levels
Antiinfective drug	Metronidazole	-
Contraceptive	Norethisterone	-
Contraceptive	Norethisterone + estradiol	-
UTI relief	Oxybutynin	-
Treatment of inflammatory processes and hypothyroidism		
Indication	**Medicine**	**Laboratory change**
Hormonal medication	Levothyroxine sodium	-
Anti-inflammatory	Prednisolone	↑ serum glucose levels ↓ serum potassium levels ↓ serum calcium levels ↑ serum sodium levels ↑ serum total cholesterol levels ↑ serum LDL-c levels ↑ serum triglyceride levels
Anti-inflammatory	Prednisone	↑ serum glucose levels ↓ serum potassium levels ↓ serum calcium levels ↑ serum sodium levels ↑ serum total cholesterol levels ↑ serum LDL-c levels ↑ serum triglyceride levels
Systemic anti-infective treatment		
Indication	**Medicine**	**Laboratory change**
Treatment of herpes infection of skin and mucous membranes	Acyclovir	↑ serum urea levels ↑ serum creatinine levels ↓ creatinine clearance

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Antibiotic	Amoxicillin	↓ hemoglobin levels Hemolytic anemia Leukopenia Agranulocytosis Thrombocytopenia ↑ urine glucose levels
Antibiotic	Amoxicillin + clavulanic acid	Clavulanic acid: false-positive Coombs test ↓ hemoglobin levels Hemolytic anemia Leukopenia Agranulocytosis Thrombocytopenia ↑ urine glucose levels ↑ serum alkaline phosphatase levels ↑ serum LDH levels ↑ serum AST and ALT levels
Antibiotic	Azithromycin	↑ prothrombin time Leukopenia Thrombocytopenia ↑ serum bilirubin levels ↑ serum AST and ALT levels ↑ serum LDH levels ↑ serum alkaline phosphatase levels ↑ serum creatine phosphokinase levels ↑ serum potassium levels ↑ serum urea levels ↑ serum creatinine levels ↑ serum glucose levels
Antibiotic	Cefalexin	False-positive direct Coombs test Neutropenia Thrombocytopenia Eosinophilia ↑ urine glucose levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↑ serum LDH levels ↑ serum urea levels ↑ serum creatinine levels
Systemic anti-infective treatment		
Indication	**Medicine**	**Laboratory change**
Antibiotic	Ceftriaxone	False-positive Coombs test ↓ hemoglobin levels Reticulocytosis Hemoglobinuria Eosinophilia Leukopenia Lymphocytosis Prolonged prothrombin time Neutropenia Agranulocytosis Thrombocytopenia ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↑ serum LDH levels ↑ serum urea levels ↑ serum creatinine levels

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Antibiotic	Ciprofloxacin	False-positive urine opiates Anemia (including hemolytic and aplastic) Thrombocytopenia Leukopenia Agranulocytosis Pancytopenia ↑ serum AST and ALT levels ↑ serum LDH levels ↑ serum bilirubin levels ↑ serum alkaline phosphatase levels ↑ or ↓ serum glucose levels
Antibiotic	Clarithromycin	↑ serum AST and ALT levels ↑ serum bilirubin levels ↑ serum alkaline phosphatase levels ↑ serum urea levels
Antibiotic	Doxycycline	False increase in urine catecholamine levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↑ serum amylase levels
Antibiotic	Spiramycin	-
Antibiotic	Erythromycin	False increase in urine catecholamines ↑ serum bilirubin levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels
Systemic anti-infective treatment		
Indication	**Medicine**	**Laboratory change**
Antifungal agent	Fluconazole	↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels
Antifungal agent	Itraconazole	↓ serum potassium levels
Antifungal agent	Metronidazole	↑ serum AST and ALT levels ↑ serum LDH levels ↑ serum triglyceride levels
Antibiotic	Nitrofurantoin	False-positive urine glucose ↑ serum bilirubin levels ↑ serum alkaline phosphatase levels ↑ serum urea levels ↑ serum creatinine levels
Antibiotic	Norfloxacin	False-positive urine opiates in immunoassays Crystalluria
Antibiotic	Benzathine penicillin	False-positive direct Cooms test False-positive urine glucose using Benedict's reagent Hemolytic anemia Agranulocytosis Leukopenia Neutropenia ↑ Proteinuria ↑ serum potassium levels after large doses ↑ serum sodium levels after large doses ↑ serum AST and ALT levels ↑ serum LDH levels ↑ serum alkaline phosphatase levels
Antibiotic	Benzathine penicillin + procaine	-
Antitubercular agent Antibiotic	Rifampicin	-

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Antibiotic	Sulfadiazine	↑ serum urea levels ↑ serum creatinine levels Hematuria Proteinuria Crystalluria
Systemic anti-infective treatment		
Indication	**Medicine**	**Laboratory change**
Antibiotic	Sulfamethoxazole + trimethoprim	False increase in creatinine levels False increase in methotrexate levels ↑ serum bilirubin levels ↑ serum potassium levels ↑ serum creatinine levels ↑ serum alkaline phosphatase levels
Treatment of musculoskeletal disorders		
Indication	**Medicine**	**Laboratory change**
Osteoporosis treatment	Alendronate sodium	-
Treatment of gouty arthritis and hyperuricemia	Allopurinol	↓ serum and urinary levels of uric acid ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↑ serum AST and ALT levels ↓ erythrocytes Thrombocytopenia ↑ serum urea levels ↑ serum creatinine levels ↓ creatinine clearance
Muscle relaxant	Baclofen	↑ serum glucose levels ↑ serum alkaline phosphatase levels ↑ serum AST and ALT levels
Anti-inflammatory	Diclofenac sodium	↓ hemoglobin levels ↓ hematocrit ↓ serum alkaline phosphatase levels ↓ serum LDH levels ↑ serum AST and ALT levels ↑ serum urea levels ↓ serum creatinine levels
Anti-inflammatory	Ibuprofen	↓ hemoglobin levels ↓ hematocrit Leukopenia Thrombocytopenia ↓ creatinine clearance ↑ bleeding time ↑ serum potassium levels ↑ serum urea levels ↑ serum creatinine levels ↑ serum alkaline phosphatase levels ↑ serum LDH levels ↑ serum AST and ALT levels ↓ serum glucose levels
Treatment of nervous system diseases and sleep disorders		
Indication	**Medicine**	**Laboratory change**
Anticonvulsant	Valproic acid	False-positive urine ketone Thrombocytopenia Leukopenia ↑ serum AST and ALT levels
Anxiolytic	Alprazolam	↓ hematocrit Neutropenia
Antidepressant	Amitriptyline	↑ serum bilirubin levels ↑ serum alkaline phosphatase levels ↑ or ↓ serum glucose levels
Antiparkinsonian drug	Biperiden	-
Antidepressant	Bupropion	False-positive urine amphetamine

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Anticonvulsant	Carbamazepine	False increase of perphenazine levels False-positive tricyclic antidepressant results Pancytopenia False-negative hCG results Thrombocytopenia Leukopenia ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum bilirubin levels ↑ serum urea levels ↓ serum sodium levels ↑ serum cholesterol levels ↑ serum HDL-c levels ↑ serum triglyceride levels Proteinuria Glycosuria
Mood stabilizer	Lithium carbonate	↑ serum sodium levels
Antidepressant	Clomipramine	Leukopenia Agranulocytosis Thrombocytopenia Anemia Pancytopenia ↑ serum ALT and AST levels ↑ or ↓ serum glucose levels
Anxiolytic	Clonazepam	↑ serum bilirubin levels ↑ serum AST and ALT levels
Antipsychotic	Chlorpromazine	False-positive phenylketonuria test False-positive salicylate in urine False-negative or-positive hCG results False-positive urine bilirubin Neutropenia Agranulocytosis ↓ hematocrit ↓ hemoglobin levels Leukopenia ↓ granulocytes Thrombocytopenia ↑ serum prolactin levels ↑ serum bilirubin levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels
Anxiolytic	Diazepam	-
Painkiller Antipyretic	Dipyrone	-
Anticonvulsant	Phenytoin	False-positive urine barbiturates Thrombocytopenia Leukopenia Agranulocytosis Pancytopenia ↓ serum T4 levels It can produce below normal dexamethasone suppression test ↑ serum glucose levels ↑ serum alkaline phosphatase levels ↑ serum GGT levels
Anticonvulsant	Phenobarbital	False increase in pentobarbital levels ↓ serum bilirubin levels

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Antidepressant	Fluoxetine	Proteinuria ↑ serum alkaline phosphatase levels ↑ serum ALT and AST levels ↑ serum urea levels ↑ serum creatine phosphokinase levels ↑ or ↓ serum glucose levels ↓ serum calcium levels ↓ serum sodium levels ↓ serum uric acid levels
Anxiolytic	Flurazepam	-
Antipsychotic	Haloperidol	↑ serum prolactin levels ↓ serum cholesterol levels Leukopenia Neutropenia Agranulocytosis
Antipsychotic	Haloperidol decanoate	-
Antidepressant	Imipramine	↑ or ↓ serum glucose levels
Antiparkinsonian drug	Levodopa + benserazide	False-negative urine glucose False-positive urine ketone False increase in catecholamines and their metabolytes in urine and plasma False-positive Coombs test
Antiparkinsonian drug	Levodopa + carbidopa	False-negative urine glucose False-positive urine ketone Falsely high levels of catecholamines and their metabolytes in urine and plasma False-positive Coombs test ↓ hemoglobin levels ↓ hematocrit Agranulocytosis Hemolytic and non-hemolytic anemia Thrombocytopenia Leukocitosis ↑ serum glucose levels ↑ serum AST and ALT levels ↑ serum bilirubin levels ↑ serum alkaline phosphatase levels ↑ serum LDH levels ↑ serum protein-bound iodine levels ↓ serum urea levels ↓ serum creatinine levels ↓ serum uric acid levels
Antipsychotic	Levomepromazine	-
Reduces smoking withdrawal symptoms	Nicotine	-
Anxiolytic	Nitrazepam	-
Antidepressant	Nortriptyline	↑ serum bilirubin levels ↑ serum alkaline phosphatase levels ↑ or ↓ serum glucose levels
Anticonvulsant	Oxcarbazepine	↓ serum sodium levels
Painkiller Antipyretic	Paracetamol	False increase in serum uric acid levels False-positive urine 5-hydroxyindoleacetic acid ↑ serum ALT and AST levels ↑ serum bilirubin levels ↑ serum LDH levels ↑ prothrombin time False decrease of serum glucose levels
Antidepressant	Sertraline	False-positive urine benzodiazepines ↓ serum uric acid levels

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Antipsychotic	Thioridazine	False-positive urine salicylate False-positive or false-negative hCG results False-positive urine bilirubin ↓ hematocrit ↓ hemoglobin levels Leukopenia ↓ granulocytes Thrombocytopenia ↑ serum bilirubin levels ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↑ serum prolactin levels
Anticonvulsant	Topiramate	↓ serum phosphate levels ↓ serum potassium levels ↑ serum alkaline phosphatase levels ↑ serum AST and ALT levels
Anxiolytic	*Valeriana officinalis*	-
Treatment of parasitic diseases		
Indication	**Medicine**	**Laboratory change**
Antiparasitic	Albendazole	Leukopenia ↑ serum AST and ALT levels
Antiparasitic	Ivermectin	Leukopenia Eosinophilia ↑ hemoglobin levels ↑ serum AST and ALT levels
Antiparasitic	Mebendazole	Leukopenia Thrombocytopenia ↓ hemoglobin levels Neutropenia (including agranulocytosis) ↑ serum urea levels transitorily ↑ serum AST and ALT levels transitorily ↑ serum alkaline phosphatase levels transitorily
Antiparasitic	Permethrin	-
Antiparasitic	Pyrimethamine	↓ serum folic acid levels ↓ serum vitamin B12 levels Leukopenia Thrombocytopenia Pancytopenia Megaloblastic anemia
Treatment of respiratory diseases		
Indication	**Medicine**	**Laboratory change**
Bronchodilator	Aminophylline	False decrease in phenobarbital levels
Anti-inflammatory	Beclomethasone	-
Anti-inflammatory	Budesonide	-
Nasal decongestant	Sodium chloride	-
Antihistamine	Loratadine	-
Antihistamine	Promethazine	False-positive salicylate in urine False-positive or false-negative hCG results Leukopenia Agranulocytosis ↑ serum glucose levels
Bronchodilator	Salbutamol	↓ serum potassium levels

ALT: alanine transaminase; ANA: antinuclear antibody; AST: aspartate transaminase; GGT: gamma-glutamyltransferase; hCG: human chorionic gonadotropin; HDL-c: high-density lipoprotein cholesterol; LDH: lactate dehydrogenase; LDL-c: low-density lipoprotein cholesterol; THC: tetrahydrocannabinol; TSH: thyroid stimulating hormone; T3: triiodothyronine; T4: thyroxine; VMA: vanillylmandelic acid; UTI: urinary tract infection.

We observed that most (67.7%) medicines of Remume can interfere in one or more laboratory tests. Among them, the main classes of medicines are diuretics, which change especially electrolyte balance; betablockers, which affect lipid profile; beta-lactams and sulfonamides, which cause change in blood count; macrolides and tricyclic antidepressants, which alter hepatic enzymes; and selective serotonin reuptake inhibitors antidepressants, which affect glucose and uric acid levels.

The main tests suffering interference were: liver function (46 medicines), blood glucose test (31 medicines), and electrolyte panel (29 medicines).

DISCUSSION

We verified that the medicines atenolol, propranolol, carvedilol, hydrochlorothiazide, carbamazepine, haloperidol, clopidogrel, medroxyprogesterone, prednisolone, and prednisone can cause alteration of the lipid profile as the major biological interference. Thus, it is important to monitor the lipid profile of the patients taking those drugs, as the increased serum levels of triglycerides and the low-density lipoprotein cholesterol (LDL-c) and the reduced serum levels of the high-density lipoprotein cholesterol (HDL-c) are associated with the increased risk of development of cardiovascular diseases[6].

Acetylsalicylic acid, atenolol, carvedilol, clonidine, furosemide, hydrochlorothiazide, propranolol, simvastatin, prednisolone, prednisone, amoxicillin, amoxicillin + clavulanic acid, azithromycin, benzathine penicillin, cefalexin, nitrofurantoin, baclofen, ibuprofen, amitriptyline, clomipramine, phenytoin, fluoxetine, imipramine, levodopa + benserazide, levodopa + carbidopa, nortriptyline, paracetamol, promethazine, ciprofloxacin, and carbamazepine are associated with alterations in the metabolism of glucose by means of decreased insulin secretion or action. As they increase blood glucose as a biological interference, it is important to monitor the glycemic levels of patients who use them. Besides, in case patients suffer from diabetes mellitus, it may be necessary to adjust the dose of the antidiabetic agent[7].

The main medicines that cause biological interference in the hepatic function are omeprazole, acetylsalicylic acid, clopidogrel, enoxaparin, heparin, captopril, losartan, methyldopa, simvastatin, ketoconazole, medroxyprogesterone, clotrimazole, amoxicillin + clavulanic acid, azithromycin, benzathine penicillin, cefalexin, clarithromycin, doxycycline, erythromycin, fluconazole, metronidazole, nitrofurantoin, sulfamethoxazole + trimethoprim, allopurinol, baclofen, diclofenac sodium, ibuprofen, valproic acid, amitriptyline, carbamazepine, clonazepam, clomipramine, chlorpromazine, phenytoin, fluoxetine, levodopa + carbidopa, nortriptyline, thioridazine, topiramate, albendazole, ivermectin, mebendazole, ceftriaxone, ciprofloxacin, pyridoxine, and paracetamol. Some of those medicines are hepatotoxic, being important to monitor liver function by measuring the hepatic enzymes alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyltransferase (GGT), and alkaline phosphatase (ALP), as well as bilirubins of the patients who use them. Moreover, in case the patient presents a liver disease, it may be necessary to adjust the dose of the medicine[8].

The medicines that cause biological interference in renal function, with the risk of increased levels of urea and creatinine and reduction of creatinine clearance, are: clopidogrel, atenolol, captopril, carvedilol, spironolactone, furosemide, hydrochlorothiazide, losartan, methyldopa, propranolol, acyclovir, azithromycin, cefalexin, clarithromycin, nitrofurantoin, sulfamethoxazole + trimethoprim, allopurinol, diclofenac sodium, ibuprofen, carbamazepine, fluoxetine, levodopa + carbidopa, mebendazole, acyclovir, ceftriaxone, and sulfadiazine. Some of these medications are nephrotoxic[9], consequently, for prevention of chronic kidney disease it is relevant to monitor renal function by means of the assessment of glomerular filtration rate and albuminuria[10]. Besides, some of those medications are contraindicated or must have the dose adjusted in patients who already present kidney disease[9].

Linagliptin, acetylsalicylic acid, clopidogrel, atenolol, carvedilol, spironolactone, furosemide, hydrochlorothiazide, methyldopa, and propranolol have as biological interference the increased levels of uric acid, being important to monitor serum levels of this analyte in patients who use those medications due to the risk of development of gout – a disease characterized by accumulation of crystals of urate in joints, synovial tissue, bones, skin, and kidneys –, regardless of the presence or absence of clinical manifestations[11].

Electrolytes are essential for basic life functioning, such as maintenance of electrical neutrality of cells, generation and conduction of action potentials in nerves and muscles[12]. The drugs that alter the levels of electrolytes (sodium, potassium, magnesium, calcium) are aluminum hydroxide + magnesium hydroxide, recombinant human insulin (NPH), regular human insulin, omeprazole, enoxaparin, heparin, atenolol, captopril, carvedilol, enalapril, spironolactone, furosemide, hydrochlorothiazide, losartan, methyldopa, propranolol, prednisolone, azithromycin, benzathine penicillin, sulfamethoxazole + trimethoprim, ibuprofen, carbamazepine, lithium carbonate, fluoxetine, oxcarbazepine, topiramate, salbutamol, and itraconazole. High or reduced levels of electrolytes can cause an imbalance in the body, interrupting the normal body functions, with risk of complications such as death; therefore, it is important to monitor serum levels in patients who are treated with these medications[12].

Acetylsalicylic acid, amiodarone, phenytoin, and medroxyprogesterone are able to interfere biologically in the levels of hormones triiodothyronine (T3) and thyroxine (T4),

responsible for metabolism regulation, and also in the levels of the thyroid stimulating hormone (TSH), produced and released by the anterior pituitary gland and responsible for regulating the secretion of thyroid hormones[13]. Thus, it is of utmost importance to monitor thyroid hormones of patients in use of the mentioned drugs. Besides, dose adjustment can be necessary in patients with hypothyroidism who are treated with levothyroxine[14].

Some drugs can even cause blood count alterations: dabigatran, hydralazine, amoxicillin, amoxicillin + clavulanic acid, benzathine penicillin, diclofenac sodium, ibuprofen, chlorpromazine, clomipramine, levodopa + carbidopa, thioridazine, mebendazole, ceftriaxone, ciprofloxacin, and silver sulfadiazine. They reduce the levels of hemoglobin, causing anemia. Metformin, pyridoxin, pyrimethamine can also cause reduction in the levels of vitamin B12 and/or folic acid, resulting in megaloblastic anemia[15]. Captopril, enalapril, hydralazine, silver sulfadiazine, amoxicillin, amoxicillin + clavulanic acid, azithromycin, benzathine penicillin, cefalexin, ibuprofen, valproic acid, alprazolam, carbamazepine, clomipramine, chlorpromazine, phenytoin, haloperidol, levodopa + carbidopa, thioridazine, albendazole, ivermectin, mebendazole, promethazine, ceftriaxone, ciprofloxacin, and pyrimethamine can cause interference in the leukocyte levels. If patients use any of these drugs, it is important to monitor them by means of blood count[16].

Regarding blood clotting, medications that interfere with the levels of platelets are heparin, hydralazine, silver sulfadiazine, amoxicillin, amoxicillin + clavulanic acid, azithromycin, cefalexin, allopurinol, ibuprofen, valproic acid, carbamazepine, clomipramine, chlorpromazine, phenytoin, levodopa + carbidopa, thioridazine, mebendazole, ceftriaxone, ciprofloxacin, pyrimethamine. As the acetylsalicylic acid, methyldopa, azithromycin, paracetamol, and ceftriaxone can cause alterations in prothrombin time, it is fundamental to monitor patients that use these drugs by means of laboratory assessment of coagulation panel. Besides, in case the patient uses the oral anticoagulant, drug dose adjustment may be necessary[17].

Metformin, omeprazole, captopril, clonidine, spironolactone, hydralazine, methyldopa, nifedipine retard, amoxicillin + clavulanic acid, benzathine penicillin, cefalexin, doxycycline, erythromycin, nitrofurantoin, norfloxacin, sulfamethoxazole + trimethoprim, valproic acid, bupropion, carbamazepine, chlorpromazine, phenytoin, phenobarbital, levodopa + benserazide, levodopa + carbidopa, paracetamol, sertraline, thioridazine, promethazine, ceftriaxone, ciprofloxacin, and pyridoxine are medications that can cause analytical interference, leading to false increase or false reduction of the following markers: antinuclear antibody (ANA), 5-hidroxi-indoleacetic acid, uric acid, amphetamine, tricyclic antidepressants, barbiturates, benzodiazepines, bilirubin, catecholamines, ketone, creatinine, digoxin, phenylketonuria, glucose, human chorionic gonadotropin (hCG), methadone, methotrexate, opiates, pentobarbital, perphenazine, salicylate, and tetrahydrocannabinol (THC). The false positive results can produce erroneous interpretations about patents' affection by a health problem they do not present or mean therapeutic failure, whereas false negative results can cause the nontreatment of a health problem that can aggravate, creating future complications to patients, physicians and laboratories. Therefore it is essential that health professionals understand alterations that each medicine can cause in tests[3].

CONCLUSION

Laboratory tests are essential for clinical diagnosis to be correctly established by the physician and the therapeutic choice to be appropriate. An incorrect test involves erroneous treatment, what can cause complications in patients' health in the future. Besides, some drugs can promote alterations in laboratory tests due to adverse effects; that is why it is so important to monitor laboratorial the patients who use them.

In this study we observed that most (67.7%) medications of Remume interfere in one or more laboratory tests. Therefore, this survey bears great relevance, because it promotes dissemination of knowledge about the interference medications cause in laboratory tests, so that pharmacists, physicians and other health professionals are attentive and learn how to identify possible interference during analysis, leading to reduction of wronged diagnoses and unsuccessful monitoring.

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