The use of Antibiotics and the Contribution to the Increase in Bacterial Resistance: A Perspective from a Research in a Health unit in Salvador

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Abstract— Antibiotics mark an era of modern medicine, after their discovery, the death rates from infections decreased 100%. However, with the potential of this class threatened by excessive and unnecessary use, associated and emerging infectious diseases arose due to the ineffectiveness of antibiotics. Bacterial resistance has become a public health problem. This paper aims to track a health care unit profile focused on medical care in a BHU in Salvador-BA, Brazil, through a descriptive exploratory study. Identifying the main antibiotics in use, if there are interactions with continuous use drugs, analyzing the factors that contribute to bacterial resistance and discussing the importance of the pharmacist in guiding the use of this class. A literature review conducted from Scielo, Journal of Public Health, WHO, ANVISA support the elaboration of a questionnaire applied to 150 participants from the community covered by the study in health unit after consent by signing the Informed Consent Form. The participants cited eight types of antibiotics, among which there was a prevalence of beta-lactams, and five types of antihypertensive drugs associated with antibiotic use. The analysis of the results identified some drug interactions. Thus, it is necessary to strengthen health education strategies, since the drug dispensing involves until the instructions given to the patient, to minimize the consequences of misuse of this class and avoid cases of bacterial resistance.

I. INTRODUCTION

The development, distribution and using of antibiotics since the 20th century has favored the control of bacterial infections, however, although the discovery of this class has favored drug therapy, the potency of antibiotics is threatened by bacterial resistance, nowadays [1,2,3]. Thus, it is necessary to use strategies that inform and raise awareness about the proper use to control of the evolution of resistant strains [4,5,6].

Bacterial resistance related to the indiscriminate use of antimicrobials is increasing, noticeable; resistance rates are higher in drugs of higher consumption[7,8,9].

Overuse of antibiotics is a serious global public health problem. Regrettable, the increase in established and emerging infectious diseases related to the ineffectiveness

of antibiotics can confirm this [10,11]. Thus, in order to avoid the expansion of this problem, it is necessary to monitor the rationalization of the use of antibiotics, especially those in which they are most used. Pay attention to the duration of treatment, the appropriate dose and the real therapeutic indication are good attitudes [6, 12,13,14].

The drug dispensing involves entire process beginning at the delivery of the medication until the instructions given to the patient. These set of actions will contribute to the rational use of medications, guiding the administration, informing duration of treatment and indicating possible adverse reactions and interactions between medicines and food[10]. Thus, drug dispensing is part of pharmaceutical care, being a guide in the pharmacist's clinical practice and provided by the health system as a service called drug therapy management. (MTM) [15, 20].

Despite pharmaceutical care to be an essential practice for a greater focus on patient, its practice is very limited in health services. Because of it, pharmacist need to be prepared to have attitudes and skills with the health team to provide to the patient and the community guidance on the appropriate use of antibiotics, improving their quality of life[3,7].

The lack of information about the rational use of antibiotics is another issue discussed. The inefficient medical assistance followed by little or no guidance in the act of medication dispensing can be the cause of the lack of information that leads the patient to leave treatment, commit administration errors and make unnecessary use[4,9].

Given the above, the present study aim to outline a profile on the use of antibiotics in patients from a basic health unit in Salvador-BA. In addition, an education intervention project was carried out that addressed the rational use of antibiotics, focusing on the discussion about the importance of the pharmaceutical professional in guiding the correct use of these drugs. This project aimed guide the correct use of these drugs, identifying the main antibiotics used possible interactions with other drugs and identifying the indicators that contribute to irrational use. This work contribute to a better quality of life of patients and the effectiveness of treatment.

II. METHODOLOGY

A. Type of study

This is an exploratory descriptive study with a bibliographic review on antibiotics, from the databases Revista de Saúde Pública, Scientific Eletronic Library Online (SciELO), and sites such as the National Health Surveillance Agency (ANVISA) and the Organization World Health Organization (WHO).

Then, data collection carried out through interviews with 150 participants who attended a Basic Health Unit in the city of Salvador.

B. Period and local study

The study was applied from October to November 2019, with people who attending a Basic Health Unit, in Salvador-Bahia.

C. Population and sample

One hundred and fifty patients contributed to the research, they were of both sexes, aged 18 years and older, who were in the drug dispensing sector, were selected. In an unintentional method, carried out with patients randomly treated at the UBS.

D. Procedures, data collection and analysis

As data, we used the questionnaire with pharmacotherapeutic variables collected during the study period. The variables studied were the characterization of the interviewees: gender, age, and education, type of infection, antibiotics in use, other medicines in continuous use and habits of use of medicines. To assess the interactions and risks associated with other drugs, we used Drugs.com and DrugBank as tools.

The data was used after be approved by the Ethics and Research Committee of Universidade Salvador the Free and Informed Consent Term and the questionnaire signed by the patients who agreed to participate after knowing the research.

Therefore, the produced Health Education Intervention Project aimed to guide patients on how to use antibiotics and raise awareness about problems that may occur due to indiscriminate use. A timetable distributed to the patients provided a guidance about how to use the antibiotic, the appropriate time to use without interfering with other medications in case of continuous use.

E. Ethical aspects

The developed project started after approval by the Ethics and Research Committee (CAEE 22076819.9.0000.5033), according to resolution 466/12 CNS / MS. The Informed Consent Form (ICF) guaranteed the research participant respect for their autonomy rights.

III. RESULTS AND DISCUSSIONS

Small businesses and a hospital complex in Salvador, which serves the population of the neighborhood and other neighbors, surround the Basic Health Unit. This unit has a team of multiprofessionals trained to meet the daily demand in the various health areas, such as clinical, dental, gynecological, nutritional, pharmacological and family

support centers, the latter in conjunction with community agents in the neighborhood.

In this unit, 150 questionnaires applied, for participants of both sexes, who signed the Consent and Clarification Term and thus the results were prepared. The interviewees' aged between 18 and over 60 years old. Most interviewed predominated in the 18 to 30 age group.

Table 1 shows the number of respondents (n = 150) according to gender, age group and education. It was possible to verify that among the interviewees 56% were female, while 44% were male. In comparison with the study carried out in a health unit in Paraíba with hypertensive patients[10], it was identified the high representation of women in relation to men. Notably, people here are able to do the treatment because they are housewives or retired.

Table 1: Characterization of patients: gender, age and education.

		Frequency	Men	Women	%
Gender	**Female**	84	-	-	56.0
	Male	66	-	-	44.0
Age	**Age (years)**				
	18 - 30	52	18	34	34.7
	30 - 40	33	11	22	22.0
	40 - 50	19	11	8	12.7
	50 - 60	24	14	10	16.0
	Over 60	22	12	10	14.7
Education	**Elemantary school incomplite**	63	26	37	42.0
	Elemantary school complite	13	5	8	8.7
	High-school incomplete	8	2	6	5.3
	High-school complete	19	7	12	12.7
	Higher education complite	29	16	13	19.3
	Higher education incomplete	18	10	8	12.0

The majority of individuals aged between 18 and 30 years old (34.7%), followed by 30 and 40 years old (22%), 40 and 50 years old (12,7%), and between 50 and 60 years (16%) and over 60 years old with a frequency of (14.7%). This data is in line with a study on the knowledge of the use of antibiotics by the population of Vizela, where there was a predominance of young people aged between 21 and 30 years[16].

The number of young women (n=34) seeking care at the unit is high when compared to other ages. It occurs because today women are more susceptible to diseases due to hormonal and circulatory changes; this demand for health services tends to be favored in terms of health promotion and prevention. While the male gender usually seeks, medical attention later or in some cases ignores the symptoms[1, 11].

Regarding the level of education, the vast majority have an incomplete elementary level (42%), a worrying data. Due to the low level of knowledge and understanding on the part of these people together the lack information about the correct use of the drugs, these people have become more subject to health problems.

According to the data presented in Table 2, the group of penicillins (Amoxicillin, Amoxicillin + Clavulonate and Penicillin G) were the most used (44%) among the antibiotics prescribed due to their effectiveness; it is generally a first-rate antibiotic choice by professionals. Therefore, the group of first generation cephalosporins (20%), quinolones (16%), macrolides (8%), fluoroquinolones (6%) and finally aminoglycosides (6%) less frequently prescribed.

Table 2: Main antibiotics used by respondents.

Antibiotics	Type	Number women	Number men	Total	%
Amoxicillin	penicillin	10	3	12	26
Amoxicillin + Clavulonate	penicillin	4	0	4	8
Azitromicin	Macrolides	3	1	4	8
Cefalexin	cephalosporin	5	6	10	20
Ciprofloxacin	Quinolones	6	2	8	16
Levofloxacin	Fluorquinolone	1	2	3	6
Penicillin G	Penicillin	3	2	5	10
Tobramycin	Aminoglycoside	1	2	3	6

Among the pharmacological classes of antibiotics prescribed, mainly for women, the most prevalent was amoxicillin (26%). this medication is an antibiotic with a broad spectrum of activity against numerous types of bacterial infections, few side effects, oral administration and stability in acid medium, so this data was expected. Previous studies pointed that this class contains the drugs most commonly used in the treatment of bacterial infections[8].

Cephalexin, belonging to the group of first generation cephalosporins, was the second most prescribed type of antibiotic (20%), mainly indicated for the treatment of the respiratory tract.

Thirdly, the quinolones represented by Ciprofloxacin (16%). This antibiotic is ideal for the treatment of urinary tract infections, prescribed for females in majority, probably due to the anatomical characteristics that make them more suitable for this type infection. A study conducted in Cuba found the inappropriately and indiscriminately use of this antibiotic, due to unnecessary self-medication. Consequently, it leads to increased bacterial resistance[14].

In a study carried out in Vitória - ES in Brazil[1], the prevalence of ciprofloxacin resistance identified at 13.4% of women indicate that if the use of this antibiotic is not judicious, the number of resistant strains will increase.

Penicillin G, prescribed in 10% of cases, is an antibiotic of first choice in the treatment of syphilis, a disease that has been affecting many people, and in rheumatic fever. According to Ordinance n. 3,161 of 12.27.2011, that recommend penicillin use in all Primary Health Care units, in situations where the use is indicated and within the scope of SUS, prescribed by nurse, doctor or pharmacist [17,18].

Morejon[12] reports that multiple mechanisms had impacts with the increase of the bacterial resistance, as the evolutions suffered by the beta-lactamase and the mutations experienced by the penicillin transport proteins causing inactivation of the beta-lactams and misuse of the antimicrobial. Thus, it is necessary to promote the appropriate use of this antibiotic in order to minimize the increase in resistant strains.

Azithromycin, belonging to the group of macrolides, prescribed in 8% of cases, has as its main characteristic a rapid uptake by the systemic circulation and by the tissues after oral administration. Thus, especially in the treatment of aggressive periodontitis, this class is widely used in dentistry due to its high penetration into soft tissues[19].

Another important data are that the antibiotics most often dispensed in a drugstore in the municipality of Jequié-Bahia, were azithromycin, amoxicillin and cephalexin, representing 20, 16 and 10%, respectively, of antibacterial prescriptions[2].

Amoxicillin + clavulonate and azithromycin, used for the treatment of rhinosinusitis, an upper respiratory tract infection, were prescribed at the same frequency (8%). Specifically for the treatment of rhinosinusitis, there is a preference for azithromycin due to the shorter duration of treatment, on a three-day basis, whereas amoxicillin + clavulonate lasts for 10 days[23].

Commonly used in the treatment of the respiratory tract, levofloxacin (6%), prescribed for patients with tuberculosis and community-acquired pneumonia, which usually occurs in winter periods. In some cases, levofloxacin can be indicate for patients who have acute pyelonephritis, a urinary tract infection.

Finally, the class of aminoglycosides, represented by tobramycin (6%), a topical antibiotic indicated for external

infections of the eyes, such as conjunctivitis, a highly contagious disease.

Regarding the infections presented, 50 infected participants were found, oropharynx infections being more prevalent (n = 12), followed by cases of urinary infections (n = 10), others (n = 8), local (n = 7), pulmonary (n = 6), orodental (n = 6) and otitis (n = 1) (Graph 1). During the study period, there were no participants with gastrointestinal infections.
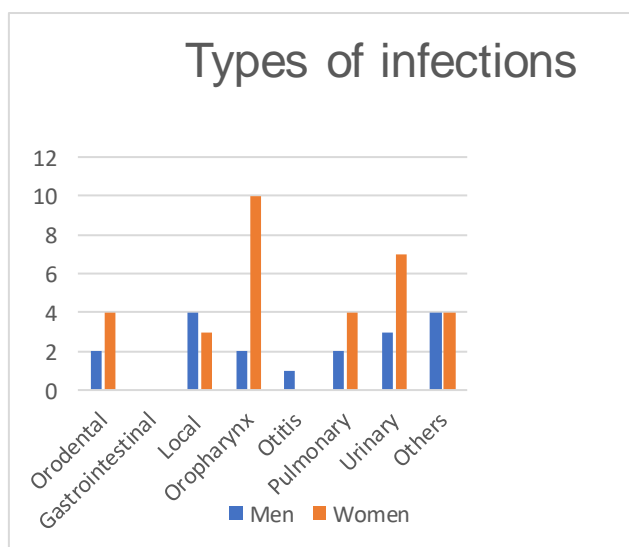
Graph 1- Types of infections presented by the interviewees

Climatic associations, changes in temperature, humidity and rainfall can increase the effects of respiratory tract infections [22]. So, it is worth mentioning that the period of data collection occurred during the months of October and November; the sudden climate change with many rainy periods in Salvador provoked many cases of oropharyngeal infections, especially in who have a previous respiratory problem.

The second most common infection was the urinary tract infection, more prevalent in women, corroborating with Costa[3], who reports that the urinary tract infection has a higher incidence in women, especially when women are sexually active, due to the greatest risk factor during intercourse. Although in males, the cause is related to prostatic pathology.

According to Graph 1, the category "Others" identified in third place, with eight cases of infection, the Sexually Transmitted Infections (STIs) being the most common. The highest incidence of cases was syphilis, a serious infection predominantly sexual, possibly passed from the mother to the fetus. It is essential that there is a counseling

service with the patient when the result of the infection is positive, to encourage adherence to treatment and the performance of tests on sexual partners, to minimize the number of cases and discuss strategies to reduce risks[18].

Among the pharmacological classes of drugs for continuous use, there is a predominance of antihypertensive drugs, highlighted in Table 3 below.

Table 3- Antihypertensive drugs used by the interviewees.

Medicines	Men	Women	Total %
Losartan	10	16	38.2
Hydrochlorothiazide	7	9	23.5
Amlodipine	6	7	19.1
Simvastatin	3	5	11.8
Enalapril	2	3	7.4

Losartan, commonly the second most used antihypertensive agent, was the most used antihypertensive medication among the participants, 38.2%. This medicine belongs to the group of blockers of angiotensin II receptors. Its action is the result of inhibition of vasoconstriction and minimization of aldosterone synthesis. Patients who use this medication must monitor renal function and potassium levels, especially patients who have chronic renal failure because they can worsen hyperkalemia[16].

Secondly, Hydrochlorothiazide, 23.5%, classified as a diuretic from the benzoatiazides class, used as an adjunct to the treatment of hypertension. Hydrochlorothiazide presents drug interaction with beta-adrenergic blockers, such as propranolol, with non-steroidal anti-inflammatory drugs, exemplifying ibuprofen, and therefore inhibitors of the angiotensin-converting enzyme, enalapril[9].

Amlodipine, considered a vasodilator of first choice for the treatment of hypertension, used by 19.1% of respondents. Simvastatin (11.8%), belong to the group of statins, has activity of inhibition of hydroxymethylglutaryl coenzyme A reductase. Finally, enalapril mechanism of action based on the conversion of angiotensin I to II, from 7.4% is the most used drug. Its use associated with a diuretic requires caution due to the risk of pulmonary edema rebound.

Some of these drugs for continuous use may have drug interactions with other antibiotics. Drug interaction,

classified as pharmacological or clinical response, occurs due to the action of a certain drug on the effect of another or in concomitance with the first. Several factors related to this type of interaction, such as prescription, with high risk in cases of polypharmacy, when using multiple medications; the health condition and age of the individual, as each organism can react in a different way.

According to literature descriptions, there are moderate interactions between antibiotics and antihypertensives. Twenty interactions were identified between antibiotics found during the study period and drugs for continuous use. Frame 1 classifies the interactions according to the degree of severity and which interaction presents; the most prominent antibiotic was Ciprofloxacino. Among the drugs of continuous use, Hydrochlorothiazide.

Frame 1: Classification of drug interactions, using the tools Drugs.com and DrugBank.

| Medicines	Interactions and risk	Classification
Amoxicillin + Hydrochlorothiazide	Decreased excretion rate of the antibiotic, resulting in a higher serum level.	Severe
Azithromycin + Simvastatin	Side effect on muscles	Moderate
Azithromycin + HCTZ Or Azithromycin + Amlodipine Or Levofloxacin + HCTZ Or Ciprofloxacin + HCTZ	The serum concentration of Losartana can be increased	Moderate
Ciprofloxacin + Simvastatin	Increased blood levels; liver damage.	Severe
Ciprofloxacin + Amlodipine	Increased blood levels; irregular heart rhythm; liquid retention; heart failure and low blood pressure.	Moderate
Ciprofloxacino + Losartana Or Ciprofloxacino + Enalapril	The risk or severity of hyperkalaemia may increase.	Moderate
Cefalexin + Losartana	Antibiotic metabolism can be decreased when combined.	Moderate
Azithromycin + Enalapril Or Levofloxacin + Amlodipine Or Levofloxacino+ Losartana Or Levofloxacin + Enalapril	Serum antibiotic concentration may be increased	Moderate

Penicillin G + HCTZ Or Penicillin G + Enalapril Or Penicillin G + Simvastatin	HCTZ excretion can be decreased	Moderate
Tobramycin + HCTZ	The risk or severity of nephrotoxicity can be increased	Severe

Amlodipine in combination with ampicillin can increase the bioavailability of antihypertensive drugs by suppressing the metabolic activity of the intestinal flora by antibiotics. Consequently, there is an increase in plasma levels of amlodipine, which can cause an increase in its potential as well as its side effects[21].

Gentamicin is an antibiotic used with caution by cardiac patients, due to its use with diuretics such as hydrochlorothiazide being responsible for causing severe damage. This is because its use leads to the minimization of serum potassium levels, developing cardiac arrhythmias.

During this study, we asked the participants whether the use of the antibiotic in use was under medical guidance and whether it was used correctly. As shown in Graph 2, 82.7% said it was under guidance and 17,3% without. Cases of self-medication, which can contribute to cases of future bacterial resistance, are common.

Graph 2: Medical guidance and use of antibiotics.
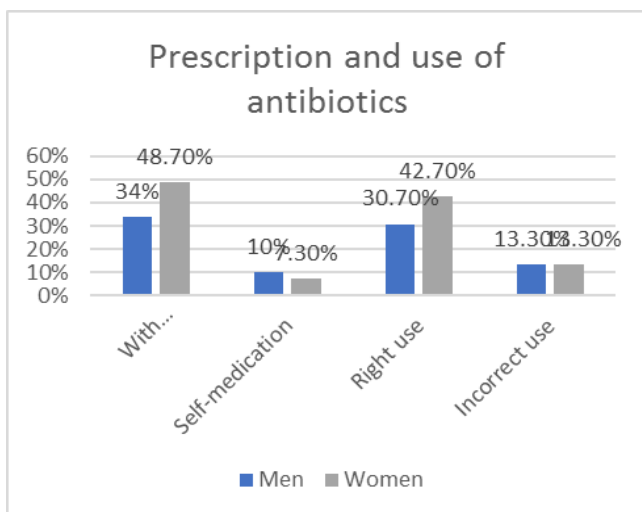
In addition, questions about the correct use of the antibiotic during the treatment period showed that among men, 30.7% said they had followed the treatment correctly and women, 42.7%. However, 26.6% of men and women reported not having followed the treatment correctly (Graph 2) for several reasons, reported in Table 4.

Table 4: Reasons for the incorrect use of the antibiotic.

Reasons				
Reasons	**Men**	**Women**	**Total**	**%**
Wrong time	2	4	6	14.3
Forgetfulness	7	6	13	31.0
They didn't know how to manage	1	6	7	16.7
Misunderstanding	2	1	3	7.0
Others	9	4	13	31.0

Table 4 shows that 31% of respondents reported having forgotten to take the medication and the same proportion reported not having followed the treatment for several other reasons, including the feeling of clinical improvement because they no longer feel the symptoms, leading to interrupting treatment.

In addition, 16.7% of respondents reported lack of knowledge about how to administer the medication, which may have been due to the lack of information. Then, 14.3% reported taking the medication at the wrong time and 7% stated that they change the medication in some situations; especially patients who use continuous medications, these lasts reported difficulties regarding the definition of schedules for each medication.

Correct medication administration is essential. Ribeiro, Pinto and Pedrosa[16] work is in agreement with these results. Situations such as forgetfulness and taken as soon as possible, identified by the authors in 45.2% of respondents, while 29.1% do not take it and continue the

treatment the next day, 18.9% do not take and redo the schedule and 7.8% abandon the treatment.

Thus, even with the passage of time, some people continue to use antibiotics incorrectly, which can contribute to the increase of resistant strains. The extensive and sometimes inappropriate use of antibiotics as well as the delay in the diagnosis of bacterial infections has favored the increase in bacterial resistance[8].

Regarding the practice of self-medication, 51.4% of participants reported using this practice, with the largest adherence of the female population being (30.7%), while (48.7) of both genders refer not to use this practice.
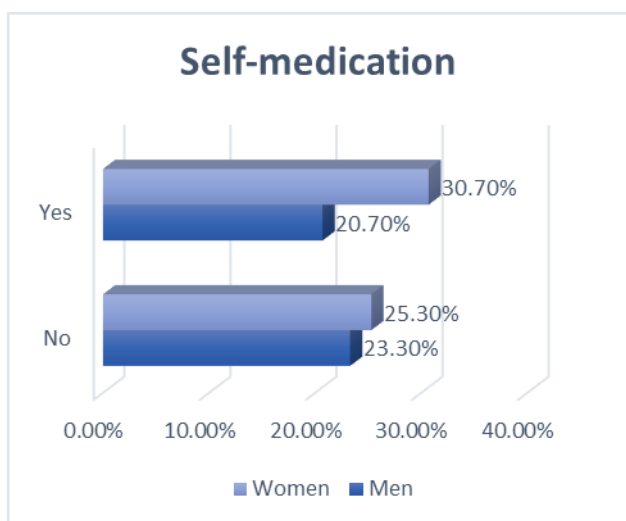
Graph 3: Prevalence of self-medication by participants.

Thus, participants after being asked about self-medication (Graph 3) reported whether they had any symptoms after using the medication on their own. Table 5 shows the frequency and symptoms related to self-medication reported by respondents at the research site.

Table 5: Classification of symptoms presented due to self-medication.

Symptoms				
Symptoms	Men	Women	Total	%
Headaches	18	13	31	20.6
Nausea	7	13	20	13.3
Dizziness	3	12	15	10
Tremors / Palpitations	4	6	10	6.7
Accelerated beats	2	8	10	6.7
	4	6	10	6.7

Hives / Allergies	24	30	54	36
None				

Only 36% of the interviewees reported that they did not feel symptoms after using medication without medical guidance, while 64% reported that they felt some symptoms. These reports are similar to a previous study who observed that, among the self-medicating participants, 15.38% had complications after self-medication[7].

Headaches were the symptoms most reported by 20.6% of participants, followed by Nausea (13.3%), Dizziness (10%), Tremors / Palpitations (6.7%), Rapid Beats (6.7%) and Hives / Allergies (6.7%). Thus, the use of medications on their own may result in serious adverse reactions. Additionally, headaches are one of the main motivators for the practice of self-medication and may be related to other health problems, such as high blood pressure[21].

There are some relations between correct medication and level of education, but also due the lack of information during the purchase of the medication contributes to the wrong use of medicines. Graph 4 shows the percentage of respondents who have knowledge about the expressions used in the prescriptions such as the interval of each dose.
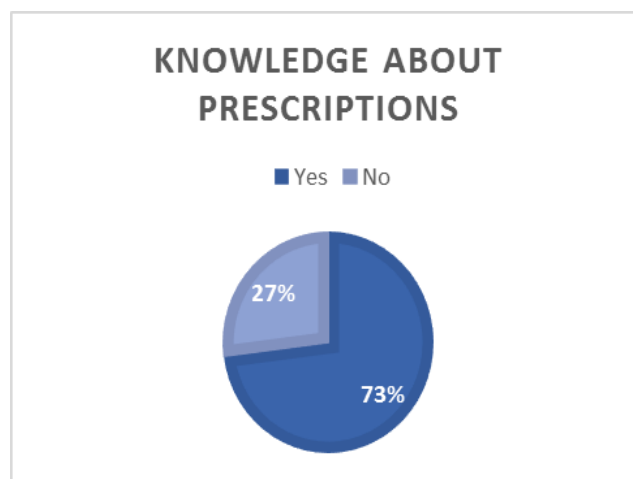
*Graph 4: Classification of respondents who have knowledge about prescriptions.*

Between men and women, 73% of the interviewees claimed to have knowledge about the expressions used in the interval of each dose, and 27% do not know its meaning. Despite being a lower percentage sample, doubts related to the use of the medication can interfere with any pharmacological treatment.

A study carried out in the state of Santa Catarina reported that a good part of the population did not have

enough information about medicines, presenting doubts about how to use them. However, in this same research in the medication dispensing doubts clarified complements the importance of the pharmacist in the orientation of these medications[13].

When asked about the opinion that the use of drugs without medical guidance can lead to health risks, 87.3% of patients (51.3% female and 36% male) stated that using drugs without medical guidance is a health risk, while 12.7% (4.7% females and 8% males) said they thought they were not at risk.
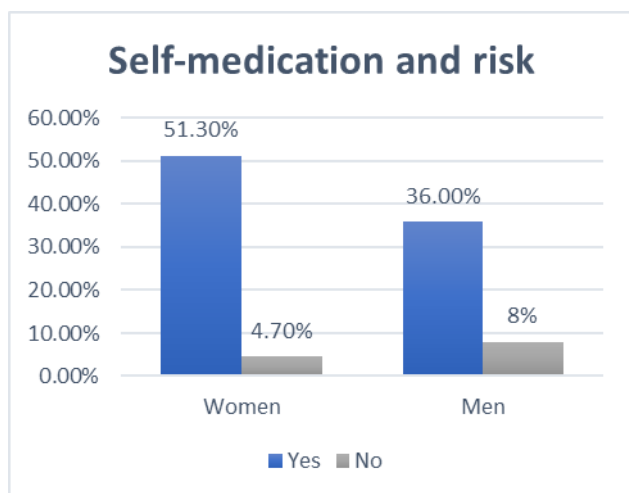
Graph 5: Relationship between medications without medical guidance and health risk.

These data corroborate the findings of Ferraz and coworkers[7] who found that among the self-medicating participants 89.85% are aware of the risks that this may present, while 10.15% are unaware, but continue to use the practice. It is worth mentioning that in this research, 61.54% are aware of the adverse effects of medications, and 38.6% are not.

Therefore, the practice of pharmaceutical care is essential for the rational use of medicines, especially antibiotics. It is through this practice that guidelines must be passed to patients with the objective of success in pharmacotherapy.

Strategies with health education can be intensified in order to guide patients about problems related to the incorrect use of antibiotics, with daily practices of monitoring the prescription, identifying, preventing and solving problems related to some medications.

According to Reginato[16], the pharmacist has a fundamental role in rationalizing the use of antibiotics; actions such as evaluating the prescription for possible occurrences of interactions with other medications,

assisting the patients regarding the dose, duration and especially the time interval between the administrations of the patients. The practice of these actions aims at the proper use of this class of drugs and thus guarantee the effectiveness of the treatment.

Based on the problems observed in the studied population, an Intervention Project was carried out in the health unit with an emphasis on the relationship between the health professional and the patient, in an attempt to help with the problems reported above regarding forgetfulness and medication administration time.

For this, guidelines on the correct use of antibiotics, that emphasizing on their rational use and the importance of adhering to the treatment correctly, respecting the interval between each dose and especially avoiding taking more than one medication at the same time, as well as following with treatment until the end without interrupting on your own were given. Then, the participants received a timetable where they could organize according their own routine the medications, dose and interval.

The presence of a pharmaceutical professional at the health center will provide effective pharmacotherapy to the patient[24]. In view of the above, the insertion and performance of the pharmacist in combating bacterial resistance is essential, since it tends to contribute to the rational use of medicines, especially antibiotics.

IV.   CONCLUSION

This study characterized the profile of the health unit related to the use of antibiotics by UBS patients. The high rate of young women using antibiotics together drugs for the treatment of hypertension is high, which reinforces the importance of the pharmaceutical professional in caring for these patients.

The antibiotics most used were those belonging to the penicillin class, and the main drugs for continuous use were antihypertensive drugs. However, with polypharmacy, it is evident that the amount of prescription drugs can affect adherence to the medication and compromise its therapeutic efficacy. The practice of self-medication is quite frequent as well as factors that contribute to the increase in bacterial resistance.

Thus, it is essential that pharmaceutical professionals follow up with patients who attend the unit for therapeutic monitoring, in addition to guiding and clarifying doubts about the prescriptions to contribute to adherence and improve the patient's quality of life.

In addition, communication must be reliable and objective, in order to minimize the risks of self-medication and the

indiscriminate use of antibiotics. The practice of pharmaceutical care must be reinforced in order to prove the importance of correct treatment, through educational strategies to provide a better understanding by patients.

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