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 (Remume) 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 Remume 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, antidepressivos tricíclicos y...
**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 (\textit{in vivo}) and analytical (\textit{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 \textit{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, \textit{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                            | -                                  |
| Antacid             | 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                           | ↑ serum AST and ALT levels ↑ serum alkaline phosphatase levels ↓ serum magnesium levels |
| Food supplement     | Pyridoxine                           | False-positive urine methadone ↑ 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 ↓ serum magnesium levels |
|                     |                                      | High doses: ↑ prothrombin time |
| Food supplement     | Folic acid                           | High continuous doses ↓ serum levels of B-complex vitamins (B1, B2, B3, B5, B6, B7, 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 |
| 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                   |                                  |
| Antiarrhythmic      |                              | ↑ 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
| Antianginal drug    | Atenolol                     |                                  |
| Antiarrhythmic      |                              | ↑ serum urea levels              |
|                     |                              | ↓ serum T4 levels                |
|                     |                              | ↓ serum T3 levels                |
| Antihypertensive medication
| Antianginal drug    | Captopril                    |                                  |
|                     |                              | ↑ serum potassium 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           |
|                     |                              | ↓ serum HDL-c levels             |
| Antihypertensive medication
| Antianginal drug    | Clonidine                    |                                  |
|                     |                              | ↑ serum glucose levels           |
|                     |                              | ↓ concentrations of urinary catecholamines and VMA |
|                     |                              | False-positive Coombs test       |
| Antiarrhythmic      | Digoxin                      |                                  |
| Cardiotonic drug    |                              |                                  |
| Antihypertensive medication
| Antianginal drug    | Enalapril                     |                                  |
|                     |                              | False increase in digoxin levels |
|                     |                              | ↑ serum potassium levels         |
|                     |                              | ↓ serum sodium levels            |
|                     |                              | ↑ serum magnesium levels         |
|                     |                              | ↑ serum uric acid levels         |
|                     |                              | ↑ serum creatinine levels        |
|                     |                              | ↑ plasma renin activity          |
|                     |                              | ↑ urinary calcium excretion      |
|                     |                              | ↑ serum cortisol levels          |
| Antihypertensive medication
| Diuretic            | Spironolactone                |                                  |
| 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 | Nifedipine retard | False-positive ANA and direct Coombs test  

| Antihypertensive medication | 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  

### Treatment of skin conditions

| Indication       | Medicine                  | Laboratory change |
|------------------|---------------------------|-------------------|
| Antifungal agent | Ketoconazole              | ↑ serum AST and ALT levels |
| Antifungal agent | Clotrimazole              | ↑ serum AST levels |
| Wound cleaning   | Collagenase + chloramphenicol | - |
| Anti-inflammatory| Decamethasone             | - |
| 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     | - |
| Contraceptive    | Anti-RH immunoglobulin    | - |
| Contraceptive    | Levonorgestrel            | - |
| Contraceptive    | Levonorgestrel + ethinylestradiol | ↑ serum alkaline phosphatase levels, ↑ serum LDL-c levels, ↓ serum T4 levels, ↑ serum T3 levels |
| Contraceptive    | Medroxyprogesterone       | - |
| Antiinfective drug | Metronidazole            | - |
| Contraceptive    | Norethisterone            | - |
| Contraceptive    | Norethisterone + estradiol| - |
| UTI relief       | Oxybutynin                | - |

### Treatment of inflammatory processes and hypothyroidism

| Indication       | Medicine                  | Laboratory change |
|------------------|---------------------------|-------------------|
| Contraceptive    | Medroxyprogesterone       | ↑ 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| 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 |
| Antibiotic                        | Amoxicillin                                      |  
|----------------------------------|--------------------------------------------------|
|                                  | ↓ hemoglobin levels                               |
|                                  | Hemolytic anemia                                  |
|                                  | Leukopenia                                        |
|                                  | Agranulocytosis                                   |
|                                  | Thrombocytopenia                                  |
|                                  | ↑ urine glucose levels                             |

| Antibiotic                        | Amoxicillin + clavulanic acid                     |  
|-----------------------------------|--------------------------------------------------|
|                                  | ↓ hemoglobin levels                               |
|                                  | Hemolytic anemia                                  |
|                                  | Leukopenia                                        |
|                                  | Agranulocytosis                                   |
|                                  | Thrombocytopenia                                  |
|                                  | ↑ urine glucose levels                             |
|                                  | ↑ serum alkaline phosphatase levels               |
|                                  | ↑ serum LDH levels                                |
|                                  | ↑ serum AST and ALT levels                        |
|                                  | ↑ 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                        | 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 LDH levels                                |
|                                  | ↑ serum alkaline phosphatase levels               |
|                                  | ↑ serum creatine phosphokinase levels             |
|                                  | ↑ serum bilirubin levels                          |
|                                  | ↑ serum LDH levels                                |
|                                  | ↑ serum urea levels                               |
|                                  | ↑ serum creatinine levels                         |

| Antibiotic                        | Ceftriazone                                       |  
|-----------------------------------|--------------------------------------------------|
|                                  | 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 creatine phosphokinase levels             |
|                                  | ↑ serum bilirubin levels                          |
|                                  | ↑ serum LDH levels                                |
|                                  | ↑ serum urea levels                               |
|                                  | ↑ serum creatinine levels                         |

| Indication | Medicine | Laboratory change |
|------------|----------|-------------------|
|            |          | 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 creatine phosphokinase levels |
|            |          | ↑ serum bilirubin levels |
|            |          | ↑ serum LDH levels |
|            |          | ↑ serum urea levels |
|            |          | ↑ serum creatinine levels |
| Antibiotic       | Laboratory change                                                                 |
|------------------|------------------------------------------------------------------------------------|
| Ciprofloxacin    | False-positive urine opiates                                                      |
|                  | Anemia (including hemolytic and aplastic)                                         |
|                  | Thrombocytopenia                                                                  |
|                  | Leukopenia                                                                         |
|                  | Agranulocytosis                                                                    |
|                  | Pancreatopathy                                                                     |
|                  | ↑ serum AST and ALT levels                                                         |
|                  | ↑ serum LDH levels                                                                 |
|                  | ↑ serum bilirubin levels                                                           |
|                  | ↑ serum alkaline phosphatase levels                                                |
|                  | ↑ or ↓ serum glucose levels                                                        |
| Clarithromycin   |                                                                                   |
|                  | ↑ serum AST and ALT levels                                                         |
|                  | ↑ serum bilirubin levels                                                           |
|                  | ↑ serum alkaline phosphatase levels                                                |
|                  | ↑ serum urea levels                                                                 |
| Doxycycline      | False increase in urine catecholamine levels                                       |
|                  | ↑ serum AST and ALT levels                                                         |
|                  | ↑ serum bilirubin levels                                                           |
|                  | ↑ serum alkaline phosphatase levels                                                |
| Spiramycin       |                                                                                   |
|                  | False increase in urine catecholamines                                             |
| Erythromycin     | ↑ serum bilirubin levels                                                           |
|                  | ↑ serum AST and ALT levels                                                         |
|                  | ↑ serum alkaline phosphatase levels                                                |
| Systemic anti-infective treatment |                                                                                 |
| Indication       | Medicine                                                                            |
| 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 alkaline phosphatase 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 immunosassys                                       |
|                  | Crystalluria                                                                        |
| Antibiotic       | Benzathine penicillin                                                              |
|                  | False-positive direct Coombs test                                                  |
|                  | False-positive urine glucose using Benedict’s reagent                              |
|                  | Hemolytic anemia                                                                   |
|                  | Agranulocytosis                                                                    |
|                  | 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 | Rifampicin                                                                        |
| Antibiotic       |                                                                                 |

Interference of medicines in laboratory exams
| Indication | Medicine | Laboratory change |
|------------|----------|-------------------|
| Antibiotic | Sulfadiazine | ↑ serum urea levels, ↑ serum creatinine levels, Hematuria, Proteinuria, Crystalluria |
| Antibiotic | Sulfamethoxazole + trimethoprim | False increase in creatinine 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 | ↓ serum and urinary levels of uric acid, ↑ serum alkaline phosphatase levels, ↑ serum bilirubin levels, ↑ serum AST and ALT levels, ↓ erythrocytes, ↑ serum urea levels, ↑ serum creatinine levels, ↓ creatinine clearance |
| 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, ↑ 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 |
### Interference of medicines in laboratory exams

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

| Antipsychotic | Haloperidol |
|---------------|-------------|
|                     | Leukopenia |
|                     | Neutropenia |
|                     | Agranulocytosis |

| Antipsychotic | Haloperidol decanoate |
|---------------|-----------------------|
|                     | ↑ or ↓ serum glucose levels |

| Antidepressant | Imipramine |
|----------------|------------|
|                     | False-negative urine glucose |
|                     | False-positive urine ketone |
|                     | False increase in catecholamines and their metabolites in urine and plasma |
|                     | False-positive Coombs test |

| Antiparkinsonian drug | Levodopa + benserazide |
|-----------------------|------------------------|
| False-negative urine glucose |
| False-positive urine ketone |
| Falsely high levels of catecholamines and their metabolites in urine and plasma |
| False-positive Coombs test |

| Antiparkinsonian drug | Levodopa + carbidopa |
|-----------------------|----------------------|
| False-negative urine glucose |
| False-positive urine ketone |
| Hemolytic and non-hemolytic anemia |
| Thrombocytopenia |
| Leukocytosis |
| ↑ 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 |

| Antipsychotic | Levomepromazine |
|---------------|-----------------|
| Reduces smoking withdrawal symptoms | Nicotine |

| Antidepressant | Nortriptyline |
|----------------|--------------|
| ↑ serum bilirubin levels |
| ↑ serum alkaline phosphatase levels |
| ↑ or ↓ serum glucose levels |

| Anticonvulsant | Oxcarbazepine |
|----------------|--------------|
| 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 |
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; beta-blockers, 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 prednisonate can cause alteration of the hepatic profile as the major biological interference. Thus, it is important to monitor the hepatic 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.

Acetylsalicylic acid, atenolol, carvedilol, clonidine, furosemide, hydrochlorothiazide, propranolol, simvastatin, prednisolone, prednisonate, 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.

The main medicines that cause biological interference in the hepatic function are omeprazole, acetylsalicylic acid, clopidogrel, enoxaparin, heparin, captopril, losartan, methylidopa, 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, albenzadone, ivertecthin, mebendazole, cefotaxime, 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.

The medicines that cause biological interference in renal function, with the risk of increased levels of urea and creatinine reduction and reduction of creatinine clearance, are: clopidogrel, atenolol, captopril, carvedilol, spironolactone, furosemide, hydrochlorothiazide, losartan, methylidopa, 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, 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. Besides, some of those medications are contraindicated or must have the dose adjusted in patients who already present kidney disease.

Linagliptin, acetylsalicylic acid, clopidogrel, atenolol, carvedilol, spironolactone, furosemide, hydrochlorothiazide, methylidopa, 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.

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. 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, methylidopa, 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.

Acetylsalicylic acid, amiodarone, phenytoin, and medroxyprogesterone are able to interfere biologically in the levels of hormones triiodothyronine (T3) and thyroxine (T4), respectively.
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, 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\(^{(16)}\).

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.

REFERENCES

1. Ceará. Secretaria de Saúde. Laboratório Central de Saúde Pública do Estado. Manual de coleta, acondicionamento e transporte de amostras. 5 ed. Fortaleza: SESA; 2019.
2. Ferreira BC, Santos KL, Rudolph SC, Alcanfor JDX, Cunha LC. Estudo dos medicamentos utilizados pelos pacientes atendidos em laboratório de análises clínicas e suas interferências em testes laboratoriais: uma revisão da literatura. Rev Eletrônica de Farmácia. 2009; 6(1): 33-43.

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3. Santos PCJL, Silva AM, Marcatto LR, et al. Interferência de medicamentos utilizados nos exames laboratoriais para monitoramento de dislipidemias e diabetes mellitus. Unisanta Health Science; 2017; 1(1): 18-32.

4. Instituto Brasileiro de Geografia e Estatística. Perfil dos municípios brasileiros. 2017. Available at: https://www.divinopolis.mg.leg.br/sobre-divinopolis/geografia. [Accessed on: 20 July 2019].

5. World Health Organization. Essential medicines and health products. Anatomical Therapeutic Chemical (ATC) classification. Available at: https://www.who.int/medicines/regulation/medicines-safety/toolkit_atc/en/. [Accessed on: 16 Dec 2019].

6. Sociedade Brasileira de Cardiologia (SBC). V Diretriz Brasileira sobre Dislipidemias e Prevenção da Aterosclerose. Departamento de Aterosclerose da Sociedade Brasileira de Cardiologia. Arquivos Brasileiros de Cardiologia. 2017; 4(2Supl. 1): 1-76.

7. Sociedade Brasileira de Diabetes (SBD). Diretrizes da Sociedade Brasileira de Diabetes 2017-2018. São Paulo: Clannad; 2017.

8. Lunardelli MJM, Becker MW, Blatt CR. Lesão hepática induzida por medicamentos: qual o papel do farmacêutico clínico? Rev Bras Farm Hosp Serv Saúde São Paulo. 2016; 7(4): 31-35.

9. Lucas GNC, Leitão ACC, Alencar RL, Xavier RMF, Daher EF, Junior GBS. Aspectos fisiopatológicos da nefropatia por anti-inflamatórios não esteroidais. J Bras Nefrol. 2019; 41(1): 124-30.

10. Porto JR, Gomes KB, Fernandes AP, Domingueti CP. Avaliação da função renal na doença renal crônica. Rev Bras Análises Clínicas. 2017; 49(1): 26-35.

11. Azevedo VE, Lopes MP, Catholino NM, Paiva ES, Araújo VA, Pinheiro GRC. Revisão crítica do tratamento medicamentoso da gota no Brasil. Rev Bras Reumatol. 2017; 57(4): 346-55.

12. Shrimanker I, Bhattarai S. Eletrólitos. [Updated on: 3 May, 2019]. In: StatPearls [Internet]. Ilha do Tesouro (FL): StatPearls Publishing; 2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK541123/.

13. Ferreira FC, Costa SHN, Costa IR. Prevalência de disfunções tireoidianas em pacientes atendidos no Laboratório Clínico do Hospital da Polícia Militar do Estado de Goiás no período de 2015 a 2016. 2018; 50(1): 57-64.

14. Barros ACS, Xavier EM, Reis IS, Carvalho PRB, Oliveira RS, Pacheco FK. Farmacêutico Bioquímico: uma abordagem voltada para o TSH e doenças da tireoide. Rev Saúde e Desenvolvimento Humano. 2018; 6(1): 67-74.

15. Sinco HBC, Peñafiel COR, Sánchez AS, Jaloma JC, Murillo CM, Figueiroa EM. Megaloblastic anaemia: folic acid and vitamin B12 metabolism. Rev Med Del Hospital General de México. 2015; 78(3): 135-43.

16. Ferreira AL, Rocha CP, Vieira LM, Dusse LMSA, Junqueira DRG, Carvalho MG. Alterações hematológicas induzidas por medicamentos convencionais e alternativos. Rev Bras Farmácia. 2013; 94(2): 94-101.

17. Wolf JM, Wolf LM. A review on oral anticoagulant therapeutics in the management of thrombosis. Rev Saude Biologia. 2017; 12(1): 66-78.

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