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Article

The effects of pharmacist interventions on health outcomes in patients with advanced prostate cancer in Brazil

Patricia M Aguiar[1], Ana Luiza PM Mori[1], Maria GF de Lima[1], Magali SPN Rossi[1], Maria Aparecida Nicoletti[1], Karina OF Martins[2], Ana Lúcia M Lopes[3], Teresa Cristina M Coan[3], Oscar Eduardo H Fugita[3], Sílvia Storpirtis[1]

[1]School of Pharmaceutical Sciences, University of São Paulo, São Paulo, Brazil, [2]Secretariat of Health of the State of Sao Paulo, São Paulo, Brazil, [3]Teaching Hospital of University of São Paulo, São Paulo, Brazil

This study examined the effects of pharmacist interventions for patients with advanced prostate cancer. A pre-post study was conducted between October 2014 and August 2017 in a community pharmacy in Brazil for outpatients with advanced prostate cancer, aged ≥ 18 years, using cyproterone acetate and/or goserelin. The patients had face-to-face meetings with a pharmacist who dispensed antiandrogenic drugs and performed interventions aimed at solving and/or preventing drug-therapy problems. Primary outcomes regarding prostate-specific antigen (PSA) and testosterone levels were compared at 0, 6, and 12 months, whereas secondary outcomes—medication adherence and quality of life—were compared at baseline and at the 12-month follow-up. Medication adherence was assessed using the Morisky–Green test, and quality of life was measured by the Medical Outcomes Study 36-item Short Form (SF-36) and the Functional Assessment of Cancer Therapy-Prostate (FACT-P). The analysis included 20 patients; 311 drug-therapy problems were identified and most of them were related to adverse reactions (78.5%). The most common adverse reactions were reduced libido, erectile dysfunction, hyperglycemia, fatigue, and gynecomastia. Testosterone levels significantly decreased at 6 months, and PSA levels at 6 and 12 months. No significant changes in adherence were noted at the end of the study. A significant increase in the "pain" domain and an improvement trend in the "physical aspects" and "vitality" domains were observed based on the SF-36 instrument. The findings show that pharmacist interventions were able to improve PSA and testosterone levels, and some domains of quality of life of patients.

Keywords: Pharmacist. Pharmaceutical care. Prostate cancer. Adverse drug reaction.

INTRODUCTION

In the year 2015, there were 1.6 million new cases of prostate cancer and 366,000 deaths related to this cancer worldwide. Aging and rising age-specific incidence rates were the key drivers for an increase of 66% in prostate cancer cases since 2005. Prostate cancer has the highest incidence and is the fifth leading cause of cancer deaths in men.[1] In Brazil, prostate cancer was not just the most frequent cancer but also the leading cancer-related death among men (Fitzmaurice *et al*., 2017). Estimates indicate that incidence and mortality rates in Brazil increased on average by 2.8% and 1.6% per year, respectively (Sierra, Soerjomataram, Forman, 2016). Thus, health systems should develop innovative and sustainable approaches that can better meet cancer patients' complex needs and improve their outcomes.

Currently, cancer care is undergoing an important paradigm shift from disease-focused management to a patient-centered approach in which increasingly

***Correspondence:** P. M. Aguiar. Departamento de Farmácia. Faculdade de Ciências Farmacêuticas. Universidade de São Paulo. Av. Prof. Lineu Prestes, 580 - Conj. das Químicas - Bloco 13. Cidade Universitária, Butantã, São Paulo, Brasil. E-mail: aguiar.pm@usp.br. ORCID: 0000-0002-3957-4533

more attention is paid to psychosocial aspects of care, quality of life, rights and empowerment of patients, and survivorship (Borras *et al*., 2014). The new paradigm also recognizes that collaborative management among health professionals in prostate cancer streamlines patient care, with rehabilitation and counseling being delivered by a team of experts (Valdagni *et al*., 2015). Clinicians appear to recognize the value of having other health professionals involved in the treatment in terms of effective communication with patients, but the dynamics inherent in multidisciplinary team-based care is still subject to debate and represents a challenge (Bellardita *et al*., 2011).

Pharmacist interventions in community pharmacies are of great importance, especially for reducing morbimortality related to medication use (Kehrer *et al*., 2013). In patient-centered care management, the need for contact with health professionals is frequent, but it can be hampered by the distance between professionals. This issue can be managed by using telephone or e-mail to maintain frequent contact. Despite any difficulties around pharmacist interventions, studies conducted in community pharmacies have shown promising results related to this aspect of patient care (Correr *et al*., 2011; Aguiar *et al*., 2012; Milosavljevic, Aspden, Harrison, 2018). The effectiveness of pharmacist intervention could be strengthened, increasing the visibility and the performance of the pharmacist, through continuous training for skills and abilities development, promotion and dissemination of the qualification of their services with validated indicators, and especially, establishing good interpersonal relationships with other health professionals (Brasil, 2015a).

With their knowledge concerning safety, efficacy, pharmacologic, and financial components of pharmacotherapy, pharmacists can play an important role in the care of patients with cancer and complement the multidisciplinary cancer care team (Liekweg, Westfeld, Jaehde, 2004). Through pharmaceutical care—a patient-centered, outcome-oriented practice—pharmacists can improve the prevention and/or management of drug-therapy problems that are very common during antineoplastic treatment (Vantard *et al*., 2015). In addition, a recent systematic review showed that pharmacist interventions have significantly improved various outcome measures in adult outpatients with cancer, such as rates of nausea and vomiting control, medication adherence, and patient satisfaction (Colombo *et al*., 2017).

To the best of our knowledge, only one study has been conducted focusing specifically on pharmacist interventions in outpatients with prostate cancer (Colombo *et al*., 2017). The research done by Patel *et al*. (2016) included patients using abiraterone, bicalutamide, or enzalutamide for metastatic castrate-resistant prostate cancer and showed significant increases in the average number of interventions per patient and adherence to lab parameter monitoring compared with patients of the control group (i.e., without pharmacist intervention). However, there is a lack of information on studies focusing on pharmacist interventions for outpatients with prostate cancer using other hormone therapies and reporting their effects on humanistic outcomes and clinical outcomes such as changes to prostate-specific antigen (PSA) and testosterone levels.

In addition, although the Sistema Único de Saúde (SUS) has been in force since 1990 in Brazil—defining a novel paradigm for public health management that is governed by universality, equality, and integrality of actions (Brasil, 1990)—the goals of this system have not been fully realized in this country. The focus on the supply of medicines does not necessarily translate into a guarantee of improved health, as obtaining medication without proper monitoring of its use can bring harm. Brazilian studies have described that after the changes allowing the supply of medicines to be managed with legal suits or administrative requests (this phenomenon is known as the judicialization of access to medicines), the conditions regarding the use of medicines, patient evolution, and achievement of the therapeutic goals are subsequently not evaluated (Figueiredo, Pepe, Osorio-de-Castro, 2010; Chieffi, Barata, 2010).

Therefore, the present study aimed to examine the effects of pharmacist interventions on health outcome measures in outpatients with advanced prostate cancer using cyproterone acetate and/or goserelin.

METHODS

Design and setting

A pre-post study of pharmacist intervention was conducted between October 2014 and August 2017 at the university pharmacy of the University of São Paulo (FARMUSP), São Paulo, Brazil. The university pharmacy was created on the campus and is linked to the School of Pharmaceutical Sciences, including a team of four clinical pharmacists and numerous pharmacy students (there are about 60 trainees throughout the year). Since October 2014 the FARMUSP has partnered with the Secretariat of Health of São Paulo along with the Teaching Hospital of the University of São Paulo for the delivery of a practice model that employs a patient-centered approach. Before this partnership, patients using prostate cancer drugs obtained by submitting administrative requests to the government of São Paulo received only a drug dispensing service. The antiandrogenic drugs available free of charge by the State of São Paulo for patients with advanced prostate cancer are goserelin and cyproterone acetate, which are prescribed by a physician following the established treatment schedule and protocol.

Patient selection

Potential participants were recruited from a teaching hospital-affiliated urological clinic by a physician, and males were referred to FARMUSP if they met the following criteria: ≥ 18 years of age; previous diagnosis and treatment (minimum time of three months) of persistent or recurrent prostate cancer after surgery or radiation therapy; and current use of government-funded cyproterone acetate and/or goserelin (intermittent or continuous therapy). Patients undergoing a change of medical treatment during this research who had any symptom or sign of hepatotoxicity, who were participating in clinical trials, or who were unable to return for scheduled appointments for three consecutive months were excluded. All patients who met our criteria and agreed to participate in the study signed a document giving written informed consent. It is important to note that eligible patients entered the study at different times, depending on the referral of the urologist physician.

Description of pharmacist interventions

Pharmacist interventions were developed for patients with advanced prostate cancer using government-funded antiandrogen drugs based on the work process proposed by the Brazilian Ministry of Health (Brasil, 2015b). Face-to-face individual monthly consultations, each lasting about 60 min, were scheduled in comfortable private rooms at FARMUSP. During these consultations, the pharmacists dispensed cyproterone acetate and/or goserelin and performed comprehensive medication reviews. The administration of goserelin by subcutaneous depot injection was performed by the nursing staff at Teaching Hospital.

Past medical history, current medication list (prescription and over-the-counter drugs) and their responses, comorbidities, information on lifestyle, and the status of therapeutic goals for diseases were collected from patients or other sources available to the pharmacists (e.g., medical records from the university hospital, prescriptions, laboratory test results, patient self-monitoring data) and used to guide the framework for necessary pharmacist interventions.

The pharmacist interventions were focused on health education and monitoring drug-therapy problems. Patients received guidance on prostate cancer and comorbidities, changes in lifestyle, and the use of the medications (e.g., medication adherence, administration, and adverse reactions). This guidance was usually verbal and, depending on the needs of the patient, educational leaflets produced by FARMSUP that elaborate on the relevant information (e.g., anemia, increased blood glucose or cholesterol, impotence, common adverse reactions due to the use of cyproterone acetate and/or goserelin) were delivered. In addition, a pill organizer was provided to patients known to have poor medication adherence.

The drug-therapy problems associated with prostate cancer or comorbidities were documented and categorized according to the document from the Brazilian Ministry of Health (Brasil, 2015b). The categories included: a) drug selection or prescription; b) administration or medication adherence; c) dispensation or manipulation of medications; d) medication discrepancies between

care levels; e) drug quality; f) monitoring procedures; g) therapy effectiveness; h) adverse drug reactions; and i) drug intoxication. If the solution to any of the problems required changing the treatment regimen or ordering laboratory tests, the patient's prescribers (from the Teaching Hospital or the community) were contacted in person or by letter. A medication list was developed and updated at every consultation by the clinical pharmacist and the patients received a medication chart to assist in the correct use of their medicines.

Outcome measures

The primary outcomes of this study were the PSA and testosterone levels. All laboratory tests were performed by the central clinical laboratory of the teaching hospital at 0, 6, and 12 months (±3 months from the start of the study). Secondary outcomes measured were medication adherence and quality of life. Medication adherence was judged by the 4-item Morisky–Green test, a validated scale that evaluates the patient's medication-taking behavior (Morisky, Green, Levine, 1986). The score was obtained by assigning one point for each "no" answer and no point for any "yes" answer (ranging from 0 to 4) and patients were classified with high (4 points), medium (2–3 points) and low (0–1 points) medication adherence. The quality of life was measured using Medical Outcomes Studies 36-item Short Form (SF-36) and Functional Assessment of Cancer Therapy-Prostate (FACT-P), which are generic and specific questionnaires, respectively. The SF-36 contains 8 domains (functional capacity, physical aspects, pain, general health, vitality, social, emotional, and mental health aspects), with each domain measured on a scale of 0 to 100 (Ciconelli *et al.*, 1999). The FACT-P consists of 27 general questions that provide assessments of physical, social or family, emotional, and functional well-being as well as 12 questions specific to prostate cancer, with a total score range of 0 to 156 (Esper *et al.*, 1997). Higher scores on both quality-of-life instruments indicate better results. The secondary outcomes were measured at baseline and at a 12-month follow-up with the pharmacist.

Data analysis

Only data of patients who completed at least 12 months of follow-up with the pharmacist and who presented results for primary outcomes were included. Data were analyzed using Graph Pad Prism 7.0 (San Diego, CA, USA). Descriptive statistics were used for patient characteristics at baseline and drug-therapy problems. For comparisons between the baseline and endpoint values, the student's t-test for normally distributed data and the Wilcoxon signed-rank test for non-normally distributed data were used for continuous variables; Fisher's exact test was used for categorical variables. Data were presented as frequency (percentage) or mean (± standard deviation). For analyses, a value of $p < 0.05$ was considered to be statistically significant.

Ethics approval

This study was approved by the Human Research Ethics Committee at the Clinical Hospital and the School of Pharmaceutical Sciences of the University of São Paulo (CAAE number: 27656514.9.3001.0067).

RESULTS

Patient characteristics

Of the 25 patients referred to FARMUSP by a urologist of the Teaching Hospital, 24 agreed to participate. During the study period, two patients died before the 12-months follow-up (lung cancer and heart attack) and two patients were referred to another hospital to treat castration-resistant prostate cancer. The remaining 20 patients were included in the final analysis and their baseline characteristics are shown in Table I. The mean age of participants was 77.1 (±7.9) years. Most patients had completed at least elementary school (75.0%) and did not regularly practice physical activity (65.0%). Hypertension (70.0%) and diabetes mellitus (30.0%) were the most common comorbidities. The mean number of medications was 5.5 (±3.3) and most patients (90.0%) received only one drug for prostate cancer care.

TABLE I - Patient characteristics at baseline

Variable	Clinical pharmacy service (n = 20)
Male gender, n (%)	20 (100.0)
Age in years, mean (±SD)	77.1 (±7.9)
Educational level, n (%)	
Elementary	15 (75.0)
Middle School	2 (10.0)
High School or College	3 (15.0)
Marital status, n (%)	
Married/partner	16 (80.0)
Divorced	4 (20.0)
Single	0 (0.0)
Widow	0 (0.0)
Comorbidities, n (%)	
Hypertension	14 (70.0)
Diabetes mellitus	6 (30.0)
Dyslipidemia	3 (15.0)
Nº of medications, mean (±SD)	5.5 (±3.3)
Treatment type, n (%)	
Cyproterone	9 (45.0)
Goserelin	9 (45.0)
Cyproterone and Goserelin	2 (10.0)

Abbreviations: SD, standard deviation.

Drug-therapy problems and interventions

311 drug-therapy problems were documented during the 12-month follow-up, with a mean of 15.5 (±7.5) per patient (Table II). All patients presented at least one problem. The problems were mainly related to "adverse drug reactions" (244; 78.5%), "medication adherence or administration" (35; 11.3%), and "drug selection or prescription" (25; 8.0%). As can be seen in Table III, most adverse drug reactions - all grades of severity (221 of 244; 90.6%) were associated with antiandrogen therapies such as: reduced libido (22), erectile dysfunction (19), hyperglycemia (18), fatigue (16), and gynecomastia (15). Most problems for medication adherence or administration occurred due to underdosing (25; 8.0%) and improper self-medication (4; 1.3%). The untreated clinical conditions (11; 3.5%) and the need for additional medications (8; 2.6%) were the most frequent problems related to drug selection and prescription. Individualized interventions involving the clinical pharmacist in cooperation with patient or physician solved most of the problems (72.3%), especially those related to dose adjustment, specific instruction on the proper use of medication, and explanation of how medication can fit the health goals. Although many drug-therapy problems related to adverse drug reactions have been identified, it has not always been possible to solve it (e.g., erectile dysfunction) considering the assessment of the risk-benefit. The physician accepted most of the suggestions made by the pharmacist (85.0%) involving prescription changes.

TABLE II - Type of drug-therapy problems identified

Drug-therapy problems	n (%)
Drug selection or prescription	
Prescription of an inappropriate or contraindicated medicine	1 (0.3)
Drug-drug interaction	3 (1.0)
Drug-food interaction	11 (3.5)
Need for additional medicine	8 (2.6)
Other selection and prescription problems	2 (0.6)
Medication adherence or administration	
Omission of doses (sub-dosage) by the patient	25 (8.0)
Addition of doses (overdose) by the patient	1 (0.3)
Incorrect patient administration technique	2 (0.6)
Frequency or time of incorrect administration (without changing daily dose)	2 (0.6)
Improper discontinuation of the medicine by the patient	1 (0.3)
Improper self-medication	4 (1.3)
Dispensation or manipulation of medications	
Medicine missing in stock (not dispensed)	2 (0.6)
Drug quality	
Improper storage	1 (0.3)
Monitoring procedures	
Need for laboratory monitoring	1 (0.3)
Need for self monitoring	2 (0.6)
Therapy effectiveness	
Ineffective treatment with identified cause	1 (0.3)
Adverse drug reaction	
Dose-dependent adverse reaction (type A)	244 (78.5)
Total	311 (100.0)

TABLE III - Frequency of adverse drug reactions (all grades of severity) associated with antiandrogen drugs (n = 221)

Adverse reactions	Cyproterone	Goserelin	Cyproterone + Goserelin	Total n (%)
Anemia	2	4	1	7 (3.2)
Atrophy of genitals	0	1	0	1 (0.5)
Breast tenderness	8	1	1	10 (4.5)
Depression	4	3	2	9 (4.1)
Diarrhea	3	0	0	3 (1.4)
Dizziness	3	1	1	5 (2.3)
Erectile dysfunction	7	10	2	19 (8.6)
Fatigue	9	5	2	16 (7.2)
Gynecomastia	7	3	5	15 (6.8)
Headache	0	1	0	1 (0.5)
Hot flashes	6	5	1	12 (5.4)
Hyperglycemia	11	5	2	18 (8.1)
Hyperlipidemia	3	4	5	12 (5.4)
Hyperprolactinemia	3	0	0	3 (1.4)
Increased blood pressure	2	1	0	3 (1.4)
Injection site reaction	0	1	0	1 (0.5)
Loss of appetite	0	1	0	1 (0.5)
Myalgia	0	2	1	3 (1.4)
Nausea	2	0	0	2 (0.9)
Peripheral edema	1	1	0	2 (0.9)
Prolonged QT interval	0	0	1	1 (0.5)
Reduced libido	9	10	3	22 (10.0)
Weakness	2	2	0	4 (1.8)
Weight gain	0	0	2	2 (0.9)
Other	16	26	7	49 (22.2)
Total, n (%)	98 (44.3)	87 (39.4)	36 (16.3)	221 (100.0)

PSA and testosterone levels

A significant mean reduction from baseline of –3.4 ng/mL (p = 0.039) in PSA levels and –153.5 ng/dL (p = 0.021) in testosterone levels was observed at 6 months of follow-up. At the 12-month follow-up, only the PSA reduction was significant (–2.7 ng/mL; p = 0.022) and there was a trend of improvement in testosterone levels (–128.9 ng/dL, p = 0.055). Many patients were able to reach the target of PSA < 0.2 ng/mL throughout this study; however, the results were not significant, as can be seen in Table IV.

TABLE IV - Changes in PSA and testosterone levels

Variables	Baseline	6 months	12 months	p value[a]	p value[b]
PSA levels, n (%)					
≤ 0.2 ng/mL	6 (30.0)	11 (55.0)	12 (60.0)	0.200	0.111
> 0.2 ng/dL and ≤ 4 ng/mL	6 (30.0)	7 (35.0)	6 (30.0)	1.000	1.000
> 4 ng/mL and ≤ 10 ng/mL	4 (20.0)	1 (5.0)	1 (5.0)	0.342	0.342
> 10 ng/mL and ≤ 20 ng/mL	3 (15.0)	0 (0.0)	0 (0.0)	0.231	0.231
> 20 ng/mL	1 (5.0)	1 (5.0)	1 (5.0)	1.000	1.000
PSA levels, ng/mL, mean (±SD)	5.0 (±7.1)	1.6 (±4.5)	2.3 (±7.8)	0.011[d]	0.022[d]
Testosterone levels, ng/dL, mean (±SD[c]	221.7 (±228.7)	68.2 (±101.5)	92.8 (±124.2)	0.005[d]	0.055[d]

Abbreviations: SD, standard deviation.
[a] Comparison between baseline and 6 months.
[b] Comparison between baseline and 12 months.
[c] Three patients were excluded because they did not have laboratory tests available at baseline.
[d] p value from the Wilcoxon signed-rank test.

Medication adherence

At the baseline, more than half of the patients (56.3%) had high medication adherence and no significant changes in adherence status were observed at the end of the study (Figure I). Similarly, there was no change in the average score from the Morisky-Green test (3.0 ±1.3 vs. 3.0 ±1.2; p = 1.000).

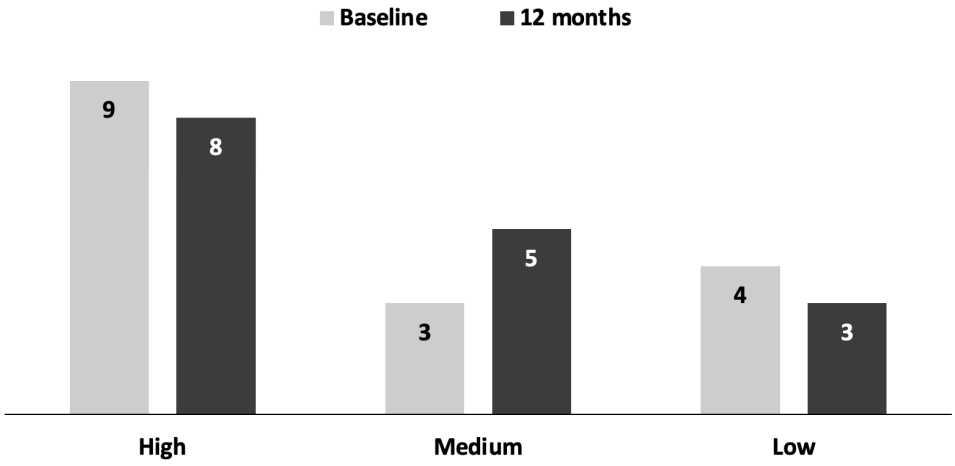

FIGURE1 - Changes in medication adherence status by Morisky-Green test for patients with prostate cancer[a].

a Four patients were excluded this analysis: one was hospitalized; one was transferred to another hospital and two patients were not using medication (intermittent treatment).
p = 1.000 for differences in baseline and 12 months for high and low adherence.
p = 0.685 for differences in baseline and 12 months for medium adherence.

Quality of life

At the 12-month follow-up, only the "pain" domain showed a significant difference (p = 0.019) and there was a tendency for improvement in "physical aspects" (p = 0.078) and "vitality" (p = 0.088) based on the SF-36 generic questionnaire (Table Va). As measured by the specific questionnaire FACT-P, no significant changes were observed during the 12 months of the study (Table Vb).

TABLE V - Changes in quality of life of patients with prostatic cancer

a. FACT-P specific questionnaire

Scale	Nº of items	Total score	Baseline	12 months	p value
			Mean (SD)	Mean (SD)	
FACT-P total [a]	39	0-156	119.9 (20.2)	119.8 (22.4)	0.982
Physical well-being	7	0-28	23.8 (3.9)	23.4 (4.3)	0.778 [b]
Social well-being	7	0-28	20.7 (4.5)	21.4 (4.5)	0.513
Emotional well-being	6	0-24	20.4 (4.2)	19.2 (4.0)	0.150
Functional well-being	7	0-28	20.1 (5.1)	19.9 (5.4)	0.913
Prostate Cancer Subscale	12	0-48	34.9 (6.6)	35.9 (7.5)	0.510

b. SF-36 generic questionnaire

Domain	Baseline	12 months	p value
	Mean (SD)	Mean (SD)	
Functional capacity [a]	65.6 (22.8)	66.9 (26.9)	0.754 [c]
Physical aspects [a]	58.3 (38.3)	76.4 (30.3)	0.078 [c]
Pain [a]	71.8 (19.3)	81.3 (18.3)	0.019 [c]
General state of health [a]	73.3 (18.5)	77.3 (18.8)	0.572
Vitality [a]	61.1 (13.5)	69.4 (17.7)	0.088 [c]
Social aspects [a]	84.7 (22.9)	83.3 (23.5)	0.999
Emotional aspects [a]	85.2 (28.5)	81.5 (34.7)	0.812
Mental health [a]	75.3 (19.2)	81.1 (20.5)	0.196 [c]

[a] Two patient were excluded: one was transferred to another hospital and one was hospitalized.
[b] p value from Wilcoxon signed-rank test; other variables were compared using parametric test.
[c] p value from Student's t-test; other variables were compared using non-parametric test.

DISCUSSION

To the best of our knowledge, this is the first research to evaluate the effect of pharmacist interventions for patients with prostate cancer on PSA and testosterone levels, medication adherence, and quality of life, besides including patients submitted to chemical castration with the use of goserelin and/or cyproterone acetate. This study is also innovative in its approach to monitoring the effect of antineoplastic drugs dispensed via administrative requests in Brazil. Despite the small sample size and the absence of the control group, the results of this investigation reinforce that the clinical pharmacist can play an important role in the collaborative management among health professionals in the care of patients with prostate cancer.

All of the patients in this study had at least one drug-therapy problem. Most of the documented problems

involved adverse reactions, which is consistent with the findings of previous studies on pharmacist interventions in cancer (Ribed *et al*., 2016; Liekweg *et al*., 2012). The main adverse reactions were reduced libido, erectile dysfunction, hyperglycemia, fatigue, and gynecomastia. As adverse reactions can reduce patients' quality of life and contribute to poor medication adherence (Nguyen *et al*., 2015; Greer *et al*., 2016), the identification and management of these reactions can be essential to optimize treatment outcomes. Many patients included in our study were elderly, had lower levels of education, and used more medication, than most of the other patients, and these factors significantly contribute to poor adherence to antineoplastic drugs (Greer *et al*., 2016). Despite these possible difficulties, medication adherence remained stable as of the 12-months follow-up with the pharmacist. In addition, a recent systematic review showed that sustainability of adherence to medications over time is dependent upon multicomponent interventions including educational, attitudinal and technical aspects to modify and enhance patient medication-taking behavior (Wiecek *et al*., 2019).

Although quality of life may be difficult to measure because the actual values may be masked by sample size, low sensitivity, or inability of the pharmacist to apply the questionnaires (Melchiors *et al*., 2005; Kheir *et al*., 2004), in our study, patients presented significant improvement in the "pain" domain and improvement tendencies in the "physical aspect"' and "vitality" domains, according to the SF-36 tool. The pharmacist should be aware that the chronicity of the pain can trigger other problems such as anxiety, fear, depression, and hopelessness, which will negatively affect the quality of life of the patients and their family (Margarit *et al*., 2012). In a recent systematic review, pharmacist interventions have significantly improved quality of life in outpatients with cancer (global scale or items of European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30) (Colombo *et al*., 2017). The analysis of quality of life is essential as cancer is considered one of the most feared diseases, involving the possibility of death and the prospect of aggressive treatments and adverse drug reactions (Donovan *et al*., 2016).

During the study period, there was a reduction in PSA and testosterone levels and most patients reached a PSA level < 0.2 ng/mL. However, only differences in PSA and testosterone levels at 6 months and PSA levels at 12 months were statistically significant. In all likelihood, the sample size of this study was simply insufficient to detect significant effects in all outcome measures. Our findings are quite promising since decreases in PSA and testosterone levels are inversely related to disease recurrence and metastasis and directly related to patient survival (Mottet *et al*., 2016).

The limitations of our study are the small sample size, single-center setting, and absence of a control group. In addition, patients may have received care from other health services in addition to the multi-professional team of the Teaching Hospital, which may have affected the observed results. These limitations are common in studies of pharmacist interventions in oncology (Colombo *et al*., 2017), and studies assessing the impact of interventions (changes from pre-to post-pharmacist interventions) in this area remain scarce. It is expected that the findings of this pioneering research may help consolidate the practice of pharmacist care in patients with prostate cancer.

CONCLUSION

The findings showed that most drug-therapy problems were related to adverse reactions and the most common of them were reduced libido, erectile dysfunction, hyperglycemia, fatigue, and gynecomastia. Testosterone levels significantly decreased at 6 months, and PSA levels at 6 and 12 months. No significant changes in adherence were noted at end of the study. A significant improvement in the "pain" domain and an improvement trend in the "physical aspects" and "vitality" domains were observed based on the SF-36 generic instrument. Future research with a randomized controlled trial design study, larger sample size, and multi-center is needed to validate the impact of pharmacist interventions in the care of prostate cancer.

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CONFLICT OF INTERESTS

The authors have no conflict of interest to declare.

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