

Pharmacist-led medication reconciliation in outpatients with breast cancer in a teaching hospital

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Abstract

Objective: to define the pharmacotherapeutic profile, drug relaxants and pharmaceutical interventions, adverse reactions in patients with breast cancer using patented intravenous chemotherapy at the pharmaceutical drug conciliation service. **Methods:** characterized as a cross-sectional observational one. Data were collected from medication reconciliation forms and data from spreadsheets of the clinical pharmacy service. **Results:** 31 pharmaceutical drug reconciliations were conducted from September to October 2022, out of a total of 70 patients with breast cancer undergoing intravenous chemotherapy. Most patients, 97% (n=30) were women, with a mean age of 52.51 years. As for education, only 32.3% (n=10) had completed high school. The AC-T protocol (Doxorubicin, cyclophosphamide and paclitaxel) was the most used (38.7% n=12). Most patients 67.7% (n=21) had other comorbidities, with arterial hypertension being the most common. The average number of medications in continuous use per patient was 3.38, with 45.2% (n=14) using 4 or more medications, which characterizes polypharmacy, in addition to the use of medicinal teas, which was identified in 50% (n =12) of patients. Discrepancies were found in these medication reconciliations in 83.9% (n=26) of the patients. In addition, 91 drug relaxants were observed, with an average of 2.9 relaxants per patient. Regarding pharmaceutical interventions, 24 possible interventions were identified, with an average of 0.77 interventions per patient. Most patients (61.3% n=19) had some adverse reaction since the last chemotherapy session. **Conclusion:** the results reinforce the importance of the pharmaceutical professional and medication reconciliation in outpatients, ensuring the safety and effectiveness of treatments.

Keywords: Drug therapy; breast neoplasms; medication reconciliation.

Conciliação medicamentosa farmacêutica em pacientes ambulatoriais com câncer de mama em um hospital de ensino

Resumo

Objetivo: definir o perfil farmacoterapêutico, interações medicamentosas e intervenções farmacêuticas, reações adversas em pacientes com câncer de mama em uso quimioterapia endovenosa submetidos ao serviço de conciliação medicamentosa farmacêutica. **Métodos:** caracteriza-se como observacional transversal sendo submetido e aprovado pelo Comitê de ética, com o número CAAE: 66439017.3.0000.5546. Foram coletados dados a partir das fichas de conciliação medicamentosa e dados de planilhas do serviço de farmácia clínica. **Resultados:** Foram analisadas 31 conciliações medicamentosas farmacêuticas no período de setembro a outubro de 2022, de um total de 70 pacientes com câncer de mama em quimioterapia endovenosa. A maioria dos pacientes, 97% (n=30) eram mulheres, a média de idade foi 52,51 anos. Quanto a escolaridade, apenas 32,3% (n=10) tinham ensino médio completo. O protocolo AC-T (Doxorrubicina, ciclofosfamida e paclitaxel) foi o mais utilizado (38,7% n=12). A maioria dos pacientes 67,7% (n=21) tinham outras comorbidades sendo hipertensão arterial a mais comum. A média de medicamentos em uso contínuo por paciente foi de 3,38, sendo que 45,2% (n=14) usavam 4 ou mais medicamentos o que caracteriza polifarmácia, além do uso de chás medicinais que foi identificado em 50% (n=12) dos pacientes. Encontrou-se discrepâncias nessas conciliações medicamentosas em 83,9% (n=26) dos pacientes. Além disso, foram observadas 91 interações medicamentosas, sendo uma média de 2,9 interações por paciente. Em relação as intervenções farmacêuticas foram identificadas 24 possíveis intervenções, apresentando uma média de 0,77 intervenções por paciente. A maioria dos pacientes (61,3% n=19) apresentou alguma reação adversa desde a última sessão de quimioterapia. **Conclusão:** os resultados reforçam a importância do profissional farmacêutico e da reconciliação medicamentosa em pacientes ambulatoriais garantindo a segurança e efetividade dos tratamentos.

Palavras-chave: quimioterápico; neoplasias da mama; reconciliação de Medicamentos.



Introduction

Cancer incidence and mortality are growing rapidly worldwide. According to estimates by the World Health Organization (WHO) in 2015, it is the first or second leading cause of death before the age of 70 in 91 of the 172 countries in the world, and this epidemiology varies substantially both across and within countries, depending on the economic development degree and on the associated social and lifestyle factors^{1,2}.

In Brazil, 66,280 new cases of breast cancer in women were estimated for 2022 according to the National Cancer Institute (*Instituto Nacional de Câncer*, INCA), the most frequent in this group when excluding non-melanoma skin tumors. However, it is worth noting that breast cancer also affects men, although it is estimated that it only corresponds to 1% of all cases of the disease^{2,3}.

After cancer has been diagnosed, most patients undergo treatments that include surgical procedures, chemotherapy and radiotherapy, which may be one of those or the combination of two or more. Systemic cancer therapy includes chemotherapy (conventional or cytotoxic chemotherapy), hormone therapy, target therapy and immunotherapy. Chemotherapy interferes with cell division through different mechanisms; it can be administered intravenously, orally, intramuscularly, subcutaneously, intrathecally, topically and intraperitoneally, and may be indicated for different purposes such as curative, disease control and palliative⁴.

Chemotherapy can be adjuvant, neoadjuvant and implemented as main treatment for the disease. In adjuvant treatment, it is performed after the surgery to destroy cancer cells that are still left after the procedure. Neoadjuvant treatment is performed before the surgery in order to reduce the tumor size. Currently, for the treatment of breast cancer the most widely used class of chemotherapeutics are as follows: taxanes (such as paclitaxel and docetaxel), anthracyclines (such as doxorubicin) and, in addition to these base analogs, alkylating agents such as 5-fluorouracil, capecitabine, cyclophosphamide and carboplatin⁵.

Many patients have other comorbidities besides cancer, mainly due to advanced age, with polypharmacy (use of 4 or more medications) thus being common since, in addition to chemotherapy, these patients also use drugs for underlying diseases in addition to medications to support the chemotherapy treatment. Polypharmacy usually occurs in 35%-80% of aged patients undergoing treatment for cancer and such medications may interfere with chemotherapy. Another factor that influences polypharmacy is self-medication and the use of herbal medicines^{6,7}.

These factors may trigger Drug-Related Problems (DRPs) that are characterized by undesired events or circumstances involving drug therapy and that may interfere with the desired therapeutic outcomes. DRPs can be classified as need, effectiveness and safety⁸.

Evaluation of the patient by the pharmacist in the process of admission to the outpatient chemotherapy service is of vital importance since, in addition to contributing to the medication reconciliation service, it provides an identification of possible Drug-Related Problems (DRPs) and/or the need for additional information about their treatment.

The medication reconciliation process consists in collecting diverse information about the patient's drug therapy, based on a comparison of the list of medications in use to another information source, such as medical records and medical prescriptions, aiming at harmonizing all the information. In addition to that, other important information is also collected such as allergies, habits, laboratory tests to monitor effectiveness and safety of the treatment and possible adverse reactions to the treatments, which includes pharmaceutical anamnesis. Therefore, it is an important service not only in the hospital environment but also in the outpatient setting, so that drug omissions, duplication, dose errors and drug interactions can be reduced^{9,10}.

In addition to that, this medication reconciliation service evaluates possible drug interactions because other drugs, chemotherapy and support therapies will be administered, in addition to those that are already for home use^{9,10}.

Drug interactions are among the potential DRPs found when analyzing the prescription of these patients. They can occur throughout the treatment and can be with medications that were already used by the patient and/or others that are added during course of the treatment. This issue is of major importance due to the intrinsic characteristics of chemotherapy drugs, such as their narrow therapeutic index and, therefore, drug interactions can increase toxicity or decrease their effectiveness, compromising treatment and patient safety¹¹.

In January 2021, the University Hospital belonging to the Federal University of Sergipe (*Hospital Universitário-Universidade Federal de Sergipe*, HU-UFS) became qualified for high-complexity Oncology care and is currently a reference in the treatment of these patients in Sergipe. Currently in this sector, a mean of 600 chemotherapy sessions/month (intravenous, oral, SC, intrathecal, IM) are performed, and breast cancer has a higher incidence with 51.6% of the cancer types. Thus, the pharmaceutical medication reconciliation service for these patients is of major importance to ensure safety of the patients undergoing chemotherapy treatments, identifying and providing the resolution of possible DRPs. Despite its importance, studies on medication reconciliation in Oncology outpatient settings are scarce, which reinforces the importance of conducting studies of this nature.

Given this context, the objectives of this study were to define the pharmacotherapy profile, to outline the sociodemographic profile, and to evaluate possible adverse reactions and drug interactions identified from the pharmaceutical medication reconciliation service in patients with breast cancer undergoing intravenous chemotherapy treated at this outpatient clinic.

Methods

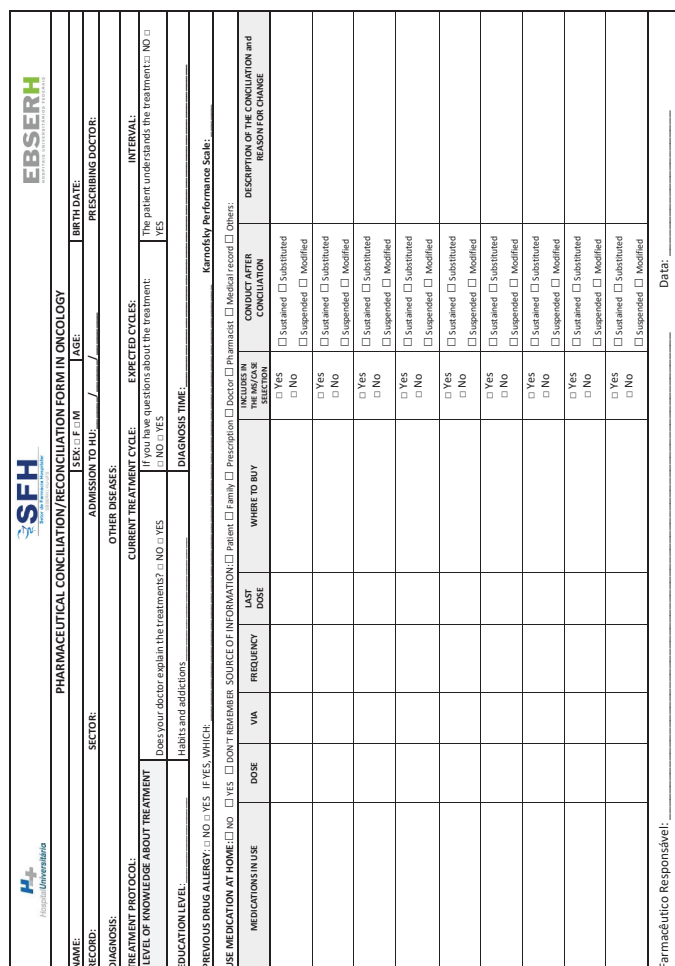
This is an observational, descriptive and cross-sectional study with a quantitative approach, in which the medication reconciliation forms (Figure 1) and data from spreadsheets of the Clinical Pharmacy service at the Oncology/Hematology outpatient clinic of the University Hospital of Sergipe (HU-UFS) were evaluated, of all patients diagnosed with breast cancer undergoing intravenous chemotherapy treatment and subjected to the medication reconciliation service, performed by a clinical pharmacist from September to October 2022.



Medication reconciliation was performed at the time the patient was undergoing intravenous chemotherapy in the outpatient Oncology service, through an interview guided by the medication reconciliation form (Figure 1). The interview was conducted directly with the patient or with his/her caregiver and/or

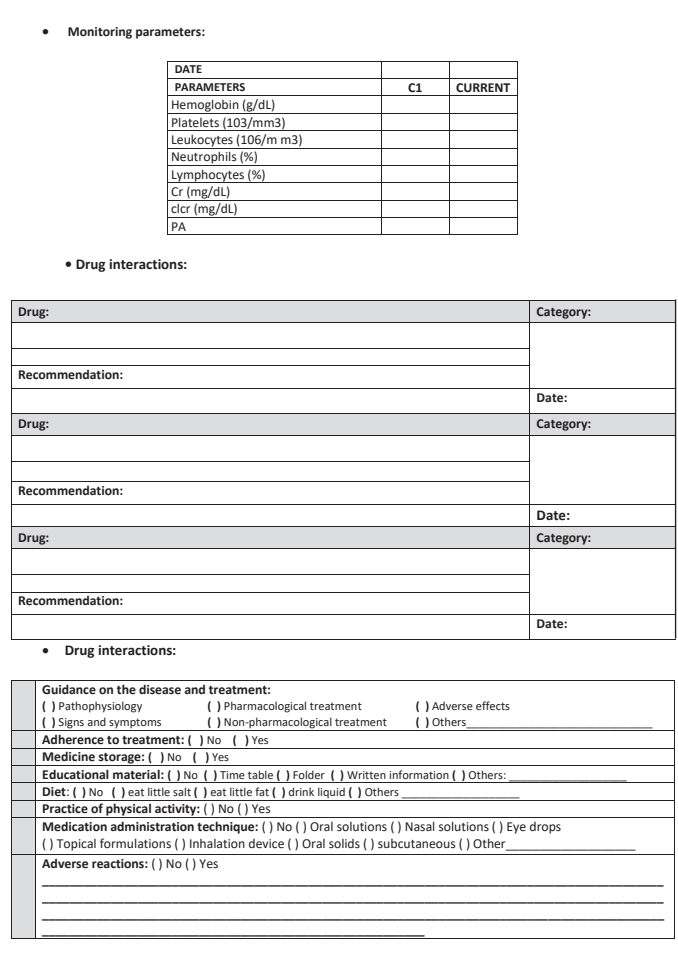
companion in cases where the patient was unable to answer such questions. The online medical records of these patients were also consulted to complement all the necessary information and compare the information provided with the medical and nursing team evolution.

Figure 1. Medication reconciliation form (front and back)



The front side of the form includes sections for:

- PHARMACEUTICAL CONCILIATION/RECONCILIATION FORM IN ONCOLOGY
- Patient information: NAME, RECORD, SEX, AGE, BIRTH DATE, PRESCRIBING DOCTOR.
- DIAGNOSIS: OTHER DISEASES, CURRENT TREATMENT CYCLE, EXPECTED CYCLES, INTERVAL.
- LEVEL OF KNOWLEDGE ABOUT TREATMENT: Does your doctor explain the treatments? YES/NO.
- EDUCATION LEVEL: Habits and addictions.
- PREVIOUS DRUG ALLERGY: YES/NO.
- USE MEDICATION AT HOME: YES/NO.
- DO NOT REASSURE SOURCE OF INFORMATION: Patient, Family, Prescription, Pharmacist, Medical record, Others.
- WHERE TO BUY: Patient, Family, Prescription, Pharmacist, Medical record, Others.
- CONDUCT AFTER RECONCILIATION: YES/NO.
- DESCRIPTION OF THE CONCILIATION AND REASON FOR CHANGE.
- CONDUCT AFTER RECONCILIATION: YES/NO.
- DESCRIPTION OF THE CONCILIATION AND REASON FOR CHANGE.



The back side of the form includes:

- Monitoring parameters: Table with columns for DATE, PARAMETERS, C1, and CURRENT. Parameters include Hemoglobin (g/dL), Platelets (103/mm³), Leukocytes (106/m³), Neutrophils (%), Lymphocytes (%), Cr (mg/dL), clcr (mg/dL), and PA.
- Drug interactions: Section for recording drug interactions with columns for Drug, Recommendation, and Date.
- Guidance on the disease and treatment: Checkboxes for Pathophysiology, Pharmacological treatment, Adverse effects, Signs and symptoms, Non-pharmacological treatment, and Others.
- Adherence to treatment: () No () Yes
- Medicine storage: () No () Yes
- Educational material: () No () Time table () Folder () Written information () Others
- Diet: () No () eat little salt () eat little fat () drink liquid () Others
- Practice of physical activity: () No () Yes
- Medication administration technique: () No () Oral solutions () Nasal solutions () Eye drops () Topical formulations () Inhalation device () Oral solids () subcutaneous () Other
- Adverse reactions: () No () Yes

Among the data collected are sociodemographic and epidemiological ones, life habits, level of understanding about the treatment, drug allergy and medication use at home. In addition to that, diverse information on the cancer classification in relation to the expression of hormone receptors was collected, together with the Karnofsky Performance Scale, which describes a patient's functionality level, being used to measure how the disease affects the patient's daily life skills.

was carried out to its linked professionals. The risk classification of the interactions in Lexicomp® Drug Interactions is an indicator that will assist in clinical decision-making and is divided into A (no interaction known), B (no action required), C (need to monitor therapy), D (consider changing the therapy) and X (avoid combination). On the other hand, the interventions were documented according to their characteristics, whether or not there was a DRP, classification of the DRP involved and description of the intervention.

Information was also collected on medications in use, possible drug interactions, pharmaceutical interventions and adverse reactions. The data were tabulated in a Microsoft Excel® spreadsheet. The medications in use by the patients were analyzed for possible drug interactions using the Lexicomp® Drug Interactions tool and recorded according to the drugs involved and to risk classification. This tool is available in the UpToDate® online database, which is currently one of the main sources of updates on medical issues in the world and is provided by the institution where this study

The data obtained in this research were initially submitted to descriptive statistics and presented in the form of graphs and tables, both in absolute and percentage values.

The study is part of a larger project entitled "Impact of Quality Management in a Hospital Pharmacy service", submitted to and approved by the Ethics Committee, with CAAE number: 66439017.3.0000.5546.

Results

During the study period (from September to October 2022), approximately 70 patients with breast cancer were undergoing intravenous chemotherapy, of which only 31 were submitted to the pharmaceutical reconciliation service as a random sample. Most of the patients were female (97%; n=30). Their mean age was 52.51 years old, with a median of 53. When assessed according to the Karnofsky Scale (KPS), the mean was 89.3% and the median was 90%.

Regarding schooling level, 38.7% (n=12) had Incomplete Elementary School, followed by 32.3% (n=10) with Incomplete High School, 9.7% (n=3) with Complete Higher Education, 6.5% (n=2) with Complete High School, and the same value was also found for Complete Elementary School and for no studies. In relation to life habits, 48.4% (n=15) of the participants denied having a sedentary lifestyle, alcoholism and smoking, whereas 16.1% (n=5) reported being sedentary and 12.9% (n=4) were former smokers.

When analyzing the classification of the breast cancer subgroups, 38.7% (n=12) of the patients in the study were HER 2 negative, 32.2% (n=10) had positive hormone receptors (HER 2, estrogen and progesterone), 16.1% (n=5) were triple-negative and 12.9% (n=4) did not have this information in the service spreadsheets. Table 1 describes the characterization of the 31 study participants.

Table 1. Characterization of the sample

Characteristics		
Gender	n	%
Female	30	97
Male	1	3
Age group		
21-30 years old	3	9.7
31-40 years old	2	6.5
41-50 years old	8	25.8
51-60 years old	11	35.5
61-70 years old	5	16.1
71-80 years old	2	6.5
Schooling level		
Incomplete Elementary School	12	38.7
Complete Elementary School	2	6.5
Incomplete High School	2	6.5
Complete High School	10	32.3
Complete Higher Education	3	9.7
No studies	2	6.5
Life habits		
They deny harmful habits	15	48.4
Sedentary lifestyle	5	16.1
Former drinker	1	3.2
Former smoker	4	12.9
Former smoker and drinker	2	6.5
Classification of the breast cancer subgroups		
HER 2 negative	12	38.7
Positive hormone receptors	10	32.2
Triple-negative	5	16.1
They did not have this information	4	12.9

The most used chemotherapeutics in this service were cyclophosphamide, doxorubicin, paclitaxel, docetaxel, carboplatin and trastuzumab, with the AC-T protocol (doxorubicin, cyclophosphamide and paclitaxel) as the most used (38.7% n=12).

Regarding other comorbidities, 67.7% (n=21) of the patients had other diseases, including systemic arterial hypertension, anxiety, diabetes *mellitus*, dyslipidemia, hypothyroidism, osteoarthritis, seborrheic dermatitis, bipolar disorder, gastritis and cardiac arrhythmia.

In relation to the use of continuous-use medications, all patients in the study had previous pharmacotherapy. The mean number of medications in continuous-use per patient was 3.38 per patient, among which 54.8% (n=17) of the patients reported using from 1 to 3 medications and 45.2% (n=14) used 4 or more medications at their homes, which characterizes polypharmacy. These medications were used to treat comorbidities and pain and/or as support for cancer treatment. Of the 14 patients who used 4 or more medications, the majority (85.7%; n=12) had other comorbidities. Many patients were observed to be on proton pump inhibitors such as omeprazole and pantoprazole. Also on continuous-use medications, 83.9% (n=26) of the patients identified unintentional discrepancies in medication reconciliation that were observed when comparing the drugs reported in the reconciliation interview and those reported in the medical evolution in the patient's online medical record.

Most of the patients (61.3%; n=19) presented some adverse reaction since their last chemotherapy session. Among the most cited are nausea, vomiting, asthenia and hypotension.

Regarding the concomitant use of medicinal and chemotherapeutic teas, most of the patients (51.6% n=16) drank teas mainly to manage adverse reactions to the cancer treatment. We can mention chamomile, lemon balm, holy grass, Chilean *boldo*, fennel, soursop, nettle and São Caetano melon among the most common.

From the data of the 31 pharmaceutical reconciliations analyzed, 24 interventions were identified, presenting a mean of 0.77 interventions per patient treated. Of those, 50% (n=12) were related to the use of medicinal teas, as most patients used them inappropriately from preparation to dosage and use mode. These data are organized in Table 2.

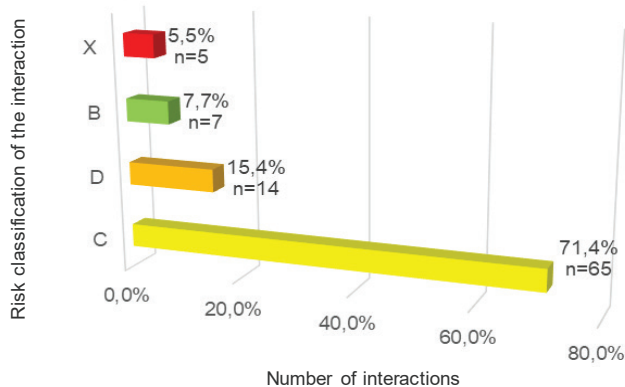
Table 2. Characterization of the pharmaceutical interventions carried out from the patients' medications conciliation

Pharmaceutical interventions identified		
Type of relationship	n	%
Related to medications	10	41.7
Related to life habits	2	8.3
Characteristics		
They were not related to DRPs	18	75%
Need DRP	2	8.3
Effectiveness DRP	2	8.3
Safety DRP		
Description of the intervention		
Health education	21	87.5
Monitor signs, symptoms and laboratory tests	2	8.3
Suggest drug therapy initiation	1	4.2

Another 41.7% (n=10) of the interventions were related to medications and 8.3% (n=2) to life habits. Regarding the characteristics of the interventions, 75% (n=18) were not related to DRPs, 8.3% (n=2) were related to need DRPs, 8.3% (n=2) to effectiveness DRPs and 8.3% (n=2) to safety DRPs. As for the description of the type of intervention performed in the face of such problems, 87.5% (n=21) were health education for patients, 8.3% (n=2) corresponded to monitoring signs, symptoms and laboratory tests and 4.2% (n=1) suggested initiating drug therapy.

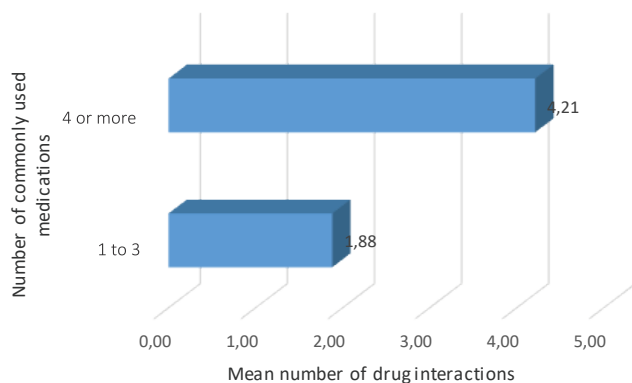
Potential drug interactions were identified in all the study patients. In total, 91 drug interactions were observed, with a mean of 2.9 interactions per reconciliation. According to Lexicomp® Drug Interactions, the risk classification of the interactions was as follows: C (need to monitor therapy) = 71.4%; D (consider changing the therapy) = 15.4%; B (no action required) = 7.7%; and X (avoid combination) = 5.5%. These data can be compared in Figure 2.

Figure 2. Risk classification of the interactions found



In relation to the drugs involved in potential interactions, 31.9% were between chemotherapeutics, 35.2% were between chemotherapeutics and other medications, and 33% were between drugs other than chemotherapeutics. When comparing the number of medications commonly used by the patients and the number of drug interactions, it was observed that patients who use 4 or more medications were exposed to more drug interactions (mean of 4.21), as described in Figure 3.

Figure 3. Comparison between the number of commonly used medications and the mean number of drug interactions.



Discussion

Before being diagnosed with cancer, many patients already have other comorbidities as underlying diseases, mainly and oftentimes due to advanced age and lifestyle, with habits such as smoking and alcohol consumption. This fact was evidenced in this study, where 67.7% (n=21) of the patients had other underlying diseases, therefore with a higher risk of polypharmacy and, consequently, of drug interactions and DRPs. Systemic arterial hypertension was the most prevalent comorbidity in the patients of this study, which is also observed in the study by Fowler *et al.* (2020)¹².

With regard to schooling level, it is important to note that only 32.3% (n=10) had Complete High School, which requires health professionals to adapt the guidelines provided in order to improve these patients' health literacy, which consequently helps to improve their quality of life¹³.

The importance of pharmacists and medication reconciliation in outpatients is also evidenced by the fact that some discrepancy was identified in 83.9% (n=26) of the medication reconciliations performed, a result that is higher than the one identified by Darci *et al.* (2022): 74.1%. Thus, it is understood that the discrepancy in such information makes it impossible to adequately monitor drug interactions and DRPs; considering that, in a systematic review, Herledan *et al.* (2023) identified that a mean of 95% of cancer patients present DRPs; in addition to Rodrigues *et al.* (2023), who found that there were potential drug interactions with clinical relevance in 27.5% of the patients treated with oral antineoplastics^{6,14,15}.

Dissemination in the service about the information of medications in continuous-use by the patients is important so that signs of adherence problems and drug interactions can be observed, and pharmacists can play a fundamental role in this context, mainly through medication reconciliation¹⁶.

According to BIBI *et al.* (2021), it was evident that the more medications a patient uses, the more likely they are to be exposed to drug interactions, thus representing a risk factor that was also observed in this research. Both situations, adherence problems and drug interaction, can interfere with the cancer treatment of these patients, with the possibility of reducing effectiveness and/or increasing toxicity, thus directly influencing the quality of life of these individuals¹⁷.

In Brazil, it is known that there is wide use of herbal medicines and medicinal plants, which is due to historical and cultural aspects and to the broad availability of species in our country. Thus, many patients reported drinking teas to manage adverse reactions during chemotherapy treatment^{11,18}.

This is relevant information for the entire multiprofessional team identified in this study, as the therapeutic index of antineoplastic chemotherapeutics is oftentimes narrow and herbal medicines and medicinal plants can alter the expression of several enzymes related to the biotransformation of medications; therefore, drug interactions can have undesirable consequences and may even compromise the person's life in some cases¹⁹.

The Memorial Sloan Kettering Cancer Center's About Herbs website (www.abouterbs.com) is currently a reliable scientific basis to seek information on medicinal plants, although the information is still insufficient. Thus, the use of medicinal plants should be judicious, mainly in patients who are undergoing chemotherapy treatments^{18,20}.

Some protocols have a greater potential for drug interactions, both with each other and with other medications. An example is the AC-T protocol (doxorubicin, cyclophosphamide and paclitaxel), where doxorubicin interacts with cyclophosphamide and may increase the cardiotoxicity of doxorubicin. Paclitaxel also interacts with several medications, with emphasis on most antihypertensives, as paclitaxel itself has an adverse reaction to hypotension that can be potentiated by the use of antihypertensives such as losartan and amlodipine, which was evidenced in this study, with the need to suspend some antihypertensives, which was a medical action independent of pharmaceutical action. Therefore, promoting health education through pharmaceutical interventions for these patients is of major importance and can be implemented through the use of tools for self-monitoring of blood pressure values, in order to help identify possible DRPs^{17,21,22}.

As study strengths, we can highlight the importance of medication reconciliation in an outpatient environment as an instrument to promote patient safety and its implementation in an environment that has been little studied, in addition to reinforcing the importance of health education. As weaknesses, we can list the reduced number of patients seen during the study period and time.

Conclusion

This study made it possible to establish the characteristics of the pharmacotherapy profile of the patients with breast cancer treated at HU-UFS. It was also observed that the use of herbal medicines and medicinal plants is widely disseminated among these patients. It is noteworthy that this use was oftentimes related to the treatment of adverse reactions from chemotherapy treatments, showing lack of information among the patients about support medications such as antiemetics. Associated with the fact that most patients have low schooling levels, the aforementioned highlights the importance of health professionals in improving these patients' health literacy in order to seek to promote a better quality of life for them.

Another important fact concerns the drug interactions, where a mean of 2.9 interactions per reconciliation was identified. In addition to that, 83.9% (n=26) of the medication reconciliations had some discrepancy.

Therefore, it is concluded that pharmaceutical professionals and medication reconciliation in outpatients are essential to ensure effectiveness and safety of the chemotherapy treatments.

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Collaborators

Authors CSA and MJS took part in design of the project and data research. CSA, FJM, SMS and MJS took part in writing and reviewing of the final text. LMA, JORM and VPC contributed to the methodological analysis, literature review and review of the final text.

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Declaration of conflict of interests

The authors declare that there is no conflict of interests.

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