

Assessment of risks of uncontrolled use of drugs with expected effectiveness against COVID-19 by patients with breast and prostate cancer at the pre-hospital stage

ABSTRACT

Aims: To reflect on the impact of self-medication in times of pandemic COVID-19 for patients undergoing treatment for breast or prostate cancer.

Study design: this is a reflective study with a qualitative approach based on the documentary analysis of the package inserts issued by ANVISA or by the manufacturers of the analyzed drugs.

Place and Duration of Study: Integrated Health Research Laboratory from the UFRJ-Macaé Multidisciplinary Center, between March 2020 and December 2020.

Methodology: The documents analyzed were the package inserts of the five main drugs used by the Brazilian population during the first year of the pandemic, from March to December 2020, as well as the package inserts of some of the main antineoplastic drugs used to treat breast and prostate cancer. All inserts were issued by ANVISA or by the drug manufacturer. We chose to reflect on the impact of self-medication on the symptoms of COVID-19 and the most common cancers in women (breast) and men (prostate).

Results: In Brazil, where, according to the Brazilian Association of Pharmaceutical Industries, around 80 million people are self-medicated, the poor quality of the supply of medicines, non-compliance with the obligation to present a medical prescription and the lack of information and education in the general population justify the concern with the quality of self-medication practiced in the country. The present study focused on the five main drugs described in the literature most used for self-medication and often with explicit contraindication by health agencies such as WHO and ANVISA, namely: chloroquine, hydroxychloroquine, ivermectin, vitamin D, dexamethasone.

Conclusion: The study suggests that the analyzed drugs can harm the health of patients undergoing cancer treatment, as it shows that they can increase the risk of liver, kidney, heart or gastrointestinal damage. It is concluded that self-medication performed by a patient with breast or prostate cancer can bring moderate to severe risks with regard to drug interaction and metabolization pathways, as some of these drugs are mistakenly used as a form of prevention and treatment for COVID-19 not only do they have dangerous adverse effects for cancer patients, but they can also potentiate the adverse effects caused by cancer treatments.

Keywords: COVID-19, Self-medication, Cancer, Adverse effects.

1. INTRODUCTION

One of the biggest public health problems in the world, Coronavirus Disease (COVID-19), was declared a pandemic disease on March 11, 2020 by the World Health Organization (WHO). His prelude took place in Wuhan (China) in December 2019 and currently acts in 188 countries/regions[1]. In view of the mechanism of this disease and the widespread spread of Coronavirus, which caused 542,798 deaths worldwide from December 2019 to

July 2020 [2] and 616,018 deaths in Brazil from February 26, 2020 to January 2, 2022 being the second country in the world with regard to deaths from Coronavirus[3].

COVID-19, caused by the SARS-CoV-2 virus, can be transmitted before (virus incubation period) and after the manifestation of symptoms, besides having numerous forms of transmission, such as: saliva droplets excreted during a dialogue, coughs, sneezing and contact with infected individuals[1]. These factors, together with the absence of vaccines and drugs for the treatment of this disease, have contributed to the increase in self-medication in the population, which has generated immeasurable adversities.

Due to the spread of COVID-19 and its pathogenicity, several existing drugs were tested to be reallocated and used in the treatment of this disease. On March 27, 2020, the Brazilian Ministry of Health defined the use of Hydroxychloroquine and Chloroquine as a complementary therapy in the treatment of critically ill patients, however, due to the high demand for these antimalarials in pharmacies, the National Health Agency (ANVISA) ordered Hydroxychloroquine and Chloroquine as special control drugs, to curb the self-medication of the population and ensure that patients have access to the drug[4].

Self-medication is the act of using a drug without recommendation or medical guidance for pain relief and health promotion, this practice is the result of numerous factors, such as difficulty in accessing the health system, conviction in the effect of the drug and urgency in pain relief[5].

In Brazil, where, according to the Brazilian Association of Pharmaceutical Industries, around 80 million people are self-medicated, the poor quality of the supply of medicines, non-compliance with the obligation to present a medical prescription and the lack of information and education in the general population justify the concern with the quality of self-medication practiced in the country.

Analogous to this, in this period of pandemic hysteria due to the scarcity of information about COVID-19 and the absence of medicines to deal with this disease, the population increasingly resorted to self-medication, however, the indiscriminate use of medications can promote various adverse effects, intoxications, generate resistant microorganisms, dependencies and in severe cases can lead to death[6].

In this context, cancer patients who are in constant contact with the health system and who, as a result of treatment and cancer itself, may present immunosuppression or even an increased immune response, in some circumstances[7], are exposed to COVID-19, self-medication and its risks, in addition to the worsening of the disease itself. From this angle, the analysis of the impact of COVID-19 on breast cancer, the second cancer with the highest incidence in the world, being the most incident among women, with the exception of non-melanoma skin cancer[8], and prostate cancer, the second type most manifested by the male population[9], in the Unified Health System (SUS) is vital.

An estimated 66,280 new cases of breast cancer are estimated for each year of the triennium from 2020 to 2022[8] and 65,840 new cases of prostate cancer for each year between 2020 and 2022[9] however, the pandemic scenario has negatively affected the health system with regard to the treatment of neoplasms, through factors such as: late diagnosis, limited access to different types of therapies and absence of a protocol to deal with the current situation[10], the tendency is that the sick have their condition worsened and that the treatments become more costly for the Single Health System (SUS).

Therefore, this article aims to reflect on the impact of self-medication in times of pandemic COVID-19 for patients undergoing treatment for breast or prostate cancer.

2. MATERIAL AND METHODS

This is a **reflective** study with a qualitative approach based on a documental analysis.

The documents analyzed were the leaflets of the five main drugs used by the Brazilian population during the first year of the pandemic, from March to December 2020, as well as the leaflets of some of the main antineoplastic drugs used for treatment against breast and prostate cancer. All leaflets were issued by ANVISA or the manufacturer of the drug.

We chose to reflect on the impact of self-medication on the symptoms of COVID-19 and the most common cancers in women (breast) and men (prostate)[11]

3. RESULTS

The present study focused on the five main drugs described in the literature most commonly used by self-medication and often with explicit contraindication by health agencies such as WHO and ANVISA, which are: chloroquine, hydroxychloroquine, ivermectin, vitamin D, **dexamethasone**.

Table 1: The main drugs used in the above-mentioned self-medication with their respective adverse effects, drug interactions, metabolic pathways and excretion pathways.

Drugs	Adverse effects	Drug interactions	Metabolic Pathways	Excretion pathways
Hydroxychloroquine	<ul style="list-style-type: none"> -Anorexia -Emotional lability -Headache -Blurred vision due to accommodation disorders that is dose dependent and reversible -Abdominal pain -Nausea -Diarrhoea -Puke -Rash -Itch 	<p>Hydroxychloroquine can increase digoxin levels in plasma. Therefore, serum digoxin levels should be carefully monitored in patients using concomitant use of these substances. Because Hydroxychloroquine may increase the effects of hypoglycemic treatment, a decrease in insulin doses or antidiabetic drugs may be required. Class IA and III antiarrhythmics, tricyclic antidepressants,</p>	<p>Hydroxychloroquine is partially converted into active metabolites in the liver.</p>	<p>Renal excretion and also bile.</p>

		<p>antipsychotics, some anti-infectives due to increased risk of ventricular arrhythmia.</p> <p>Halofantrin should not be given with Hydroxychloroquine.</p> <p>Cyclosporine.</p> <p>Anticonvulsants.</p> <p>Antiepileptics.</p> <p>Praziquantel</p>		
Chloroquine	<ul style="list-style-type: none"> -<u>Hipotension</u> -Vasodilation -Suppression of myocardial function -Cardiac arrhythmias -Cardiac arrest -Confusion -Seizures -Coma -<u>Cefaleia</u> -Irritation of the tract -Gastrointestinal -Visual disturbances -<u>Urticária</u> -Retinopathy -Irreversible ototoxicity -Toxic myopathy 	<p>Potential of its direct blocking action at neuromuscular junction by aminoglycoside antibiotics; Inhibition of its metabolism by cimetidine, which can increase the plasma concentration of the substance; Antagonism of the effect of neostigmine and pyridostigmine; Reduction of humoral response (antibody-mediated) to primary immunization with human intradermal antirabid vaccine; As with chloroquine, antacids can reduce the absorption of Hydroxychloroquine and it is advisable to observe a 4-hour interval between the administration of Hydroxychloroquine and antacids.</p>	Metabolized in the liver.	It occurs mainly through urine.
Dexamethasone	-Water retention	-The risk of hepatotoxicity is	Dexamethasone is quickly absorbed	It is eliminated mainly by

	<ul style="list-style-type: none"> -Weight gain -Electrolyte imbalances -High blood pressure -High blood sugar levels -Increased need for diabetes medicines -Osteoporosis -Increased appetite -Menstrual irregularities -Delay in wound healing -Some skin diseases -Swellings of the lips or tongue -Seizures -Psychic disorders (such as mood swings and difficulty in judgment) -Increased sensitivity to infections -Muscle weakness -Gastrointestinal ulcer 	<p>increased when dexamethasone is used simultaneously with high doses of paracetamol or in chronic treatments.</p> <p>-Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. Dexamethasone increases the risk of ulcer or gastrointestinal bleeding with nonsteroidal anti-inflammatory (NSAID).</p> <p>-Parenteral amphotericin B may cause severe hypokalemia in combination with glucocorticoids.</p> <p>The use of antacids decreases the absorption of dexamethasone. Due to intrinsic hyperglycemic activity of dexamethasone, it may be necessary to adjust the dose of insulin or oral hypoglycemic agents.</p> <p>-Diphenylhydantoin (phenytoin), phenobarbital, ephedrine and rifampicin may accentuate metabolic clearance of corticosteroids, causing reduced blood levels and decreased physiological activity, which will</p>	<p>orally. It metabolizes in the liver, but slower than other corticosteroids</p>	<p>metabolism, by renal excretion of inactive metabolites.</p>
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		<p>require adjustment in corticosteroid dosage. These interactions may interfere with dmetry inhibition tests, which should be interpreted with caution during the administration of these drugs.</p> <ul style="list-style-type: none">-False-negative results have been reported in the dmeperhasone suppression test in patients treated with indomethacin.-Prothrombin time should often be checked in patients receiving corticosteroids and coumarin anticoagulants simultaneously, given references that corticosteroids have altered response to these anticoagulants. Studies have shown that the usual effect of corticosteroid addition is to inhibit response to coumarins, although there have been some confl potentiating references of potentiation, not proven by studies.-When corticosteroids are administered simultaneously with potassium-spolitic diuretics, patients should be observed strictly for their development of		
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		<p>hypokalemia.</p> <ul style="list-style-type: none"> -The joint use of drachmahasone with digitalis glycosides increases the possibility of arrhythmias. -Dmethhasone increases the metabolism of mexiletine by decreasing the concentration of mexiletine. 		
Ivermectin	<ul style="list-style-type: none"> -<u>Diarrhoea</u> -Nausea -Asthenia -Abdominal pain -<u>Norexia</u> -<u>Constyping</u> -<u>Vomitos</u> -Dizziness -Sleepiness -Vertigo -Tremor -Itch -Rashes -Urticaria 	<p>There are no reports on drug interactions with Ivermectin; however, it should be administered with caution to patients using drugs that depress the Central Nervous System.</p>	<p>Hepatic Route Adipose tissue</p>	<p>Exclusively by feces.</p>
Vitamin D	<ul style="list-style-type: none"> -Dryness of the mouth -<u>Cand headache</u> -Polydipsia -Polyuria -Loss of appetite -Nausea -<u>Vomitos</u> -<u>Fadiga</u> -Feeling weak -Muscle pain -Itch -Weight loss 	<ul style="list-style-type: none"> - Antacids containing magnesium and/or aluminum when used concomitantly with vitamin D may result in increased serum levels of aluminum and magnesium, especially in the presence of chronic renal failure. - The concomitant use of vitamin D with analogues, especially calciferol, is not recommended due to the additive effect 	<p>It is first hydroxylated in the liver; subsequently metabolism occurs in the kidney.</p>	<p>They are excreted mainly in bile and feces, appearing only small amounts in the urine.</p>

		<p>and increased toxic potential.</p> <ul style="list-style-type: none"> - There is an increased risk of hypercalcemia in the co-administration of vitamin D with thiazoid diuretics, calcium or phosphate. Calcium concentrations should be monitored in these situations. - Some antiepileptics may increase the need for vitamin D (e.g. carbamazepine, phenobarbital, phenytoin and primidone). - Rifampicin and isoniazid may reduce the effectiveness of vitamin D. - Corticosteroids can counteract the effect of vitamin D. 		
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Table 2: The antineoplastic drugs used in the treatment of breast cancer with their respective adverse effects, drug interactions, metabolic pathways and excretion pathways.

Drugs	Adverse effects	Drug interactions	Metabolic pathways	Excretion pathways
Anastrozole	<p>Hypertension Peripheral edema Vasodilation Rash Diarrhoea Intestinal tract disorder Nausea Puke</p>	<p>No clinical or unknown relevance.</p>	<p>Hepatic; via N-desalkylation, hydroxylation and glucoronidation; inactive metabolite, triazole.</p>	<p>Feca and renal.</p>

	Lymphedema Arthralgia Arthritis Low back pain Bone pain Osteoporosis Asthenia Headache Insomnia Depression Mood disorders Flushing of menopause Dyspnoea Increased cough frequency Pharyngitis Pain STROKE Precordial pain Ischemic heart disease Myocardial infarction Myocardial ischemia Thrombophle bitis Venous thromboembo lism Multiform erythema Skin lesion Skin ulcers Steve- Johnson syndrome Breast CA Serum			
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	cholesterol elevation TVP Thromboembolic alteration			
Capecitabine	Oedema Dermatitis Abdominal pain Constipation Diarrhoea Anorexia Nausea Stomatitis Puke Anaemia Leukopenia Lymphocytopenia Neutropenia Thrombocytopenia Hyperbilirubinemia Paresthesia Fatigue Cardiotoxicity Hand-foot syndrome Diarrhoea grade 3 and 4 Gastrointestinal bleeding Grade 3 and 4 anemia Bleeding grade 3 and 4 lymphocytopenia Grade 3 and 4 neutropenia Thrombocytopenia grade 3	Warfarin due to the low regulation of CYP2C9	Hepatic to active metabolites 5-fluorouracil, 5-desoxy-5-fluorocytidine (5-DFCR), 5-dFUR, 5-fluoro-2-desoxyuridine monophosphate (FdUMP), 5-fluorouridine triphosphate (FUTP).	Renal and fecal

	and 4 Grade 3 and 4 hyperbilirubinemia Neurotoxicity			
Carboplatin	Alopecia Hypocalcemia Hypokalemia Hypomagnesemia Hyponatremia Abdominal pain Diarrhoea Nausea Puke Anaemia Leukopenia Neutropenia Thrombocytopenia Elevated alkaline phosphatase INCREASED AST Abnormal urea Elevated serum creatinine Myelosuppression Hypersensitivity reaction Unexplained visual loss Visual disturbances	None of the 5 drugs mentioned.	Hepatic, minimal.	Renal
Cyclophosphamide	Alopecia Facial	CYP34A inducers and	Through active and	Through enzymatic

	flushing Hyperpigmentation of the skin and nails Rash Urticaria Toxic epidermal necrolysis Abdominal discomfort Diarrhoea Nausea Puke Anorexia Mucositis Leukopenia Neutropenia Amenorrhoea Cardiac tamponade Cardiotoxicity ICC Pericardial effusion Multiform erythema Malignant tumor of the dermis Steve Johnson Syndrome Toxic epidermal necrolysis Lma CML Malignant tumor related to hematopoietic tissue and lymphoid	inhibitors. CYP2C8/9 inhibitors CYP2B6 inducers	inactive metabolite microsomatic enzymes in the liver via P450, primarily by CYP2B6.	oxidation to active and inactive metabolites, which are excreted mainly in the urine. Fecal.
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	<p>SMD Hepatic angiosarcoma Anaphylaxis Nasal congestion and watery eyes Runny Bladder fibrosis Hemorrhagic cystitis Malignant bladder tumor Pielite Renal hematuria Secondary malignant neoplasm of the renal pelvis Azoospermia Oligozoospermia Interstitial pneumonia Pulmonary fibrosis Infectious diseases</p>			
Cisplatin	<p>Anaemia Leukopenia Thrombocytopenia Nausea Puke Myelosuppression Hypersensitivity reaction Brain hernia</p>	None of the 5 drugs mentioned.	Non-enzymatic conversion to various inactive metabolites occurs, which are highly plasma proteins.	Urine

	<p>Encephalopathy Neuropathy Neurotoxicity Reversible posterior leukoencephalopathy Convulsion Nephrotoxicity Ototoxicity</p>			
Docetaxel	<p>Oedema Vasodilation Alopecia Skin and/or subcutaneous tissue alteration Nail changes Itch Rash Diarrhoea Nausea Stomatitis Puke Anaemia Leukopenia Neutropenia Asthenia Neuropathy Amenorrhoea Fever of unknown origin Severe edema Stevens-Johnson Syndrome Toxic epidermal necrolysis Colitis</p>	CYP3A4 inducers and inhibitors	Primarily hepatic via CYP3A4 to inactive metabolites.	Fecal and urinary.

	<p>anemia Febrile neutropenia Thrombocytopenia Hepatotoxicity Anaphylaxis GO Interstitial pneumonia Pulmonary embolism Infectious diseases</p>			
Doxorubicinol	<p>Alopecia Nausea Puke Acute-onset cardiomyopathy Late-onset ICC Left ventricular insufficiency WOULD Myocarditis Pericarditis Local complications due to extravasation Pancreatitis Colon ulceration Grade 3 and 4 leukopenia Neutropenia Thrombocytopenia grade 3 and 4 Hepatitis Veno-</p>	None of the 5 drugs mentioned	Liver and other tissues by an enzyme aldoketoreductase to the active metabolite doxorubicinol.	Predominantly biliary, biliary and fecal.

	occlusive disease Anaphylaxis Septic shock Pneumonitis by rooted Lma SMD			
Epirubicin	Alopecia Blush Itch Rash Diarrhoea Inflammatory disease of the mucous membrane Nausea Puke Anaemia Leukopenia Neutropenia Thrombocytopenia Lethargy Conjunctivitis Keratitis Amenorrhoea Infectious diseases Cardiotoxicity Thrombophlebitis Local complications resulting from extravasation Hyperuricemia Nausea and vomiting grade 3 or 4 Lma Grade 3 or 4	None of the 5 drugs mentioned.	Hepatic intense and fast; reduction, conjugation, hydrolysis, redox. Metabolites: derivative 13 (S)-dihydro, epirubicinol, doxorubicin aglicona, doxorubicinol aglicona, 7-deoxy-doxorubicin aglycon, 7-deoxyrubicinol aglicona.	Fecal and renal

	leukopenia Grade 3 or 4 neutropenia Anaphylaxis Hypersensitivity Pulmonary embolism			
Everolimo	Hypertension Peripheral edema Acne Rash Hypercholest erolemia Hypertriglycer idemia Hypoalbumin emia Hypophosfate mia Hyperglycemi a Constipation Anorexia Diarrhoea Nausea Stomatitis Puke Grade 3 or 4 anemia Decreased grade 3 or 4 lymphocyte count Increased astrocytoma subependimá rio of giant cells Thrombocyto penia Increased alkaline	CYP3A4 inductors and inhibitors	Hepatic via CYP3A4 and glycoprotein P.	Fecal and renal

	phosphatase INCREASED ALT Increased ASR Asthenia Mental disorder Elevated serum creatinine Infectious diseases of the urinary tract Amenorrhoea Menstrual change and menorrhagia Cough Dyspnoea Sinusitis Upper respiratory tract infection Fatigue Fever Hemorrhage Leukopenia Thrombosis Thrombotic microangiopathy Thrombotic thrombocytopenic purpura Infectious diseases Convulsion Hemolytic uremic syndrome GO			
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	<p>Interstitial pulmonary disease, pleural effusion Pneumonia Noninfectious pneumonitis.</p>			
Exemestano	<p>Alopecia Diaphoresis Flushing of menopause Increased appetite Nausea Elevated alkaline phosphatase Arthralgia Headache Insomnia Anxiety Depression Fatigue IC WOULD Gastric ulcer Cholestatic hepatitis Hepatitis Decreased bone mineral density Bone fracture STROKE</p>	CYP3A inducers	hepatic via CYP3A4; metabolite active, 17-dihydro.	Fecal and renal
Fluorouracil	<p>Alopecia Hand-foot syndrome Maculopapular eruption Itch Photosensitivity Diarrhoea</p>	Decreased synthesis of P450C9 enzymes.	Hepatic, via dihydropyrimidine dehydrogenase (DPD).	Renal and respiratory.

	<p>Anorexia Nausea Puke Stomatitis Headache Angina Cardiotoxicity Coronary arteriosclerosis Thrombophlebitis Gastrointestinal ulcer Bleeding Myelosuppression Anaemia Leukopenia Thrombocytopenia Anaphylaxis Hypersensitivity Acute cerebellar syndrome Nystagmus Blurred vision Tearing Photophobia Tear system susthesis</p>			
Fulvestranto	<p>Vasodilation Pain at the injection site Reaction to injection site Abdominal pain Constipation Diarrhoea Nausea Puke</p>	No clinical or unknown relevance	hepatic via CYP3A4.	Fecal and renal

	<p>Increase in the level of liver enzymes Back pain, bone pain Asthenia Headache Flushing of menopause Cough Dyspnoea Increased cough frequency Pharyngitis Pain Thromboembolic disease Hepatitis and liver failure Hypersensitivity Angioedema</p>			
Lapatinib	<p>Hand-foot syndrome Rash Diarrhoea Indigestion Nausea Puke Anaemia Thrombocytopenia Depression of left ventricular systolic function Extended QT interval Diarrhoea grade 3 or 4 Hepatotoxicity</p>	<p>CYP3A4 inducers and inhibitors Tricyclic antidepressants.</p>	<p>mainly via CYP3A4 and 3A5.</p>	<p>Renal and fecal.</p>

	Hypersensitivity Interstitial lung disease Pneumonitis			
Megestrol	Hypertension Rash Sweating Weight gain Diarrhoea Flatulence Indigestion Nausea Puke Insomnia Mood swings Impotence Spontaneous uterine bleeding Adrenal insufficiency Anaemia TVP Thrombophlebitis Pulmonary embolism	CYP3A4 inducers and inhibitors (Drecessionh asone)		Fecal and renal
Methotrexate	Thromboembolic disease Multiform erythema Steve Johnson Syndrome Toxic epidermal necrolysis Agranulocytosis Aplastic anemia Leukopenia Pancytopenia	None of the 5 drugs mentioned.	Hepatic and intracellular to active metabolites polyglutamates and 7-hydroxymethoprolin.	Biliary and renal

	<p>Liver cirrhosis Hepatic fibrosis Hepatotoxicity Opportunistic infection GO Interstitial pneumonia</p>			
Paclitaxel	<p>Alopecia Diarrhoea Inflammatory disease of the mucous membrane Nausea Puke Anaemia Leukopenia Neutropenia Thrombocytopenia Hypersensitivity reaction Arthralgia Myalgia Peripheral neuropathy Peripheral neuropathy seizure grade ≥ 3 Pulmonary embolism Respiratory failure</p>	<p>CYP3A4 inducers and inhibitors (Drecessionh asone) CYP2C8 inhibitors</p>	<p>Hepatic via CYP2C8 (fundamentally) and CYP3A4; metabolite, 6-alpha-hydroxypaclitaxel.</p>	<p>Fecal and urine</p>
Ribocycline	<p>Alopecia Constipation Diarrhoea Nausea Puke Grade 3 or 4 leukopenia</p>	<p>CYP3A4 inhibitors and strong inducers Drugs that prolong the QT interval</p>	<p>Hepatic cyp3a4 route.</p>	<p>Urine and fecal</p>

	Grade 3 or 4 neutropenia Low back pain Headache Fatigue Extended QT interval Sudden cardiac death Syncope Anaemia Febrile neutropenia Lymphocytopenia	(Chloroquine)		
Tamoxifen	Menopause flushing Irregular menstruation Vaginal discharge Multiform erythema Steven Johnson Syndrome Breast CA TVP Thromboembolic disease Cataract Uterine CA Interstitial pneumonia Pulmonary embolism	CYP2D6, CYP3A4, CYP2C9 inhibitors CYP3A4 inducers	Hepatic, substrate of CYP3A, CYP2C9 and CYP2D6; metabolite, N-demethyl tamoxifen.	Biliary/fecal and renal

Table 3: The antineoplastic drugs used in the treatment of prostate cancer with their respective adverse effects, drug interactions, metabolic pathways and excretion pathways.

DRUGS	ADVERSE REACTIONS	INTERACTIONS MEDICINAL	METABOLIC PATHWAY	EXCRETION PATHWAYS
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APALUTAMIDA	Hypertension Peripheral edema Rash Blush Weight reduction Decreased appetite Diarrhoea Nausea Arthralgia Fatigue Bone fracture Convulsion Fall	CYP3A4 and CYP2C8 inhibitors	Hepatic, primarily to the active metabolite N-desmethyl apalutamide (major); inducer (moderate to strong) of CYP3A4 and CYP2B6; P-gp, BCRP and OATP1B1 inducer inducer; CYP2B6 (moderate) inhibitor and CYP2C8; CYP2C9, CYP2C19 and CYP3A4 inhibitor(weak); OCT2 inhibitor, OAT3 inhibitor and MATEs (no clinical effect on OAT3 substrates); cyp2c8 (40%) and CYP3A4 substrate (37%); p-gp substrate (no clinical effect on bioavailability).	Renal and fecal
BICALUTAMIDA	Peripheral edema Sweating Abdominal pain Constipation Diarrhoea Nausea Infectious diseases Back pain Pelvic pain Asthenia Haematuria Nocturia Dyspnoea Pain ICC		Glucoronidation and oxidation	Fecal and renal.

	Myocardial infarction Hepatitis Hepatotoxicity Liver failure			
CABAZITAXEL	Alopecia Constipation Diarrhoea (grade 3 or 4) Anorexia Nausea Puke Anemia (grade 3 or 4) Leukopenia (grade 3 or 4) Neutropenia (febrile) (grade 3 or 4) Thrombocytopenia Back pain Asthenia Peripheral neuropathy Haematuria Cough Dyspnoea Fatigue Fever GO	CYP3A4 inhibitors and inducers	hepatic, primarily via CYP3A4/5; to a lesser extent via CYP2C8.	Fecal and renal
DEGARELIX	Sweating Injection site reaction Weight gain Increased hepatic aminotransferase Gammaglutamylase Extended QT interval Hypersensitivity reaction		Hepatobiliary via hydrolysis to peptides.	Fecal and renal
DOCETAXEL	Oedema Vasodilation Alopecia Skin and/or subcutaneous tissue alteration Nail change Itch	CYP3A4 inhibitors and inducers	Primarily hepatic via CYP3A4 to inactive metabolites.	Fecal and urinary

	<ul style="list-style-type: none"> Rash Diarrhoea Nausea Stomatitis Puke Anaemia Leukopenia Neutropenia Asthenia Neuropathy Amenorrhoea Fever of unknown origin Severe edema Steve-Johnson syndrome Toxic epidemic necrolysis Colitis Anaemia Febrile neutropenia Leukopenia Neutropenia Thrombocytopenia Hepatotoxicity Anaphylaxis GO Interstitial pneumonia Pulmonary embolism Infcciosa diseases 			
ENZALUTAMID A	<ul style="list-style-type: none"> Peripheral edema Blush Diarrhoea Neutropenia (grade 3 or 4) Arthralgia Back pain Musculoskeletal pain Asthenia Fatigue Cauda equina syndrome Convulsion Spinal cord compression Infectious 		<ul style="list-style-type: none"> Liver via CYP2C8 and CYP3A4; N-desmethyl enzalutamide, active metabolite 	<ul style="list-style-type: none"> Renal and fecal

	diseases			
GOSSERRELIN E	Peripheral edema Acne Seborrhea Sweating Breast atrophy Headache Depression Mood change Erectile dysfunction Blush Reduced libido Sexual dysfunction Vaginitis Pain ICC Diabetes mellitus Pituitary apoplexy Hypoherotic tumor Tumor flare Anaphylaxis Hypersensitivity STROKE GO COPD		liver, hydrolysis of C-terminal amino acids and metabolites 1-7 fragment and 5-10 fragment.	Renal
LEUPRORRELIN/ LEUPROLIDA	Oedema Hypertension Acne Pain at the injection site Injection site reaction Rash Blush Increased transient testosterone level Elevated seeric triglycerides Constipation Nausea Puke Anaemia Arthralgia Arthropathy Decreased bone		Hydrolysis via peptidase enzyme.	Renal

	mineral density Myalgia Asthenia Dizziness Headache Insomnia Lethargy Depression Mood change Dysuria Testicle atrophy Vaginitis Cough Constipation Malaise Fatigue Pain IC WOULD Pituitary apoplexy Liver injury Anaphylactic reactions Fracture of the spine Convulsion Suicidal thoughts Pulmonary embolism			
OLAPARIBE	Rash Constipation Decreased appetite Diarrhoea Indigestion Nausea Stomatitis Change in taste Anemia (grade 3 or 4) Arthralgia Low back pain Myalgia Headache Cough Nasopharyngitis Fatigue LM Pneumonitis	CYP3A4 inhibitors and inducers	Hepatic, via CYP3A4	Fecal
TRIPTORRELIN E	Hypertension Peripheral	No clinical or unknown	Unknown, unlikely	Urine, liver.

	<p>edema Pain at the injection site Sweating Nausea Puke Arthralgia Back pain Bone pain Pain in the lower limbs Dizziness Headache Insomnia Dysuria Urination retention Infectious diseases of the urinary tract Testicle atrophy Erectile dysfunction Impotence Chest pain Reduced libido Fatigue Pain Pituitary apoplexy Anaphylaxis Hypersensitivity immune reaction Sepsis Convulsion Angiodema Tumor flare</p>	relevance.	participation of CYP	
ABIRATERONA	<p>Oedema Hypertension Blush Hypercholesterolemia Hyperglycemia Hypertriglyceridemia Hypocalcemia Diarrhoea Puke Anaemia Lymphocytopenia High ALT High AST</p>	<p>CYP3A4 inhibitors and inducers CYP2D6 substrates</p>	<p>Abiraterone is metabolized by CYP3A4.</p>	<p>Fecal and renal.</p>

	Swelling in the joints Infectious diseases of the urinary tract Nocturia Cough Dyspnoea Fatigue Cardiac arrhythmia Chest pain Myocardial infarction Sudden cardiac death Adrenal insufficiency Elevated seeric bilirubin			
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UNDER PEER REVIEW

The adverse effects of antineoplastic drugs associated with medicines used in the treatment of COVID-19 are predominantly gastrointestinal and dermatological. However, some chemotherapy drugs used in the treatment of breast and prostate cancers, and some medicines used in COVID-19 therapy have more severe frequent adverse reactions, such as:

In breast cancer:

1. Cardiovascular disorders: Chloroquine, Anastrozole, Capecitabine, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin, Everolimus, Exemestan, Fluorouracil, Fulvestrant, Lapatinib, Megestrol, Mettopy, Paclitaxel and Ribocyclib
2. Ophthalmological: Hydroxychloroquine. Chloroquine, Carboplatin, Cyclophosphamide, Epirubicin, Everolimus, Fluorouracil and Tamoxifen
3. Musculoskeletal: Dexamethasone, Vitamin D, Anastrozole, Capecitabine, Exemestano, Fulvestrant, Lapatinib, Paclitaxel and Ribocyclib
4. Psychiatric: Hydroxychloroquine and Anastrozole,
5. Renal: dexamethasone, Anastrozole, Capecitabine, Carboplatin, Cyclophosphamide, Cisplatin and Metoprolol.
6. Neurological: Hydroxychloroquine, Chloroquine, dexamethasone, Vitamin D, Ivermectin, Anastrozole, Capecitabine, Cyclophosphamide, Cisplatin, Docetaxel, Epirubicin, Paclitaxel and Ribocyclib. Exemestano, Fluorouracil, fulvestrant, Lapatinib, Megestrol and Methotrexate.
7. Immunological: dexamethasone, Anastrozole, Capecitabine, Carboplatin, Cyclophosphamide, Cisplatin, Docetaxel, Doxorubicin, Epirubicin, Everolimus, Fluorouracil, Fulvestrant, Methotrexate and Paclitaxel

In prostate cancer

1. Cardiovascular disorders: Bicalutamide, Cabazitaxel, Degarelix, Goserelin, Leuprorelin, Triptoreline, Abiraterone and Chloroquine.
2. Ophthalmological: Hydroxychloroquine and Chloroquine.
3. Skeletal: Apalutamide, Bicalutamide, Cabazitaxel, Docetaxel, Enzalutamide, Goserelin, Leuprorelin, Olaparib, Triptoreline, Abiraterone, dexamethasone and Vitamin D.
4. Psychiatric: Triptoreline, Leuprorelin, Goserelin, Triptoreline, Hydroxychloroquine and dexamethasone.
5. Renal: Abiraterone and dexamethasone.
6. Hepatic: Bicalutamide, Degarelix and Leuprorelin

7. Neurological: Apalutamide, Cabazitaxel, Docetaxel, Enzalutamide, Goserelin, Leuprorelin, Triptorelin, Hydroxychloroquine, Chloroquine, dexamethasone, Vitamin D and Ivermectin.

8. Immunological: Bicalutamide, Enzalutamide, Triptoreline and dexamethasone.

9. Pulmonary: Bicalutamide, Cabazitaxel, Docetaxel, Leuprorelin, Olaparib, Abiraterone.

4. DISCUSSION

As a consequence of the association of drug reactions, adverse effects are potentiated, generating disorders in the cardiovascular, nervous, excretory, muscular and skeletal systems. Moreover, monitoring the toxicity of drugs in the patients' bodies is essential to elect the most appropriate pharmacological administration conduct in each scenario.

Metabolization pathways

From the reading of the table that correlates the metabolization pathways of antineoplastic drugs and the drugs used in COVID-19 therapy, it is possible to observe that several drugs have the same metabolization pathways, which can generate severe hepatic and renal dysfunctions. The metabolism of the aforementioned drugs occurs mainly in a hepatic way through one of the metabolic pathways of the cytochrome P450 system (CYP), which arouses in a competition for the active site for subsequent metabolization. This dispute results in an inhibition by competition generating the increase of drugs and their remnants at the serum level. Thus, the elevation of drugs in plasma can promote toxicity and carcinogenic effects in the body, greater than those of the initial drug, especially if the drug in question is not metabolized through phase 1 reactions (oxyreduction, reduction or hydrolysis)[12]. In this context, the side effects related to the hepatic system, manifested by most chemotherapy drugs used as a treatment for breast cancer, together with the adversities related to inhibition of drug metabolism accentuate the dysfunctions and failures of this system[13].

Inductive isoenzymes

Dexamethasone, as well as Vitamin D, act as inducers of CYP3A4, the consecutive induction of this enzyme by specific drugs causes a reduction in the effects of medications, due to the decrease of drugs at serum levels due to the intensification of metabolization[14,15].

Inhibitory isoenzymes

All the aforementioned drugs used as therapy for COVID-19 are metabolized by cyp3a4 isoenzyme, however, isoenzymes such as CYP2C8, CYP2D6, CYP2R1, CYP27B1 and CYP24A1 also act in this process through the conversion of several drugs. The overload of these enzymes as a result of competition for the active site promotes its inhibition and, consecutively, increases the half-life of these drugs intensifying its effect and toxicity[16,17,18,19,20].

Excretion pathways

Chemotherapy, as well as the medicines used in the treatment of Coronavirus are excreted mainly by the renal and biliary route through urine and feces. Considering that only two routes are used for the excretion of several drugs, the overload of the renal and hepatic system is evident, and may lead to significant and critical collapses in these systems in cancer patients[21].

Drug interactions

BREAST CANCER

The main interaction with regard to Chloroquine and Hydroxychloroquine is associated with qt-prolonging drugs such as Ribocycline, Lapatinib and Tamoxifen. The concomitant use of these drugs may promote the extension of QT and, consequently, cause intense ventricular arrhythmias and cardiac disorders, classifying the severity of this interaction as high risk. Therefore, the aforementioned drugs acquire additive effects in increasing the QT interval when co-administered and, therefore, ECG monitoring is indicated. Similarly, the use of Tamoxifen in concomitance with Chloroquine or Hydroxychloroquine culminates in an increased risk of retinopathy due to the ocular toxicity generated by these drugs, especially in therapies with high doses of Chloroquine[22,23,24,25,26].

Dexamethasone is a corticosteroid with anti-inflammatory, immunosuppressive and antiallergic action that acts by inhibiting several cytokines and biochemical pathways[27]. Due to the mechanism of action of dexamethasone, this drug is administered as a therapy for various types of neoplasms and, currently, in some cases, as a treatment for COVID-19. However, dexamethasone interacts with several chemotherapy drugs given in breast cancer therapy, such as Everolimus, Doxorubicin, Exemestano, Lapatinib, Letrozol, Megestrol and Paclitaxel. Drug interactions in this scenario may be severe (Everolimus, Doxorubicin, Exemestano and Lapatinib) or moderate (Letrozol, Megestrol and Paclitaxel)[28,29,30,31,32,23,34]. The concomitant use of the aforementioned antineoplastic drugs with dexamethasone promotes the reduction of antineoplastic drugs at the serum level, consequently, in order to obtain the necessary levels of these cytostatics, higher doses should be administered. The superdosis of these drugs can promote several adversities with regard to toxicity, besides generating additive effects such as: musculoskeletal, neurological, immunological disorders and etc [14].

PROSTATE CANCER

Similar to what occurs with drugs used for the treatment of breast cancer, the main interactions with regard to Chloroquine and Hydroxychloroquine are associated with qt-prolonging drugs such as Degarelix, Gosserreline and Triptorrelina. The concomitant use of these drugs may promote the extension of QT and, consequently, cause intense ventricular arrhythmias and cardiac disorders, classifying the severity of this interaction as high risk. Therefore, the aforementioned drugs acquire additive effects in increasing the QT interval when co-administered and, therefore, ECG monitoring is indicated[35,36,37,25,26].

Due to the mechanism of action of dexamethasone, this drug is administered as a therapy for various types of neoplasms and, currently, in some cases, as a treatment for COVID-19. However, dexamethasone interacts with several chemotherapy drugs given in prostate cancer therapy, such as Apalutamida, Enzalutamida. Drug interactions in this scenario can be severe. The concomitant use of the antineoplastic drugs mentioned above with dexamethasone may lead to decreased serum levels and the efficacy of antineoplastic drugs, thus increasing their dosage. The superdosis of these drugs can cause it to increase

toxicity, besides generating additive effects such as: musculoskeletal, neurological, immunological disorders and etc[23,38,39].

Although they do not present severe or moderate drug interactions in relation to the drugs used in the treatment of breast and prostate cancer, Ivermectin and Vitamin D may potentiate adverse effects, such as diarrhea, vomiting, nausea, headache, among others.

In this scenario, marked by the disorder with regard to the administration of medications and self-medication, compliance with pharmaceutical care is paramount. Pharmaceutical care is based on communication between the pharmacist and the patient, at this juncture, the pharmacist acts through the elucidation of medications to the population, through the mitigation of the side effects presented and the recovery of the patient[16].

Today, the application of this concept in Brazil is not usual due to the initial investment required and the scarcity of studies in Brazil that prove the effectiveness of the application of this method[16]. However, numerous countries show the validity of this resource and, in addition, express several positive points of the applicability of this tool, such as: the improvement in the quality of life of the patient, the savings acquired through the inclusion of the pharmacist in the long-term health service and better results with regard to the treatment of the patient in question[17]. The fulfillment of pharmaceutical care, in view of the above-mentioned results, in the current scenario of contagion, especially in relation to cancer patients, would benefit the attenuation of the current crisis and improve the current therapy.

It is also essential to point out that pharmaceutical care acts as a barrier with regard to self-medication. From the detailed and individual contact between the pharmacist and the patient, the pharmacist is able to provide clarification regarding the medication and, consequently, contain the unbridled and harmful consumption of medications [16].

According to the National Continuous Household Sample Survey - Information and Communication Technology, mobile devices are the main means of internet access in Brazil. Data show that 79.3% of Brazilians aged ten years or older have mobile phones for personal use, with or without internet. This percentage was 78.2% in 2017 and in that same year, 84.4% of individuals with mobile devices also had access to the network through them. This rate increased to 88.5% in 2018 [40].

The technology has provided many changes in the forms of communication around the world, ensuring access to information that generates education and help in building the knowledge of the population. On the other hand, with technological evolution and the expansion of the Internet together with social media, the citizen not only consumes the content of the Internet but also interacts, creates and shares content with great scope [41].

In cases of health, communication is essential and accurate information of the facts helps the responsible agencies to take more effective measures (BRASIL, 2020). However, the ease of access, dissemination, creation and sharing of information provided by the Internet began to bring complications to the online environment through the popularization of fake news, the so-called Fake News[41].

Fake News consists of fake content shared by means of messages and social networks in order to attract the attention of the population and inform it, without a certain true source, but presenting a makeup that generates an apparent veracity for those who receive them [41].

The dangers posed by this false information during the COVID-19 pandemic vary, among the contents that deserve attention the most are those that have spread in Brazil, the advice on how to "prevent" or "cure" the virus from a treatment with a specific substance, such as chloroquine and ivermectin [42].

In this sense, a new concern has drawn the attention of the WHO, the use of these drugs without medical prescription and without scientific basis by those who want to prevent or feel one or more symptoms of Covid-19. This fear is due to the indiscriminate use of these drugs by people who are often in other types of treatments, such as patients undergoing cancer treatment [43].

Hydroxychloroquine and chloroquine are associated with many drug and disease interactions, as well as dexamethasone, which also has a high degree of risk. On the other hand, vitamin D and ivermectin have small interactions, but with a possible potentiation of the adverse effects suffered by cancer patients[44].

In addition, it is essential to highlight, in this context, the aforementioned adverse effects related to self-medication, such as: prolonged effect of QT, intensification of the adverse effects of antineoplastic drugs and inhibition from competition for metabolic pathways. This scenario is able to aggravate the condition of debilitated patients due to antineoplastic treatment and, by virtue of this, should be treated with due severity and austerity.

However, it should be pointed out that there are those who say that such drugs used prophylactically have some benefit, based on preliminary, observational and in vitro studies. Some people with a high power of influence over the population claim that there is an "early treatment" for COVID-19, even without robust scientific basis with good plausibility, or even using as an argument laboratory tests that have not even passed the testing phase on living beings. The biggest problem in this case is that a good part of the population strongly believes in these influencers, and with this, end up processing this information as an absolute truth, and consequently assume, even indirectly, a risk to their health, when they self-medicate.

5. CONCLUSION

The study suggests that the drugs analyzed may cause damage to the health of patients undergoing cancer treatment, as it shows that it may increase the risk of liver, renal, cardiac or gastrointestinal injury.

It is concluded that self-medication performed by patients with breast or prostate cancer may bring moderate to severe risks with regard to drug interaction and metabolization pathways, because some of these drugs used erroneously as a form of prevention and treatment for COVID-19 not only have dangerous adverse effects for cancer patients, may also potentiate the adverse effects caused by cancer treatments. That said, it is of paramount importance to stress that no medication should be used without a medical prescription, and that one should filter out all the information that is disclosed, so that no one puts their own health at risk.

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