v. 4, n. 26, 2024

International Journal of Health Science

MAIN INTERACTIONS WITH ANTIBIOTICS

Jessica Julia de Mendonca de Moura
Universidade Paulista UNIP
Novo Horizonte-SP
http://lattes.cnpq.br/2461347762136310

Helen Mariana Baldan Cimatti
Universidade Paulista UNIP
Araraquara-SP
http://lattes.cnpq.br/6943066177591497

Abstract: The work aims to expose the main interactions caused by the concomitant use of antibiotics and other allopathic medicines, nutrients and alcohol, highlighting the adverse effects, harmful damage to the patient's health, the effectiveness of the treatment, and in the case of hospitals, the high incidence of hospitalizations for an unnecessary length of time, in addition to discomfort, the appearance of simultaneous pathologies and lack of control of those that already existed. In a simplified way, the topics present the most common cases, exemplifying the antimicrobial classes, their drug interactions (DIs) and the mechanisms that are susceptible to the mutual occurrence of action between two or more substances. Aiming to improve the quality of individual health care, in a conscious and responsible way, playing the role of guiding and monitoring the patient as a whole, which guarantees their well-being. The research was developed through a bibliographical review of a descriptive and qualitative nature, bringing together academic articles by some authors who share similar results. Classes such as Penicillins, Celafosporins, Quinolones, Macrolides, among others, most commonly used in commercial and hospital settings, are also those most likely to interact with other substances in therapy. Therefore, concern during the medical consultation until dispensing and adherence is the point that minimizes the possible risks that the patient can avoid as long as they follow and are correctly guided.
Keywords: Drug interactions, adverse reactions, biotransformation, antibiotics.

INTRODUCTION

Drug interactions are pharmacological responses, where the effects of one or more drugs are altered by the simultaneous administration of drugs or even through concurrent administration with foods, supplements and other substances (FONSECA, 1994; OGA; BASILE, 1994; HANSTEN; HORN, 1996). The responses resulting from the interaction can generate enhancement of the therapeutic effect, reduction of efficacy, appearance of adverse drug reactions (ADR) with different degrees or even cause no change in the desired effect of the medication (OGA; BASILE, 1994). Therefore, the interaction between medications can be useful (beneficial) or cause unpleasant responses not anticipated in the therapeutic regimen (adverse), or even have little clinical significance.

The identification of these interactions is difficult due to the fact that there is great variability between patients (age, biotype), difficult and even late detection, in addition to the degree of dose-dependent complications.

Interactions can be classified into pharmacokinetics, referring to the movement of the drug within the organism, relating (a) changes in distribution speed, biotransformation, absorption and excretion potential; (b) pharmacodynamics, which suggest changes in drug binding sites, decreased action due to competition between receptors and their ligands; (c) effect, when the administration of more than one drug occurs at the same time, which can produce synergy (association) or antagonism reactions (one interferes with the effect of the other); (d) physical-chemical interactions, which occur before the patient comes into contact with the substances, caused by temperature, agitation, pH, inactivating or increasing the therapeutic effect. (OLIVEIRA, 2009).

It is important to highlight the interactions that occur between drugs and food and even with alcohol, as, as they are often common in the individual's diet, they go unnoticed and overlooked, and can cause major problems. Interactions can interfere with the biotransformation of nutrients, in most cases, administering the medicine with a

meal brings some benefits, such as reducing post-disintegration stomach damage, favoring better absorption depending on the physicochemical properties of the drug, or maintaining the stable plasma concentrations of the drug, which could be destroyed by the pH of the medium. However, in certain cases, the presence of food in the gastrointestinal tract can lead to delayed gastric emptying, favoring high toxic absorption, changes in the solubility of the compound, as well as the formation of precipitates and chelates. Simultaneous consumption with alcohol only triggers harmful effects, as it interferes with the process of biotransformation of substances, acts on neurological receptors that alter sensory and motor characteristics, in addition to causing hepatotoxicity, which is often lethal. (LOMBARDO/ESERIAN, 2014).

One of the most alarming cases in terms of drug interactions is the interaction with antibiotics. As it is one of the most used classes in treatments, around 12% of prescriptions in outpatient clinics prevent the proliferation of bacteria or lead to death. It is a comprehensive and effective class, studied since the beginning of medicinal advances to combat pathologically resistant microorganisms. The risk of combining antibiotics is high due to the great action potential and spectrum that most have. Therefore, the dose and route of administration are of paramount importance when choosing the drug combination to obtain a better therapeutic effect. There are many cases of prescriptions that present drug interactions in the same prescription, with inappropriate dosages. The choice of antibiotics that maximize the desired effects and minimize side effects must be analyzed according to the patient's profile based on examinations and observation of responses to associated medications. This reduces the risk of interaction. (FONSECA, 2008; HOEFLER, 2012)

Some consequences of these interactions are the high risk of nephrotoxicity, delayed antibiotic excretion, vascular arrhythmia, hypo or hyperglycemia, among others. Generating discomfort and causing coexisting illnesses. Consequently, hospital stays are longer than expected, costs increase and so do new medications. The pharmaceutical professional working clinically can study these medications and their associations, being able to guide the patient and the medical team to provide improvements in the individual's treatment, also helping in similar future cases. (NEVES/COLET, 2015)

GOALS

GENERAL GOALS

Analyze the action of the main interactions with antibiotics in patients in order to minimize side effects.

SPECIFIC OBJECTIVES

- Identify medications and foods with potential for interaction.
- Check the incidence of cases in hospitals.
- Compare the increase in side effects when there are simultaneous pathologies.

METHODOLOGY

The research was developed through a bibliographical review, or literature review, seeking to show the problem and preventive measures based on published references. However, the method is the set of activities that allow achieving the proposed objective, determining possible errors and assisting in the preparation of the project. (GIL, 2002; MARCONI AND LAKATOS, 2003).

It is based on a descriptive and qualitative nature, developed through articles accessed in the SCIELO databases and CAPES portal and various bibliographical research for this review.

The following criteria were used to select articles that contained the following keywords: drug interaction, allopathic medicines, self-medication, they were used alone and in combination in the research, with the following inclusion criteria: Being published in Portuguese, available online in full and free of charge, and be published in the period between 1994 and 2018.

The procedures for carrying out this work followed the following steps: bibliographic survey, search for articles on the subject, analytical reading, selection, summary and archiving of pertinent information, followed by interpretation of all information collected. From the analysis of a list of references and review articles, those mentioned and the most characteristics on the proposed subject were selected.

The studies addressed issues about possible interactions between allopathic medicines. The work was carried out in accordance with ABNT standards and specifications of the Pharmacy Course at Universidade Paulista – UNIP.

RESULTS AND DISCUSSIONS

In related studies, we analyzed different opinions that complement each other in a final consent that aims at the patient's well-being.

DRUG-NUTRIENT AND DRUG-ALCOHOL INTERACTIONS:

According to Farina and Polleto (2010), the antimicrobial class has a greater focus on interactions with food, directly interfering with the absorption of nutrients depending on the time of administration, which determines whether or not the medication is effective and whether the patient's nutrition will be affected by it.

Some of the main classes of antibiotics in this study are:

- Penicillins (except amoxicillin) have reduced action with food interactions;
- Cephalosporins have a delayed effect, but do not change effectiveness;
- Tetracyclines have reduced action with some minerals that provide the formation of insoluble chelates;
- Chloramphenicol does not interact and taking it with food reduces the - quinolones (cipro and norfloxacin) minimized effect with milk and dairy products.

The authors Moura and Reyes (2002) conclude that oral administration is the most used due to practicality. However, the patient must be aware of the possible consequences, such as interactions between drugs and foods, which in this case will use the same first-pass metabolism for bioavailability. Remembering that the nutritional status must be in balance to achieve successful treatment (for better pharmacokinetic and dynamic performance), as the use of antibiotics is generally more aggressive to the body. In addition to the lack of guidance or correct adherence at home, in hospitals the rates are alarming, as the times between medication administration and meals served rarely undergo supervision. While some drugs depend on this interaction to work at their best, others must have at least an interval of one hour to achieve good performance.

Some examples are cited as:

- Rifampicin: requires an interval of 2 hours before or 3 hours after meals to avoid delaying gastric emptying and reducing absorption, as does ampicillin, which requires an interval of 1 hour before or 2 hours after.
- Ciprofloxacin and tetracycline: they need an interval of 2 hours before or 3 hours after, otherwise they reduce absorption due to complexation of divalent cations in foods such as milk,

yogurt and others rich in Fe, Mg, Ca.

- Isoniazid: needs to be administered on an empty stomach to avoid an increase in gastric pH and a decrease in solubility and absorption.

In addition to food, interactions with alcohol and the damage caused by it also show high rates. In some cases, it may result in a decrease or failure of the therapeutic effect (Table 1). On the other hand, it can also worsen the patient's situation, being classified into 5 severity scales, where 1 is the most dangerous with a consequent decrease.

The article by Lance (2014) reports in detail some of these interactions. About 24% increase in adverse effects comes from these reactions. An antibiotic widely used, mainly in outpatient clinics, subject to these risks is metronidazole, classified as an interaction of severity three (moderate - potentially serious), responsible for unwanted effects such as nausea, cramps, headaches and flushing. Erythromycin's effect is compromised by delaying gastric emptying (orally) and increasing blood alcohol levels through intravenous administration (Table 2).

INTERACTIONS BETWEEN ANTIBIOTICS AND OTHER DRUGS:

The antimicrobial class is extremely broad and complex, important for considerations in drug interactions as it is present in most prescriptions, especially hospital prescriptions, as it establishes microbial control in the body and prevents mild to dangerous infections. Using the concepts of Zanini –Oga (2002) on the associations of this class, we find the main antibiotics most commonly used, and their risks and benefits. Depending on the receptors and binding sites, drugs may have different responses than they would have alone, as shown by some associations:

Penicillins together with gentamicin have a highly effective, beneficial synergistic reaction for endocarditis. Unlike the combination of gentamicin with chloramphenicol, which causes a decrease in the effectiveness of one or both drugs. With erythromycin, protein synthesis is inhibited, interfering with the action; reduce the effect of contraceptives; increases methotrexate toxicity; with lithium the amount of sodium in the blood increases; with diuretics there is an increase in potassium in the circulation; with clavulanate beneficial association for better therapeutic effect.

- Amphotericin B, clindamycin, cyclosporine interacting with aminoglycosides are nephrotoxic; Amphotericin B also potentiates the effect of acyclovir.
- Beta-lactams interact with trimetropin synergistically.
- Cephalosporins with penicillins generate antagonism; with furosemide nephrotoxicity.
- Ciprofloxacin with antacids (Mg/Al/Ca) within four hours reduces absorption.
- Clindamycin with anti-inflammatories, risks of adverse effects on the Central Nervous System (CNS); with erythromycin they compete for the binding site; with muscle relaxants enhances and prolongs the effect.
- Chloramphenicol associated with tetracyclines and penicillins generates antagonism; with barbiturates, it potentiates their effect, and decreases the effect itself; with anticoagulants the risk of bleeding increases; with phenytoin and paracetamol it generates toxicity.
- Erythromycin with carbamazepine generates toxicity; with lincomycin it causes antagonism;
- Levofloxacin with haloperidol generates an additive effect and causes arrhythmia; with insulin R can generate hypo or hyperglycemia.
- Metronidazole together with anticoagulants increase bleeding rates;

International Journal of Health Science ISSN 2764-0159 DOI: https://doi.org/10.22533/at.ed.15942624180310

Most common adverse reactions resulting from drug-alcohol interactions
• Change in drug metabolism • Increased blood alcohol levels • Exacerbation of adverse effects • Gastrointestinal bleeding and inflammation • Hepatoxicity • Disulfiram-type reaction • Reduction in the effectiveness and safety of the medicine • Sedation

Table 1: Side effects due to drug-alcohol interactions.

Alcohol / Drug	Main mechanism of interaction	Gravity	Management	Sources of information
Metronidazole	Pharmacokinetic interaction	Class 3: contraindicated	Reduce consumption of alcohol; survey	*Stockley's Micromedex Hansten&Horn*
Erythromycin	Pharmacokinetic interaction	Class 3	Reduce consumption of alcohol	*Stockley's Hansten&Horn*

Table 2: Classification of the severity of interactions with alcohol.

Source: Teresa Martins Nobre Lança (2014)

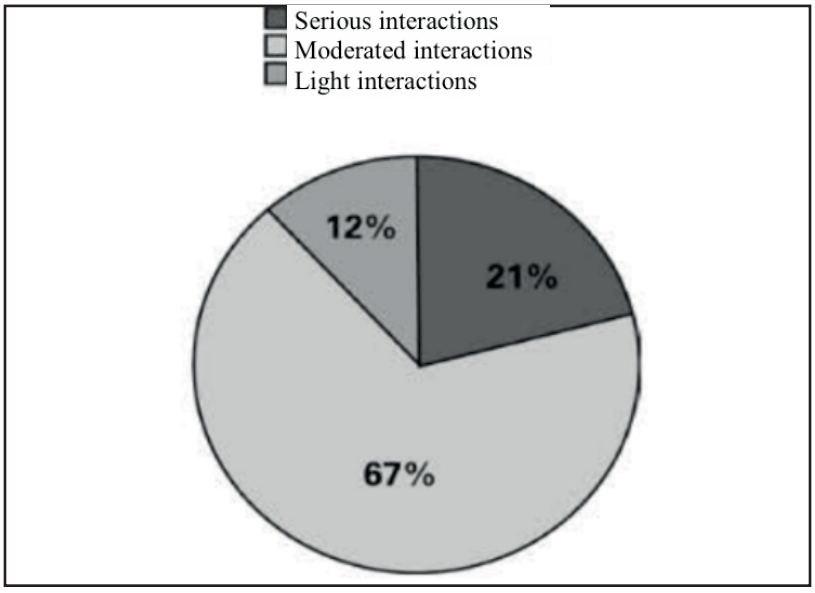

Figure 1: Potential drug interactions in patients' prescriptions at the emergency clinic at Hospital São Paulo, March to July, São Paulo, 2012.

with clindamycin generates synergism.

- Norfloxacin with antacids (Mg/Al) decreases absorption.
- Neomycin enhances the effect of anticoagulants; decreases absorption of vitamin B12.
- Sulfamethoxazole + trimetropine with amiodarone, clarithromycin, amitriptyline, fluconazole generates cardiotoxicity and arrhythmia, with an additive effect.
- Tetracyclines with antacids impair absorption; the effect of oral contraceptives decreases; iron damages intestinal absorption; with barbiturates it generates liver overload.
- Tobramycin increases miconazole concentration.

Antibiotics, because of their high potency, also interfere with oral contraceptives, completely or partially inhibiting their effect. The consequent destruction of the intestinal microbiota caused by antimicrobials acts directly on the metabolism of contraceptives, which lose the release of estrogen resulting from enzymes. Therefore, another form of contraceptive prevention during treatment is necessary (AMADO, CARNIEL, RESTINI, 2011).

MAIN INTERACTIONS WITH ANTIBIOTICS IN HOSPITALS:

According to the studies presented in Moura's thesis (2010), in hospitals, due to the large number of associations in the treatments of patients who spend a few days in hospital, side effects and therapeutic failures arising from interactions are one of the biggest problems faced, and can reach 70% of events. Generally due to lack of knowledge and guidance from the team.

The more serious the case, the more medications are needed to ensure the individual's improvement, in addition to the constant change of employees on duty and consequently changes in treatment depending on the evolution of the pathology, that is, new medications. Even so, such an exchange is necessary to analyze whether the previous treatment was really the most appropriate and the possible changes to be made to improve it. There are also situations in which the use of some pharmacological classes increases the primary health problem, further weakening the patient. For example: gastritis, which can be affected by taking aggressive medications such as antibiotics without proper gastric protection; neurotransmitter diseases that require constant medication and can generate interactions in the treatment of infections; development of adverse effects resulting from the pathology and initial treatment, which will require analgesics, antiallergics, anti-inflammatories, or even other antibiotics. Everything makes drug interactions likely to occur.

Complementing this subject, the main antibiotics used on a large hospital scale, in addition to those already mentioned above, were listed in the Practical Guide to Drug Interactions by Oliveira (2009). Some for exclusive use in hospitals such as:

- Cefazolin with warfarin (moderate degree) increases the risk of bleeding.
- Imipenem + cilastatin interacts with valproic acid (to a greater degree) reducing the action of the anticonvulsant effect of valproic acid; with ganciclovir (higher degree) it causes seizures; associated with cyclosporine (moderate degree) causes neurotoxicity.
- Linezolid with antidepressants, methyldopa, carbidopa is contraindicated as it exerts a potentiating function, with a risk of serotonin syndrome; with rifampicin (moderate degree) efficacy decreases.
- Meropenem and valproic acid (higher

grade) decrease effectiveness against seizures.

- Oxacillin reacts to contraceptives by decreasing hormonal effectiveness.
- Piperacillin + tazobactam with neuromuscular blockers (higher grade) can cause paralysis and respiratory depression; associated with methotrexate increases toxicity.
- Vancomycin with gentamicin (higher degree) and amikacin (moderate) generates nephrotoxicity; interacts with metformin increasing hypoglycemia; with warfarin bleeding may occur; with cefuroxime nephrotoxicity occurs.

FINAL CONSIDERATIONS

It is concluded, from this information survey, that interactions with antibiotics are extremely important, that is, they have a significant impact on the effectiveness and safety of treatment, requiring analyzes of pre-existing comorbidities, use of medications and other substances prior to starting the desired treatment or ensuring its continuity. The wide variety of the class, common prescription and numerous unwanted side effects that can occur, contribute to this.

The negative points of these DIs, in most cases, outweigh the positive points as they reduce the absorption of both nutrients and drugs, resulting in the inhibition of the effect and generating poor functional performance in the body. On the other hand, these interactions can increase absorption, increasing expected or adverse effects, resulting in toxicity and worsening of the clinical picture with longer hospitalization, more health problems and costs that could be avoided.

This highlights the concern in the use of these drugs, which depend on a series of knowledge and adjustments from prescription to administration, through several trained and oriented professionals to then dispense and administer in the safest way possible, knowing the imminent risks and, thus, transmit all the necessary information to guarantee the effectiveness of the treatment, and the patient must also play his role and correctly follow the care given to him.

Many adverse effects occur as if they were a natural part of the pharmacokinetic process, when, in fact, they must be understood as the result of an interaction and not a simple consequence.

At this point, the need for specialized clinical pharmacy in hospitals is evident, so that, together with doctors and nurses, they can perform more specifically the function of monitoring the patient's complete picture and the best therapy to follow. Just like in drugstores at the time of dispensing, guiding the customer to follow the recommendations for their well-being and minimize possible ADRs. However, it depends on establishments providing more training, easily accessible information and educational programs.

REFERENCES

AMADO, L. R.; CARNIEL, T. Z.; RESTINI, C.B.A. **Interações medicamentosas de anticoncepcionais com antimicrobianos e álcool relacionando à pratica de automedicação**. Ribeirão Preto, 2011, p 1451-1460.

BALEN, E.; GIORDANI, F.; KLEIN, K.A.; outros .Disponível em http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0047-20852017000300172&lang=pt/. Acesso em 10 de março de 2018.

FARINA, L.O.; POLETTO, G. **Interações entre antibióticos e nutrientes: uma revisão com enfoque à saúde. Visão acadêmica.** Curitiba, Jan/Jun 2010, p 91-97.

FONSECA, A.L, **Interações medicamentosas**. Rio de janeiro, EPUC, 1994.

GIL, A.C. **Como elaborar projetos de pesquisa**. São Paulo, 2002, p 59-87.

GONÇALVES, F.S. Disponível em https://www.infoescola.com/farmacologia/acao-das-drogas-antimicrobianas/ . Acesso em 25 de março de 2018.

HANSTEN, P.D.; HORN, JR. **Drug interactions monographs**. Vancouver, Applied Therapeutics Inc, 1996.

HOEFLER, R. **Interações medicamentosas. Secretaria de ciência**. Ministério da saúde, Brasília 2008 p. 30-33.

LAKATOS, E. M.; MARCONI, M.A. **Fundamentos da metodologia cientifica**. São Paulo, 2003, p 44-70.

LANÇA, T.M.N. **Interações medicamentosas – álcool com relevância clínica no ambulatório.** Portugal, out/2014, p 54-56.

LOMBARDO, M.; ESERIAN, J.K. **Fármacos e alimentos: interações e influencias na terapêutica.** São Paulo, 2014, p 188-192.
MOURA, C.S. **Interações medicamentosas em pacientes hospitalizados: exposição, relação com indicadores de internação e intervenção.** Belo Horizonte- MG, 2010, p16-64.

MOURA, M.R.L.; REYES, F.G.R. **Interação fármaco-nutriente: uma revisão. Revista de nutrição.** Campinas-SP, Maio/Ago. 2002, p 223-238.

MOURAND, A.M. Disponível em http://www.afepa.org.br/antigo/videos/interacoes-medicamentosas-afepa-on-line/hwLkQCD7_A4.html/. Acesso em 13 de abril de 2018.

NEVES, C.; COLET, C. **Perfil de uso antimicrobiano e suas interações medicamentosas em uma uti adulto do Rio Grande do Sul. Revista de epidemiologia e controle de infecção**. Santa Cruz, Abr/Jun 2015, p 65-71.

OGA, S.; BASILE, A.C.; CARVALHO, M. F. **Medicamentos e suas interações.** Atheneu. São Paulo, 1994.

OKUNO, M. F. P.; CINTRA, R. S.; CAMPANHARO, C. R. V.; BATISTA, R. E. A. **Interação medicamentosa no serviço de emergência.** São Paulo, 2013.

OLIVEIRA, H. C. **Guia prático das interações medicamentosas dos principais antibióticos e antifúngicos utilizados no hospital Julio muller.** Cuiabá, julho de 2009, p1-29.