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# **DRUG INTERACTIONS GUIDE – A TOOL IN HEALTH EDUCATION**

GUIA DE INTERAÇÕES MEDICAMENTOSAS - UMA FERRAMENTA DE EDUCAÇÃO EM SAÚDE

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## ABSTRACT

**Objective:** The present study intended to list the medications used in a Hospital, in order to elaborate a guide for drug interaction and promote a measure of health education. **Methods:** This research was obtained from on-site research of all drugs used and analyzed the interactions between them through the Drugdex (Micromedex)® database. **Results:** There were 60 drug varieties, of which 85% had drug interactions, with 237 possible combinations. The drugs that presented the most interactions were: propranolol hydrochloride, phenobarbital and phenytoin, representing 8.2% each, followed by diclofenac potassium 7.6%, dogoxin 7.6%, diclofenac sodium 7.2%, ciprofloxacin 6.7% and 6.3% levofloxacin. 53% of the interactions were shown to be of the major type, 40% moderate and 6% were the minor type. **Conclusions:** From these data a guide was developed and present to hospital professionals and distributed in the sectors. This study highlighted the relevance of health education as a pharmaceutical service and improving the quality of life of drug users.

Keywords: Drug interactions. Pharmaceutical care. Health education.

#### RESUMO

**Objetivo:** O presente estudo pretendeu listar os medicamentos utilizados em um Hospital, a fim de elaborar um guia para interação medicamentosa e promover uma medida de educação em saúde. **Métodos:** Este estudo foi realizado a partir de pesquisa in loco de todos os fármacos utilizados e foram analisadas as interações entre eles através do banco de dados Drugdex (Micromedex) (B). **Resultados:** Havia 60 variedades de medicamentos, dos quais 85% tinham interações medicamentosas, com 237 combinações possíveis. Os medicamentos que apresentaram mais interações foram: cloridrato de propranolol, fenobarbital e fenitoína, representando 8,2% cada, seguido por diclofenaco potássico 7,6%, digoxina 7,6%, diclofenaco sódico 7,2%, ciprofloxacina 6,7% e 6,3% levofloxacina. 53% das interações mostraram ser do tipo principal, 40% moderado e 6% do tipo menor. **Conclusões:** A partir desses dados, um guia foi desenvolvido e apresentado aos profissionais do hospital e distribuído nos setores. Este estudo destacou a relevância da educação em saúde como serviço farmacêutico e melhoria da qualidade de vida dos usuários de medicamentos.

# **Palavras-Chave**: Interação medicamentosa. Cuidados farmacêuticos. Educação em Saúde.

# 1. Introduction

An intense social struggle, known as sanitary reform, began in the 1970s to build a new national health system: the Unified Health System (UHS), held at the VIII National Health Conference in Brasilia, having as principles the universal and equal access to the actions and services for the promotion, protection and recovery of health care and its maintenance.<sup>1</sup>

Historically, with the development of anatomy, contributions have been initiated to understand the structure of organic systems. At the end of the nineteenth century, with the appearance of the microscope, the existence of microorganisms was discovered as possible causers of diseases, forming, therefore, the essential pillar of the pathology, besides providing contribution and enabling the exploration and understanding of physiology. From then on, the basis for the progress of Pharmacology as an intervention for restoring health was obtained, given the advances that had made possible the studies on diseases, their causes and methods of treatment, as well its prevention.<sup>2</sup>

Health, with a vision focused on the understanding of the pathological processes and the forms of intervention for the resolution of these clinical pictures, can be defined when the individual presents a complete state of physical, mental and social well-being.<sup>3</sup> The quest for the early restoration and maintenance of it has become frequent and for centuries has been the goal of several researchers.

In this context, it is important to highlight the importance of Pharmaceutical Assistance (PA), which is not restricted to the production, acquisition and distribution of medicines, but includes a set of procedures necessary for the promotion, prevention and recovery of individual and collective health, with a shared focus between the drug and its user.<sup>1</sup>

Treatment resulting from the use of drugs is often essential for the cure of diseases in the hospital, but it can also be a cause of illness and death if not administered correctly, which includes the indication, the moment and the way appropriate. The result of the use of various drugs may lead to the increase or decrease of the desired effects as a consequence of pharmacological interaction or to cause adverse effects on the user,<sup>4</sup> and are linked to non adherence to pharmacotherapy. All these occurrences represent types of drug related problems (DRPs), causes of negative results (RNMs), both correlated to pharmacotherapeutic failure.

According to the World Health Organization (2008), the irrational use of drugs involves several behaviors that include: the simultaneous use of many drugs without technical criteria, the inappropriate use of pharmacological classes and inadequate medical prescriptions. Given the importance of the correct use of these active principles, the pharmacist becomes a key player in contributing to the success of pharmacotherapy.<sup>5</sup>

Within the scenario of DRPs, highlighting the drug interactions, which according to the concept given by the Agency of Sanitary Surveillance (ANVISA), through RDC 140/2003, is a pharmacological or clinical response, caused by the combination of drugs, different from the effects of two drugs given individually, and their end result may be the increase or decrease of desired effects and / or adverse events. They occur between medicine-medicine, medicine-food, medicine-laboratory tests and medicine-chemicals. It is worth mentioning that a large number of occurrences were observed in prescriptions given to hospitalized patients, with at least one serious interaction being reported, causing life-threatening drug users or leading to relevant clinical adverse reactions; and 6 moderate ones, that cause changes in the clinical picture of the individual and require a change in their therapy. Research has shown that the interactions of the severe type occur around 1%, and approximately 10% are moderate interactions.

Pharmaceutical care, with the philosophy of practicing approaching the patient's pharmacist - the drug user - provides appropriately indicated, effective and safe drug therapy, when associated with the understanding, willingness and openness of the patient to use it properly, and has real value in the identification of the PRMs, like the drug interactions.<sup>5</sup>

The health care process includes the reception of the complaint, the anamnesis and pharmaceutical semiology, which enables the characterization of the symptoms, identification of the problems and the elaboration of a plan of action for the resolution, through the interventions, in some cases with the participation of other members of the multiprofessional team. The ultimate goal is to meet the health needs of the individual, the family and the community, as well as reduce the morbidity and mortality associated with the use of medicines, bringing to the fore the essence of promotion, protection, recovery and maintenance of health, as well as disease prevention.<sup>5</sup>

To do so, we use pharmaceutical services such as drug reconciliation, therapeutic drug monitoring, pharmacotherapy review, pharmacotherapeutic monitoring, self-limited health problem management, dispensing, health condition management, health screening and education in health,<sup>7-10</sup> as well as various procedures such as the verification / monitoring of clinical parameters and the organization of medications in use by the patient.

With regard to the resolution of drug interactions, it is possible to use many of these services and pharmaceutical procedures concurrently, with emphasis in this work, for the promotion of health education for the professionals of the team, through the elaboration of instructional and clarification materials, with updated references and consolidated, so that the knowledge acquired leads to optimization of pharmacotherapy, verified by the cure or the interruption of the pathological process or the amelioration of signs and symptoms, besides the prevention of the affections, which leads to the accentuation of the quality of life of the individual.

For these purposes to be achieved, the management of the practice of pharmaceutical care must be very well structured, to guarantee the pharmacist all the necessary resources - human, training, financing, infrastructure, provision and maintenance of high quality services.<sup>11-14</sup>

The clinical assignment of the pharmacist is a primordial practice for the promotion of the rational use of medicines (RUM), being fundamental in the prevention or resolution of DRPs, be they drug interactions and / or adverse events. <sup>15</sup>And there is no doubt that the well-performed clinical role will culminate in the appreciation and recognition of the social and differentiated function of this professional by his colleagues and, above all, by society.

It is clear that the inclusion of this professional to healthcare teams providing assistance to users is essential, since differentiated pharmaceutical care is a practice that contributes to the proper use of medicines and to improving clinical parameters of diseases.<sup>15</sup>

In this way, we highlight the mission of this specialist in the chain of patientcentered care, by assuming great responsibility for the improvement of the health services provided, which guarantee safety, better quality and therapeutic adherence and, above all, reaching the rational use of medicines. <sup>16</sup> The preparation of a medication guide for the multiprofessional team can contribute positively and effectively to this patient therapy process, meeting the individual needs of each one of them and as a consequence, avoid medication errors. In view of the above, the objective of this study was to list the drugs used in the Sofia de Castro Hospital, in Alagoa Nova - PB, Brazil, with the purpose of elaborating a drug interaction guide that guides health professionals (physicians, pharmacists, nurses and nursing technicians) and eliminate or reduce the possibilities of these problems related to the concomitant use of drugs, thus constituting a measure of health education, within the philosophy and plan of action of pharmaceutical care.

#### 2. Methods

#### 2.1 Type of research

This study is characterized as descriptive and qualitative, which sought to verify the occurrence, to identify the types of interactions between the medicines available and used in sectors of a municipal hospital, then to elaborate an informative guide approaching and later to carry out the a time of health education for the professionals in the hospital with the intention of promoting health education, by presenting the results obtained, clarifying and making available, for consultation, the prepared guide.

## 2.2 Research location

The research was carried out at the Sofia de Castro Hospital, located in the municipality of Alagoa Nova - PB, located in the mesoregion of Borborema and in the Brejo Paraibano microregion, distant 148.6 km from the capital João Pessoa and 28 km from the municipality of Campina Grande, with territorial area of approximately 120 km<sup>2</sup>, representing 0.30% of the total area of the state. The research was conducted in the following sectors: emergency, delivery room and nursing station.

## 2.3 Data analysis

The data were obtained from in loco research of all the medicines used. The list of medications was organized alphabetically and pharmacologically. The verification of the occurrence and the classification of the interactions was carried out by the Drugdex database (Micromedex<sup>®</sup>), available on the CAPEs website. Lastly, the Drug Interactions Guide was drawn up.

## 2.4 Elaboration of the Guide

With the results, tables and an illustrative and didactic material were prepared to be presented to the hospital management so that it could be analyzed and filed by a multidisciplinary team. After this, the moment of health education was held to expose the Drug Interactions Guide, instruction and clarifications for hospital professionals, and then, availability of the material in the various existing sectors.

## 3. Results

The existing drugs were identified and counted in the hospital, 60 varieties were found, as indicated in Table 1. From this list, the associations between them were analyzed, of which 51 (85%) presented drug interactions, and 9 (15%) did not show any type of combination: trenexamic acid, ipratropium bromide, scopolamine, ambroxol hydrochloride, biperiden hydrochloride, clindamycin phosphate, oxytocin, atropine sulfate and vitamin K.

	Concontration	Pharmaceutical	Thorspoutic class
Medical product	concentration	form	merapeutic class
Trenexamic acid	50 mg/ml	Injectable	Anti-hemorrhagic
Aminophylline	24 mg/ml	Injectable	Bronchodilator /
			antiasthmatic
Amoxicillin	500 mg – 250	Tablet /	Antibiotic
	mg/5ml	suspension	
Bromazepam	3 mg	Tablet	Psychotropic
ipratropium bromide	0.25 mg/ml	Solution	Bronchodilator /
			antiasthmatic
Scopalamine	20 mg/ml	Injectable	Antispasmodic
fenoterol hydrobromide	5 mg/ml	Solution	Bronchodilator
Captopril	25 mg	Tablet	Antihypertensive
Cimetidine	150 mg/ml	Injectable	Antiulcerous
Chloramphenicol	1000 mg/ml	Injectable	Antibiotic
Ambroxol hydrochloride	30 mg/5 ml	Syrup	Expectorant
biperiden hydrochloride	2 mg	Tablet	Psychotropic
ketamine hydrochloride	50 mg	Injectable	Anesthetic
ciprofloxacin hydrochloride	500 mg	Tablet	Antibiotic

#### Table 1 - List of medicines used in the Hospital Sofia de Castro Alagoa Nova/PB.

lidocaine hydrochloride 20 ml Injectable Anesthetic metoclopramide 10 mg/2 ml Solution Antiemetic	ve c c
lidocaine hydrochloride 20 ml Injectable Anesthetic metoclopramide 10 mg/2 ml Solution Antiemetic	c c
metoclopramide 10 mg/2 ml Solution Antiemetic	С
ondansetron 2 mg/ml Injectable Antiemetic	С
Promethazine 50 mg/2 ml Injectable Antiallergi Hydrochloride	с
propranolol 40 mg Tablet Antiarrhythr hydrochloride	nic
Diazepam 10 mg Injectable Psychotrop	ic
Deslanoside 0.2 mg/ml Injectable Cardiotoni	С
diclofenac potassium 50 mg – 25 Tablet / Injection Anti-inflamma	atory
mg/mi	
sodium diclofenac 50 mg – 25 Tablet / Injection Anti-inflamma	atory
mg/ml	
Digoxin 25 mg Tablet Cardiotoni	С
Epinephrine 1 mg/ml Injectable Vasoconstric	tor
Spirolactone 25 mg Tablet Antihyperten	sive
they are 2 mg Tablet Psychotrop	ic
Phenytoin 100 mg Tablet Psychotrop	ic
Fenorbital 200 mg Injectable Psychotrop	ic
Clindamycin phosphate 150 mg/ml Injectable Antibiotic	
dexamethasone sodium 2 mg/ml - 4 Injectable Anti-inflamma phosphate mg/ml	atory
Furosemide 40 mg – 20 Tablet / Antihyperten	sive
mg/2 ml Injectable	
Haloperidol 5 mg Tablet Psychotrop	ic
heparin sodium 5000 UI Injectable Anticoagula	int
Hydrochlorothiazide 25 mg Tablet Antihyperten	sive
Levofloxacin 5 mg/ml Injectable Antibiotic	:
Lorazepam 2 mg Tablet Psychotrop	ic
Losartan 50 mg Tablet Antihyperten	sive
enalapril maleate 10 mg Tablet Antihyperten	sive
Mebendazole 100 mg Tablet Antiparasit	ic
Methyldopa 500 mg Tablet Antihyperten	sive
Metformin 850 mg Tablet Hypoglycen	nic
Metronidazole 250 mg Tablet Antibiotic	:
Midazolam 5 mg/ml Injectable Psychotrop	ic
Nifedipine 10 mg Tablet Vasodilato	r

Norfloxacin	400 mg	Tablet	Antibiotic
Olanzapine	2.5 mg	Tablet	Psychotropic
Omeprazole	20 mg	Tablet	Antiulcerous
Oxytocin	5 ml	Injectable	(stimulant / inducer of
			labor)
Prednisone	20 mg	Tablet	Anti-inflammatory
hydrocortisone sodium	100 mg – 500	Injectable	Anti-inflammatory
succinate	mg		
amikacin sulfate	250 mg	Injectable	Antibiotic
atropine sulfate	0.25 mg/1 ml	Injectable	Anticholinergic
gentamicin sulfate	40 mg/1 ml	Injectable	Antibiotic
morphine sulfate	10 mg	Injectable	Analgesic
terbutanil sulfate	0.5 mg/ml	Injectable	Bronchodilator /
			antiasthmatic
Tenoxicam	20 mg	Injectable	Anti-inflammatory
Tramadol	100 mg	Injectable	Analgesic
vitamin k	10 mg/ml	Injectable	Vitamin
	<b>.</b>	1 1 (2020)	

Source: survey data (2020).

The drugs that showed the most interactions can be seen below (table 2).

Table 2 - Distribution of drugs with the highest number of drug interactions.					
Medication	Ν	%			
Propranolol hydrochloride	19	8.2			
Phenobarbital	19	8.2			
Phenytoin	19	8.2			
Diclofenac potassium	18	7.6			
Digoxin	18	7.6			
Sodium diclofenac	17	7.2			
Ciprofloxacin	16	6.7			
Tenoxicam	16	6.7			
Levofloxacin	15	6.3			
Source: survey data (2020)	15	0.5			

In figure 1, it is possible to observe the level of severity of drug interactions.



The guide on drug interactions can be seen below (figure 2).



# Figure 2 - Section of the drug interactions Guide

Source: survey data (2020).

# 4. Discussion

According to the Micromedex<sup>®</sup> database, there were 237 possible interactions between the 51 drugs shown in Table 1. The drugs that presented the most possibilities of interactions were: propranolol hydrochloride, phenobarbital and phenytoin

representing 8.2%, followed by diclofenac potassium 7.6%, dogoxin 7.6%, diclofenac sodium 7.2%, ciprofloxacin 6.7%, tenoxicam 6.7%, levofloxacin 6.3%, aminophylline 6.3% (Table 2).

Regarding the classification of the interactions by gravity, it is observed that 53% of the interactions are of the severe type, 40%, moderate and 6% constitute the mild type (figure 1).

The severity classified as contraindicated was found in 1% of the situations, pointing to these interactions with the drug metoclopramide hydrochloride, which, when interacting with haloperidol, olanzapine and promethazine hydrochloride causes, if co-administered, an increased risk of extrapyramidal symptoms . Metoclopramide is an active ingredient used as an antiemetic and has a structure similar to chlorpromazine acting as  $D_2$  antagonist.<sup>17</sup>

From then on, the drug interactions guide was elaborated, dividing it by therapeutic classes, the drugs that interact, the severity and the characteristics of the association (Figure 2), and later the material was sent to the hospital and the multiprofessional team (pharmacist, physicians, nurses and nursing technicians) for the promotion of the health education stage, with an explanation of the results obtained, explanation and sensitization, being well accepted, causing reflections on the professionals who position themselves closer to the patient within this scope,

The predominance of the occurrence of interactions between the medications proves the importance of studies with this theme and focus, mainly on medical prescriptions that may present potential "severe" and "moderate" interactions of severity.

Pivatto Júnior et al. <sup>18</sup> presented a study related to drug interactions between drugs prescribed in clinical and surgical wards in a school hospital using the Micromedex<sup>®</sup> database, and identified 485 interactions, with emphasis on propranolol, an antihypertensive drug prescribed in 17 recipes that added 41 interactions, as well as the active digoxin that appeared in 9 prescriptions, promoting 33 interactions.

Lima <sup>17</sup> obtained prescribing data from 102 patients hospitalized in the ICU, where it was verified that 72.5% of these had 311 drug interactions. The principles digoxin, phenytoin and levofloxacin were present in the interactions that occurred. It was also verified that 54.7% of the interactions were of moderate severity, a value higher than that obtained in our study, which according to figure 1 was 40%.

Santos et al. <sup>19</sup> identified 1,440 drug interactions, with 192 different potential interactions. The prescriptions analyzed contained 0 to 15 different potential drug combinations, with the following drugs being present: propranolol and diclofenac.

These data obtained in the literature show that there may be several interactions of drugs prescribed within the hospitals where the patients are submitted to polypharmacotherapy, corroborating the data presented in the present study, which calculated 237 possible combinations to occur among the 51 medicines in the hospital.

Prado et al. <sup>15</sup>, in an analysis of diabetes in the elderly, have shown that for the larger interactions, the drug propranolol interacts with metformin causing hypoglycemia, hyperglycemia or hypertension. This result certifies the data obtained in this research, whose propranolol was the active principle that most presented interactions, going according to the interaction that is expressed in the elaborated guide.

In a study carried out at the Hospital das Clínicas of the University of Minas Gerais, Brazil, 154 potential interactions were observed in the prescriptions, which corresponds to 308 drugs involved, among which phenytoin was one of the most frequent <sup>20</sup>. A similar result was obtained in this study, since phenytoin is one of the drugs used in the Alagoa Nova hospital, as can be seen in Table 1. Thus, it is justified the importance of evaluations and studies in the prescriptions of said hospital, being able to use as source the IM information guide, which has been elaborated.

To Backes <sup>21</sup>, the interactions with metoclopramide are classified, mainly as important or contraindicated, and it was reported among the five most common medications found in prescriptions. A similar result was obtained in the present study, since metoclopramide interacts in a manner contraindicated with haloperidol, olanzapine and promethazine hydrochloride (data set forth in the Drug Interaction Guide). Concomitant prescription of this active principle with other drugs may compromise the patient's life if the prescribing professional does not have the necessary knowledge.

The results of the interactions according to severity obtained in the present study, resemble those described by Evangelista et al. <sup>22</sup> which identified 321 drug interactions, 206 being considered serious (64.2%), 103 moderate (32.1%) and 12 minor (3.7%). It should be noted that 96.3% of the interactions are of the severe and moderate type, and this may represent life threatening or result in a worsening of the patient's condition, requiring medical intervention, he reports.

Drug interactions cannot always be prevented. It is important to disseminate knowledge among health professionals, starting with the pharmacist, which is one of the main tools to prevent these sometimes undesirable events. It is imperative that, based on the information acquired, they opt for safer therapeutic regimens, thus offering quality care and free of damage to the patient's health.<sup>23</sup>

It is indispensable to propose intervention strategies that involve health professionals, especially physicians and pharmacists, who are responsible for identifying potential negative associations <sup>24</sup>, with the pharmacist having to analyze drug interactions and prevent related problems, with the objective of promoting the therapeutic success of the patient <sup>25</sup>. All this can be done through the review and conciliation of pharmacotherapy and, in cases that require greater dedication of study

and to the patient, the pharmacotherapeutic follow-up, being, therefore, examples of pharmaceutical services also available to the family and the community.

The preparation of guides can ease these problems, especially when used to promote health education, as performed at the Sofia de Castro Hospital. On the occasion, the participants learned about the didactic material, clarified doubts about drug interactions and were open to future discussions among the members of the team, placing this topic in order to, therefore, study the IMs more emphatically and, in this way, offer patients of the hospital a safe, rational and effective pharmacotherapy.

It is certified that the drug interactions are a real and worrying fact, since they increase the morbimortality of the patients. Therefore, it is interesting that the hospital guarantees the quality of the care provided to the community, promoting permanent educational actions, by providing tools that guide the health team in relation to the IM, being essential, for this, the role of the pharmacist, besides of course , to stimulate the participation of professionals in scientific events and refresher courses.<sup>4</sup>

#### 5. Conclusion

Based on this study, the relevance of health education as a type of pharmaceutical service and a work tool for and by the multiprofessional team, through which professionals have the opportunity to learn, gain security to instruct other colleagues within the team, as well as the patient who resorts to it, with the purpose of mitigating or eradicating, mainly, those interactions of greater gravity.

The pharmaceutical professional has the fundamental responsibility to control these occurrences, as well as other problems related to drugs, to guide other professionals and to promote instructional measures, as well as to monitor polypharmacy patients, whether in the hospital setting or in any other sector that enabling clarification and rescue of health, establishing and ensuring the well-being of the population.

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