Drugs that interfere with the results of laboratory tests: an integrative review of the literature

Medicamentos que interferem nos resultados de exames laboratoriais: uma revisão integrativa da literatura

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Abstract
Objective: *To gather scientific knowledge about the use of drugs that cause interference in the results of laboratory tests. This is an integrative review of the literature that used Lilacs, SciELO and Medline as databases and to search for articles; the keywords in Portuguese and English were selected using Bireme's (DeCS) tests: tests Laboratory interactions, drug interactions and interferences. Research published in English, Portuguese or Spanish was published in the form of articles, reviews, dissertations and theses published between 2009 and 2016. Interference caused by medication is a major problem because the patient may be in use of several prescribed drugs, and mainly by self-medication. Among the most commonly used medications, paracetamol causes an increase in alkaline phosphatase and bilirubin, as well as some corticosteroids, such as hydrocortisone that elevates chlorine through salt and water retention. In hematological examinations the reduction of erythrocytes can be provoked by the use of acyclovir, amitripilina, captopril, cimetidina or levodopa. It emphasizes the importance of an effective clinical evaluation of the patient, so that the use of medicines is seen and thus, guarantee quality in the results of the laboratory tests.*

Keywords
Laboratory; Laboratory test; Drug

INTRODUÇÃO

A quality test result depends on the success of all processes involving the laboratory examination, since the collection of material to review and release the result. In the study of metabolism and the action of drugs in the body, it is known that this process leads to some changes in the organic operation itself and also produce metabolites (active or not). The metabolites have the aid of the circulatory system for transport (on excretion and/or site of action) of the urinary system (on excretion), among other systems.[1]

In laboratory diagnostic tests used in most cases of blood and urine, the tests search the type and quantity of substances that indicate or quantify for definition of the diagnosis of a particular disease. These substances and medicines are chemical origin and often resemble in structure. The diagnostic equipment and even chemical reagents using this information to identify and quantify, although not so accurate to differentiate them. Thus, any medicine can be identified as another substance, leading to an erroneous result.[2]

The verification of the quality of the sample according to the material and the tests requested by the doctor is extremely important, because pre-analytic factors may interfere in the results significantly such as medicine, hemolysis, lipemia, hyperbilirubinemia, collection time, practice, time of fasting, alcohol consumption and cigarette use.[3]

It is worth mentioning that the drugs interferes with the harmonious organic operating during the period of use or prolonged use, which this lack of control can also lead to altered lab results, positively or negatively. With that, a high consumption of drugs by the population with both order preventive as the most diverse pathologies, dressing andyess, the study aims to present the drugs that cause interference results in the context of the webbing.

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MATERIAL AND METHODS

The present study uses as integrative literature review method, which presents the objective to gather and summarize scientific knowledge already provided on the use of medicines that cause interference on the results of laboratory tests, allowing to evaluate and condense the evidence available in order to contribute to the development of knowledge on the subject.

For the development of this integrative review the following steps were covered: defining the guiding question (problem) and aims of research; establishment of criteria for inclusion and exclusion of publications (sample selection); Search in the literature; analysis and categorization of studies, presentation and discussion of results.[4] To guide the research, formulated the following question: what medicines cause interference on the results of laboratory tests?

The search was conducted in the following databases: Latin American literature and Caribbean Health Sciences (Lilacs), electronic library Scientific Electronic Library Online (SciELO), Medline – Medical Literature Analysis and Retrieval System online and VHL – Virtual Health Library. For the search of the articles were used keywords in Portuguese and English selected by consulting the health sciences descriptors (DeCS) of Bireme: laboratory tests, drug interactions and interference. Inclusion criteria were: research that cover the use of medications that cause interference in laboratory results, types of these interactions and approaches of innovations, which were published in English, Portuguese or Spanish; in the form of articles, reviews, dissertations and theses published from 2009 to 2016. As exclusion criteria: jobs that do not submit abstracts in their entirety in the databases and the library surveyed, it was in previous years and publications with duplicity.

The productions that established the criteria were selected for this study, and analyzed in their entirety. And so, proceeded with the analysis and organization of publications, in order to describe the results, showing the knowledge produced on the theme proposed.

RESULTS AND DEBATES

The laboratory tests that are used for several purposes in diagnosis of diseases, provide results should be interpreted with the concomitant problems identified in the clinical evaluation of the patient. Thus, the decision of the medical clinic with the help of the examination, confirms or excludes the diagnosis, and thus, set the appropriate therapeutic alternative. In addition, the test can also be used in diagnostic monitoring, that is, the professional has the monitoring of therapy and the development of Pathology.[1]

However, there is no absolutely precise examination, several factors that may interfere with test results such as: patient preparation (such as time of day, fasting or fed, drug injection, smoking), the sample collection form (such as venipuncture method, suitable for collection, identification of the sample), the sample handling (transport, processing, storage), analysis (such as accuracy of the method , accuracy of the method, automation), the issue of the results (with erroneous calculations, printed or verbal communication without clarity), effect of medicines.[5]

The interference caused by medicines constitutes a big problem, because the patient may be in use of multiple prescription drugs, and especially by self-medication. These drug interference can be divided into: *in vivo* physiological effects of the drug and its metabolites, and *in vitro* effects resulting from a physical-chemical property in analytical processes.[6,7] Table 01 presents examples of various medicines with their respective changes in laboratory tests.

The *in vivo* physiological effects can manifest themselves when the drugs induce lesions in tissues or organs, such as the anfoterencina B-induced Nephrotoxicity by medicines that alter organ functions such as simvastatin that increases levels of alanine aminotransferase and aspartate aminotransferase, by the effect of competition for medicines, as the offset of the thyroxine-binding proteins by phenytoin, and the interaction between medications, like amiodarone which increases the effect of Digoxin which, in turn, raising your serum concentration. The *in vitro* effects are manifested in interference of medicine with the method of analysis, as for example, ascorbic acid which in large quantity reduces the level of glucose in serum glucose oxidase method.[7,8]

Even with analysis technologies that have changed over the decades, it is still susceptible to interference by medicines for both enzymatic and immunological methods methods. With the knowledge of these interferences, new methods and apparatus to quantify or identify substance, are entered into the world market. These means of analysis are previously tested and have manuals that indicate the type of medicine interference. These tests follow a study that has a selection of medicine through eligibility criteria. They include in such judicious, items such as: high serum concentration of medicine, knowledge of interference in the method, the frequency of use of the medicine, the *in vivo* relevance, recent documentation.[9]

It is important to note that a medication may interfere with the determination of an analyte specifically for a methodology, without interfering the results of tests for the same analyte accomplished through other methods. As an example, the dosage of glucose in the urine, when performed by enzymatic methods, have their values reduced by Ascorbic acid and levodopa. However, if you used method with Benetict solution, glucose levels can be increased with the use of Ascorbic acid, chloral hydrate and cefalosporima.[1]

Table 01 - Examples of drugs with his appointment, the possible changes in laboratory tests and its mechanism. (Part 1)

Medicine	Indication	Laboratory	Changes	Mechanism of action
Paracetamol	Antipyretic	Alkaline phosphatase	Increase	High dosage associated with ???
	Analgesic1	Bilirubin	Increase	Hepatic injury due to high dosage
		Glucose	Decrease	
		Chlorine	Increase	
		Uric acid	Increase	
		Sodium	Decrease	
		Bicarbonate	Decrease	
		Calcium	Decrease	
		Chlorine	Increase	
Acetazolamide	Ocular hypotensive; Diuretic	Bilirubin	Increase	
		Uric acid	Increase	
		Glucose	Increase	
		Ammonia	Increase	
		Alkaline phosphatase	Increase	
		Sodium	Decrease	
		Bicarbonate	Decrease	
		Calcium	Decrease	
Acyclovir	Initial treatment and prophylactic treatment of mucosal and cutaneous herpes infection	Urea	Increase	Leukopenia
		Alkaline phosphatase	Increase	
		Bilirubin	Increase	
		Creatinina	Increase	Reversible renal failure
Amitriptyline	Antidepressant	Alkaline phosphatase	Increase	
Ascorbic acid	Food supplement	Bilirrubin	Increase	
		Urinary glucose	False (+)	Reagent cupric sulfate
			False (-)	Glucose oxidase method
Baclofen	Relaxing skeletal muscle	Glucose	Increase	
		Ammonia	Increase	
		Bilirubin	Decrease	
Corticosteroids	Anti-inflammatory steroid	Chlorine	Increase	Salt-water Retention
Dexamethasone		Glucose	Increase	Gluconeogenesis
Hydrocortisone		Phosphor	Decrease	Glucose spending
Betamethasone		Potassium	Decrease	Renal loss
Methylprednisolone		Sodium	Increase	Salt-water Retention
Prednisone		Amylase	Increase	
Prednisolone		Cholesterol	Increase	
		Protein	Increase	
		Thyroxine	Decrease	
Buspirone	Anxiolytic	AST	Increase	
		ALT	Increase	
Calcitriol	Food supplement	Cholesterol	Increase	
		Magnesium	Increase	
		Urea	Increase	
Captopril	Antihypertensive	Direct coombs	Increase	
		Cholesterol	Decrease	
		Urinary acetone	False (+)	Use of the reagent based on sodium nitroprusside
		Potassium	Increase	Hypoaldosteronism
		Urea	Increase	
		Creatinine	Increase	
Cephalexin	Antibiotic	Urinary glucose	False (+)	Reagent cupric sulfate
Chlorpropamide oral	Antidiabetic	Direct coombs	Positive	
		Cholesterol	Decrease	
		Sodium	Decrease	Uncontrolled increase secretion of ADH5
Cimetidine	Antiulceroso	AST	Increase	
		ALT	Increase	
Cyclosporine	Immunosuppressant	Potassium	Increase	Decreased excretion
Diazepam	Anxiolytic	Urinary glucose	False (-)	Method of glucose oxidase
Diltiazem	Antianginal	Bilirubin	Increase	
		Uric acid	Increase	Leads to the appearance of the drop

Table 01 - Examples of drugs with his appointment, the possible changes in laboratory tests and its mechanism. (Part 2)

Medicine	Indication	Laboratory	Changes	Mechanism of action
Enalapril	Antihypertensive	Potassium	Increase	Hypoaldosteronism Decreased renal excretion
Ethambutol	Antitubercular agent	Uric acid	Increase	
Furosemida	Antihypertensive Diuretic	Magnesium	Decrease	Diuretic action
		Potassium	Decrease	Diuretic action
		Sodium	Decrease	Diuretic action
		Ammonia	Increase	
		Amylase	Increase	
		Uric acid	Increase	
Gentamicin	Antibiotic	Magnesium	Decrease	Urinary loss of potassium, magnesium
		Potassium	Decrease	Renal tubular toxicity
		Protein	Increase	
		Urea	Increase	
		AST	Increase	
		Alkaline phosphatase	Increase	
		Creatinine	Increase	
		Sodium	Decrease	
		Calcium	Decrease	
Glibenclamide	Antidiabetic oral	Prothrombin time	Decrease	
		Sodium	Decrease	
Indapamide	Antihypertensive diuretic	Glucose	Increase	
		Uric acid	Increase	
		Chlorine	Decrease	
		Magnesium	Decrease	
		Potassium	Decrease	
		Sodium	Decrease	
Insulin	Antidiabetic	Potassium	Decrease	
		Catecholamine	Increase	
Levothyroxine	Repositor hormone	Glucose	Increase	
		Calcium	Increase	Promoter mobilization
Mannitol	Laxative	Sodium	Decrease	Diuretic effect
Metformin	Antidiabetic oral	Bicarbonate	Decrease	Acidosis
		Iron	Decrease	Bad absorption of vit. B12
Metronidazole	Antifungal	Glucose	Decrease	
Omeprazole	Antiulcerous	Gastrin	False	
Oxacillin	Antibiotic		False (+)	
		Urinary protein	False (+)	
Penicillin	Antibiotic	Albumin	Decrease	
		Urinary protein	Increase	
		Protein	False (+)	
		Urinary protein	False (+)	
		Direct Coombs	Positive	
Piroxicam	Anti-inflammatory	Chlorine	Increase	
		Sodium	Increase	
Reserpine	Antihypertensive	Catecholamine	Decrease	
Risperidone	Antipsychotic	Potassium	Decrease	Hypokalemia
		Sodium	Decrease	Hyponatremia
Spironolactone	Anti -hypertensive diuretic	Potassium	Increase	
		Digoxin	False ?	
		Sodium	Decrease	Diuretic Effect
Sulfamethoxazole	Antibiotic	Protein	Increase	
		Uric acid	Increase	
Vancomycin	Antibiotic	Urea	Increase	Nephrotoxicity
Valsartan	Antihypertensive	Potassium	Increase	

Source:Barros; Barros[10]; Santos; Torriani[3]

There are many drugs that interfere in laboratory tests, both *in vitro* as *in vivo*, being the latest also called adverse reactions to medicines. An example of analytical interference is the false increase of the values of fructosamine in serum for patients using the captopril. As an example of interference by physiological effect can cite the enalapril and hydrochlorothiazide that cause changes in dosages of uric acid in serum. Other interference by physiological effect is observed in the use of propranolol and/or levothyroxine on examination of thyroxine (T4) free serum.[11]

It should be emphasized also that several classes of medications, besides the possibility of causing dyscrasias, can interfere with laboratory tests and, consequently, the clinical diagnosis. Hematologic changes induced by drugs can be avoided through measures such as monitoring of medicines, consisting of a pharmacovigilance practice that can be optimized through the mutual cooperation of different health professionals, always seeking the welfare of the patients.[12] Table 02 presents examples of hematologic changes that some medications can cause.

Studies show that the antihypertensive drug class represents complications for the profile lipid. The use continuous of diureticos thiazide (e.g.hydrochlorothiazide and chlorthalidone) raises the levels of total cholesterol (TC), the lipoproteina of low density (LDL) and lipoproteins of very low density (VLDL-C). However, the levels of lipoproteins of high density (HDL) does not suffer changes. The patients with hipertension and diabetes type 2 that make use of these medicaments are at risk before their interference in lipid metabolism.[13]

Table 02 - Haematological Examinations that have interference with medicines

Exam	Interference	Examples of medicines
Protombina time	Increases	allopurinol, cimetidine, diclofenac, dypirone, erythromycin, fluconazole, isoniazid, methyldopa
	Decreases	acetylsalicylic acid, azathioprine, doxycycline, penicillin, rifampicin
Fibrinogen	Increases	salicylates, pyrazinamide
	Decreases	atenolol, prednisone, sinvastantina
Globular sedimentation speed	Increases	carbamezepina, cyclosporine, dexamethasone, misoprostol
	Decreases	budesonide, cortisone, trimethoprim
Mean Corpuscular hemoglobin concentration	Increases	acyclovir
	Decreases	multivitamin
Red cells	Increases	danazol, erythropoietin, hydrochlorothiazide
	Decreases	acyclovir, amitripilina, captopril, cimetidine, levodopa, prilocaine, piroxicam
Mean corpuscular hemoglobin	Increases	oral contraceptives
	Decreases	acetylsalicylic acid
Hematocrit	Increases	atropine, clozapine, carvediol, cefoxitin
	Decreases	enalapril, dypirone, phenytoin, losartan, ofloxacino, theophylline
Hemoglobin	Increases	interferon, ivermectin, hydroxyurea
	Decreases	ampicillin, acetazolamide, ketoprofen, clozapine
Platelets	Increases	cefazolin, danazol, lithium, meropenem, miconazole
	Decreases	albendazole, amioridona, azathioprine, buspirone

Source: Ferreira [12]

It is vital that drug interventions in laboratory tests are evaluated through clinical studies that have purpose to quantify the impact of variations in patient care and laboratory professionals know the limitations of the methodologies employed and the appropriate instructions.

CONCLUSION

Good practices in clinical and toxicological analysis are important to identify, reduce and/or eliminate the sources of potential errors in laboratory diagnosis. This will require continuing education of working professionals in clinical and toxicological analysis. One must be careful with the use of vitamins by the patient, since many of them may interfere with laboratory tests, such as Ascorbic acid which can cause false-negative results for determination of glucose, cholesterol, triglycerides and uric acid.

It is observed that many variables can interfere with the performance of the analytical phase and, consequently, the accuracy and precision of the results of the examinations, vital to medical conduct and, ultimately, for the well-being of the patient.

With that stresses the importance of enhancing the knowledge of professionals to be transmitted the required information to the population and to reduce the occurrence of these interferences.

Resumo

Objetivo: Obter conhecimento científico sobre o uso de drogas que causam interferência nos resultados de testes laboratoriais. Trata-se de uma revisão integrativa da literatura que utilizou bancos de dados da Lilacs, da SciELO e Medline, e, para a busca de artigos, foram selecionadas as palavras-chave em Português e Inglês utilizando-se os testes da Bireme (DeCS): testes interações laboratoriais, interações medicamentosas e interferências. A pesquisa publicada em Inglês, Português ou Espanhol foi publicada sob a forma de artigos, resenhas, dissertações e teses publicadas entre 2009 e 2016. A interferência causada pela medicação é um grande problema porque o paciente pode estar usando várias drogas prescritas e automedicação. Entre os medicamentos mais utilizados, o paracetamol provoca um aumento da fosfatase alcalina e bilirrubina, bem como alguns corticosteroides, como a hidrocortisona, que eleva o cloro devido à retenção de sal e água. Nos exames hematológicos, a redução dos eritrócitos pode ser provocada pelo uso de aciclovir, amitripilina, captopril, cimetidina ou levodopa. Enfatiza-se a importância de uma avaliação clínica efetiva do paciente, de forma que o uso de medicamentos seja observado e, assim, seja possível garantir a qualidade nos resultados dos testes laboratoriais.

Palavras-chave

Laboratório; Teste de laboratório; Medicamento

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