

Oral Antineoplastics: Treatment Adherence and Medication Beliefs

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Antineoplásicos Oraís: Adesão ao Tratamento e Crenças sobre os Medicamentos

Agentes Antineoplásicos Orales: Adherencia al Tratamiento y Creencias sobre los Medicamentos

Vânia Mari Salvi Andrzejewski¹; Sérgio Lunardon Padilha²; Jorge Vinícius Cestari Felix³; Francisco Diego Negrão Lopes Neto⁴; José Zanis Neto⁵

ABSTRACT

Introduction: Adherence to oral antineoplastics (OA) is an important indicator of therapeutic response related to personal, social, and structural factors. **Objective:** To determine rates of adherence to OA, investigating possible risk factors for nonadherence and to assess patient beliefs about medication, identifying opportunities for pharmaceutical intervention. **Method:** An analytical study was conducted with cancer patients using OA in 2015. Adherence to Refills and Medication Scale (ARMS) and Beliefs about Medicines Questionnaire (BMQ) were applied to assess adherence and beliefs about medication and treatment. Mann-Whitney, Chi-square, and Fisher's Exact tests were used for data analysis. **Results:** A total of 222 patients were interviewed, with a 92.8% adherence rate according to ARMS and 84.7% according to BMQ, in which the necessity-beliefs exceeded the concerns with the treatment and use of OA. Family income, treatment interruption, number and causes of interruptions, depression, and medication possession ratio were the risk factors identified. Comparison of BMQ domains showed that, in the adherent group, patient beliefs in the necessity of the medication exceeded their concerns about it. **Conclusion:** Understanding the patient's beliefs is a decisive factor in comprehending the risks related to nonadherence as well as in defining strategies to deal with it.

Key words: Medication Adherence; Pharmaceutical Services; Administration, Oral; Antineoplastic Agents; Culture.

RESUMO

Introdução: A adesão aos antineoplásicos orais (AO) é um importante indicador de resposta terapêutica relacionada a fatores pessoais, sociais e estruturais. **Objetivo:** Determinar as taxas de adesão aos AO, investigando possíveis fatores de risco para a não adesão, e avaliar as crenças dos pacientes sobre medicamentos, identificando oportunidades de intervenção farmacêutica. **Método:** Estudo analítico realizado com pacientes com câncer em uso de AO em 2015. Escala de Adesão e Recarga dos Medicamentos (ARMS) e Questionário de Crenças sobre Medicamentos (BMQ) foram aplicados para avaliar a adesão e crenças sobre medicamentos e tratamento. Os testes de Mann-Whitney, qui-quadrado e exato de Fisher foram usados para análise de dados. **Resultados:** Foram entrevistados 222 pacientes, com taxa de adesão de 92,8%, segundo o ARMS e 84,7%, segundo o BMQ, no qual as crenças de necessidade excederam as preocupações com o tratamento e o uso de AO. Renda familiar, interrupção do tratamento, número e causas das interrupções, depressão e razão de posse de medicamentos foram os fatores de risco identificados. A comparação dos domínios do BMQ demonstrou que, no grupo aderente, as crenças dos pacientes sobre a necessidade do medicamento excederam suas preocupações quanto a isso. **Conclusão:** Considerar as crenças do paciente é um fator decisivo para compreender os riscos relacionados à não adesão, bem como para definir estratégias para lidar com ela.

Palavras-chave: Adesão à Medicação; Assistência Farmacêutica; Administração Oral; Antineoplásicos; Cultura.

RESUMEN

Introducción: La adherencia a antineoplásicos orales (AO) es un indicador importante de la respuesta terapéutica relacionada con factores personales, sociales y estructurales. **Objetivo:** Determinar tasas de adherencia a AO, investigar posibles factores de riesgo de incumplimiento y evaluar creencias de los pacientes sobre la medicación, identificando oportunidades para intervención farmacéutica. **Método:** Estudio analítico con pacientes con cáncer que usaban AO en 2015. Se aplicó Adherencia a la Recogida y Administración de la Medicación (ARMS) y Cuestionario de Creencias sobre Medicación (BMQ) para evaluar el cumplimiento y las creencias sobre medicación y tratamiento. Las pruebas de Mann-Whitney, Chi-cuadrado y Exacto de Fisher se utilizaron para análisis de datos. **Resultados:** Se entrevistó un total de 222 pacientes, con una tasa de adherencia de 92,8% según ARMS y 84,7% según BMQ, en la cual las creencias de necesidad excedieron preocupaciones con el tratamiento y uso de AO. Ingreso familiar, interrupción del tratamiento, número y causas de interrupciones, depresión y proporción de posesión de medicamentos fueron los factores de riesgo identificados. La comparación de los dominios de BMQ mostró que, en el grupo adherente, las creencias sobre necesidad de la medicación excedieron preocupaciones. **Conclusión:** La consideración de las creencias del paciente es un factor decisivo para comprender los riesgos relacionados con la no adherencia, así como para definir estrategias para afrontarla.

Palabras clave: Cumplimiento de la Medicación; Servicios Farmacéuticos; Administración Oral; Antineoplásicos; Cultura.

¹⁻⁵Federal University of Paraná (UFPR). Hospital of Clinics. Curitiba (PR), Brazil.

¹E-mail: salviavania@gmail.com. Orcid iD: <http://orcid.org/0000-0003-3877-1487>

²E-mail: serlunarpadi@hotmail.com. Orcid iD: <https://orcid.org/0000-0001-6532-0062>

³E-mail: jvcfelix@hotmail.com. Orcid iD: <http://orcid.org/0000-0002-0086-674X>

⁴E-mail: francisco.negrao@ebserh.gov.br. Orcid iD: <https://orcid.org/0000-0003-2094-5928>

⁵E-mail: zanisneto@gmail.com. Orcid iD: <https://orcid.org/0000-0002-0322-737X>

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Corresponding author: Vânia Mari Salvi Andrzejewski. Setor de Farmácia Hospitalar do Complexo do Hospital de Clínicas da Universidade Federal do Paraná. Rua General Carneiro, 181 - Alto da Glória. Curitiba (PR), Brazil. CEP 80060-900. E-mail: salviavania@gmail.com



INTRODUCTION

The significant increase in the number and complexity of oral medication regimens for cancer patients in recent years has radically changed the management of these products¹⁻⁵. Consequently, new concerns have emerged, prompting changes of the roles, responsibilities, and priorities of patients and health professionals. Such changes have urged the adequacy of the healthcare system, especially regarding patient safety, communication, and treatment adherence, requiring new controls and guidelines for satisfactory results²⁻⁷. The treatment with oral antineoplastics (OA) is preferred over traditional regimens such as intravenous infusion for being less invasive, painful, and risky, besides waiving the need to be performed in a health institution^{2,5-7}.

Adherence to OA is an important indicator of therapeutic response^{2,3,6,8,9}. Several studies have shown that poor adherence may affect treatment efficacy, toxicity, public health expenditures, patient survival time, and increase mortality risk^{1-3,5-12}. For women with hormone receptor-positive breast cancer, for example, mortality can reach up to 49% of nonadherents⁸.

For the International Society for Pharmacoeconomics and Outcomes Research, adherence to medication is defined as “the degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency”¹⁻³. The Medication Possession Ratio (MPR) is a validated method for measuring adherence by tracking pharmacy dispensing records and dates^{5,10,13}, counting the number of days that the patient is in possession of the medication and serving as a basis for assessing the quality of the administrative phases of the processes related to pharmacotherapy and not strictly for adherence¹⁴. In oncology, there is some variation in the desirable value for MPR according to the type of cancer, where patients with MPR values between 0.8 and 1 (80% and 100%) are considered adherent^{3,5,9,12,13}. The closer to 1, more certainty of pharmacological response to the proposed treatment will be.

Noncompliance with cancer treatment is complex and multifactorial, being related to personal, social, and structural factors^{1,3,8}. Barriers to adherence and persistence are linked to self-efficacy, social support, continuity of follow-up care, patient-health professional relationship, and side effects^{4-6,8}. In addition, from the patient's point of view, nonadherence is also influenced by beliefs about the necessity of treatment, risk-benefit analysis, fear of disease recurrence, information about diagnosis and treatment, as well as their previous experiences^{4,8}.

Implementing strategies to improve adherence to OA is a major challenge and involves patient education, understanding nonadherence risks, and proper management of adverse events with real-time OA-related problem resolution^{9,12}. In this sense, the oncology clinical pharmacist specialist plays an essential role in this process, since the professional maintains continuous and systematic contact with the patient throughout the treatment, guiding, educating, monitoring, managing adverse effects, and making the necessary referrals for problem solving^{6,11,13}.

Considering that the nonadherence to OA treatment is a complex and multidimensional process that can compromise the therapeutic efficacy and even increase the risk of mortality, especially in cancer patients, this study aims to determine rates of adherence to OA agents, investigating possible risk factors for nonadherence and to assess patient's beliefs about medication, identifying opportunities for pharmaceutical intervention.

METHOD

Analytical quantitative approach cross-sectional study conducted at the Oncology and Hematology Outpatient Clinic of a teaching hospital in a Brazilian southern capital.

The survey was performed from October 2013 to March 2015 by convenience sampling. The inclusion criteria were: patients aged 18 years or older undergoing outpatient cancer treatment with OA for at least one month; ability to understand, verbalize, and answer the questions or availability of a companion who can answer the requested information. Exclusion criteria were: pregnancy, mental/psychiatric illness, and inability to attend the hospital.

During a visit to the outpatient clinic, participants were invited for an interview to answer a questionnaire, addressing clinical and sociodemographic variables, questions related to the health system care, plus two specific instruments for assessing treatment adherence and beliefs. The first instrument, called Adherence to Refills and Medication Scale (ARMS) consists of 12 items in 4-point Likert scale: never, sometimes, often, and always, addressing the patient's concern about buying their medicines, refilling them at the health system (refill), and forgetting to take them (taking)¹⁵. The final result is obtained by summing the values of the answers and the score ranges from 12 to 48 points. The adherence rate was classified according to the following values: (a) total adherence when the sum reached 12 points; (b) partial adherence when scores ranged between 13 and 21 points; and (c) nonadherence when the score exceeded 21 points. Patients who scored between 12 and 21 points

were considered adherent, which corresponds to 80% of the maximum score that could be obtained through the instrument.

The second instrument is the Beliefs about Medicines Questionnaire (BMQ), which assesses the patient's beliefs over the disease and treatment, as well as their behavior in respect to adherence. The BMQ was validated for the Portuguese language in 2013 and consists of two subscales and 11 items in 3-point Likert scale: agree, not sure, and disagree, addressing issues related to the patient necessity and concerns regarding the disease and proposed treatment¹⁶⁻¹⁸. The final result is obtained by dividing the necessity score by the concerns score and indicates a tendency to adhere or not to the treatment. The best adherence occurs as high is the value of necessity versus concerns. Results higher than one indicate that the patient's beliefs about the necessity of treatment outweigh the concerns about medication use and its consequences.

The Medication Possession Ratio (MPR) value was calculated by the number of days that the medication was prescribed divided by the number of days covered, evaluating patient refill electronic records at the pharmacy responsible for dispensing the OA. Patients who obtained MPR values greater than 0.8 were considered adherent.

To complement the information, the institution's computerized database was consulted, and the patients' medical charts were reviewed. Data were analyzed using IBM SPSS V.25 software. Continuous numerical variables were presented as mean and standard deviation or median and interquartile range, while categorical variables were described as frequencies and percentages. The classification of patients into adherent or nonadherent groups was performed using the results obtained by the ARMS instrument. The variables were compared using the Mann-Whitney, Chi-square, and Fisher's Exact tests, assessing possible associations among categorical variables. The equality of proportions test was also used to evaluate the heterogeneity of patient frequency in both groups. For all tests, 5% significance was adopted.

The Institutional Review Board of the Federal University of Paraná Clinic's Hospital Complex approved the study (number CAAE 23362213.7.0000.0096). All interviewed patients agreed to join the study and signed the Informed Consent Form.

RESULTS

From the total of 222 patients interviewed, with mean age of 59.7 years (± 13.5 SDM – standard deviation of the mean), 75.7% earned up to 3 minimum wages per family. Most adherent patients (72.5%) had family income of less than or equal to 3 minimum wages ($p=0.005$). However,

there were no significant differences between groups regarding origin, gender, age, ethnicity, marital status, religion, education, and employment status.

The results obtained with ARMS are presented in Table 1. An adherence rate of 92.8% was observed, indicating that the patients were quite aware about having the drug for use, besides low medication-intake forgetting rates or concern about the treatment ($p<0.001$).

Regarding clinical variables, adherent and nonadherent groups were not different. The drugs the interviewed patients used were aromatase inhibitors (17%), Capecitabine (10.4%), Flutamide (10.4%), hydroxyurea (16.7%), and tamoxifen (45.5%). The presence of other comorbidities was reported for 87.8% of the patients, where 30.6% had four or more health problems besides cancer and 59.4% were polymedicated. The most prevalent diseases were systemic arterial hypertension (49.5%), depression (30.2%), and hyperlipidemia (24.3%). Proportionally, depression rates were higher among nonadherents ($p = 0.025$) (Table 2).

Treatment discontinuation was observed in 50.9% of the patients and was more frequent among adherents ($p = 0.008$). The frequency of treatment interruptions was once for 21.6%, twice for 17.6%, three times for 10.4%, and more than three times for 1.3% of the participants ($p = 0.001$). For adherent patients, the most important reasons for each interruption (once, twice, and three times, respectively) were lack of medication in the pharmacy (27.5%, 12.6%, and 4.5%), followed by personal problems (4.5%, 5.8%, and 3.6%) and adverse drug reactions (3.6%, 1.8%, and 0.5%) ($p = 0.001$). For nonadherent patients, personal problems were the most common (3.1%, 2.7%, and 2.2%), followed by several reasons such as adverse drug reactions (1.3%), transportation problems (0.9%) and pharmacy drug shortages (0.5%) ($p = 0.001$) (Table 2).

Also, 82.9% of the patients had a medication possession ratio considered adequate (MPR > 80%), where 79.7% of them were adherent, versus only 3.1% of nonadherents ($p < 0.05$). Besides, it was observed that 69.3% of the female patients had breast tumors. Treatment with OA lasted for 12 months or more for 53.2% of the patients, while 17.1% were under treatment for less than 3 months (Table 2).

Table 3 presents the patients' beliefs regarding cancer treatment and their influence on necessity of treatment and concerns about OA use. Four of the five necessity-related questions were significant: "my life would be impossible without these medications" ($p = 0.006$), "without these medications, I would be very sick" ($p = 0.012$), "my future health will depend on these medications" ($p = 0.004$), and "these medications prevent me from getting worse" ($p <$

Table 1. Distribution of responses by items and adherence classification according to the instrument Adherence to Refills and Medications Scale (ARMS)

ARMS questionnaire items	Never		Sometimes		Often		Always	
	A	NA	A	NA	A	NA	A	NA
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Do you...								
T1 – forget to take your medications?	126 (56.8)	2 (0.9)	74 (33.3)	7 (3.2)	4 (1.8)	5 (2.3)	2 (0.9)	2 (0.9)
T2 – decide not to take them that day?	181 (81.5)	5 (2.3)	23 (10.4)	8 (3.6)	2 (0.9)	3 (1.4)	0 (0)	0 (0)
R3 – forget to go to the pharmacy to get them?	190 (85.6)	4 (1.8)	15 (6.8)	7 (3.2)	0 (0)	3 (1.4)	1 (0.5)	2 (0.9)
R4 – run out of them?	179 (80.6)	4 (1.8)	24 (10.8)	7 (3.2)	0 (0)	2 (0.9)	3 (1.4)	3 (1.4)
T5 – not take them because of a doctor’s appointment?	188 (84.7)	6 (2.7)	18 (8.1)	4 (1.8)	0 (0)	3 (1.4)	0 (0)	3 (1.4)
T6 – stop taking them when you feel better?	191 (86)	6 (2.7)	12 (5.4)	6 (2.7)	3 (1.4)	4 (1.8)	0 (0)	0 (0)
T7 – stop taking them when you feel sick?	194 (87.4)	6 (2.7)	12 (5.4)	7 (3.2)	0 (0)	3 (1.4)	0 (0)	0 (0)
T8 – stop taking them when you are more careless with yourself?	196 (88.3)	6 (2.7)	10 (4.5)	6 (2.7)	0 (0)	4 (1.8)	0 (0)	0 (0)
T9 – change their dose for any need?	179 (80.6)	10 (4.5)	26 (11.7)	3 (1.4)	0 (0)	1 (0.5)	1 (0.5)	2 (0.9)
T10 – forget to take them when you must take it more than once a day?	181 (81.5)	5 (2.3)	20 (9)	4 (1.8)	4 (1.8)	4 (1.8)	1 (0.5)	3 (1.4)
R11 – stop buying them if they are expensive?	113 (50.9)	5 (2.3)	26 (11.7)	3 (1.4)	9 (4.1)	0 (0)	58 (26.1)	8 (3.6)
R12 – refill before finishing the ones you have at home?	175 (78.8)	3 (1.4)	20 (9)	3 (1.4)	4 (1.8)	7 (3.2)	7 (3.2)	3 (1.4)

Captions: A: adherents (ARMS score ≥ 12 and ≤ 21), n = 206 (92.8%); NA: nonadherents (ARMS score > 21), n = 16 (7.2%).

Table 2. Distribution of clinical and pharmacotherapy-related variables associated with adherence of patients using oral antineoplastic agents. n = 222

Variables	Adherence		Total	p-value
	Yes n (%)	No n (%)	n (%)	
Disease classification				0.831 ^b
Breast	143 (64.4)	11 (4.9)	154 (69.3)	
Hematologic	33 (14.9)	4 (1.8)	37 (16.7)	
Prostate	22 (9.9)	1 (0.5)	23 (10.4)	
Other	8 (3.6)	0 (0)	8 (3.6)	
Treatment time				0.565 ^b
≤ 3 months	37 (16.6)	1 (0.5)	38 (17.1)	
> 3 and ≤ 12 months	61 (27.5)	5 (2.2)	66 (29.7)	
≥ 12 months	108 (48.7)	10 (4.5)	118 (53.2)	
Medication				0.214 ^b
Anastrozole	38 (17.1)	0 (0)	38 (17)	
Tamoxifen	91 (41)	10 (4.5)	101 (45.5)	
Hydroxyurea	33 (4.9)	4 (1.8)	37 (16.7)	
Capecitabine	22 (9.9)	1 (0.5)	23 (10.4)	
Flutamide	22 (9.9)	1 (0.5)	23 (10.4)	
Interruptions of OA use?				0.008 ^{b*}
Yes	100 (45)	13 (5.9)	113 (50.9)	
No	106 (47.8)	3 (1.3)	109 (49.1)	

to be continued

Table 2. continuation

Variables	Adherence		Total	p-value
	Yes n (%)	No n (%)	n (%)	
Interruption frequency				0.001 ^{b*}
None	106 (47.7)	3 (1.3)	109 (49.1)	
Once	45 (20.3)	3 (1.3)	48 (21.6)	
Twice	35 (15.8)	4 (1.8)	39 (17.6)	
Three times	20 (9)	3 (1.3)	23 (10.4)	
More than three times	0(0)	3 (1.3)	3 (1.3)	
Interruption reason (1 st time)				0.001 ^{b*}
Did not interrupt	106 (47.7)	3 (1.3)	109 (49.1)	
Drug shortage	61 (27.5)	2 (0.9)	63 (28.4)	
Personal problems	10 (4.5)	7 (3.1)	17 (7.6)	
Administrative problems	9 (4)	1 (0.5)	10 (4.5)	
Adverse drug reactions	8 (3.6)	3 (1.3)	11 (4.9)	
Transport problems	5 (2.2)	0 (0)	5 (2.2)	
Hospitalization	3 (1.3)	0 (0)	3 (1.3)	
Exams	2 (0.9)	0 (0)	2 (0.9)	
Pregnancy	1 (0.5)	0 (0)	1 (0.5)	
Hospital strike	1 (0.5)	0 (0)	1 (0.5)	
Interruption reason (2 nd time)				0.001 ^{b*}
Did not interrupt	149 (67.1)	6 (2.7)	155 (69.8)	
Drug shortage	28 (12.6)	0 (0)	28 (12.6)	
Personal problems	13 (5.8)	6 (2.7)	19 (8.6)	
Hospitalization	5 (2.2)	1 (0.9)	6 (2.7)	
Transport problems	4 (1.8)	2 (0.9)	6 (2.7)	
Adverse drug reactions	4 (1.8)	0 (0)	4 (1.8)	
Administrative problems	1 (0.5)	0 (0)	1 (0.5)	
Exams	1 (0.5)	0 (0)	1 (0.5)	
Pregnancy	1 (0.5)	0 (0)	1 (0.5)	
Hospital strike	0 (0)	1 (0.5)	1 (0.5)	
Interruption reason (3 rd time)				0.001 ^{b*}
Did not interrupt	186 (83.8)	10 (4.5)	196 (88.3)	
Drug shortage	10 (4.5)	1 (0.5)	11 (4.9)	
Personal problems	8 (3.6)	5 (2.2)	13 (5.8)	
Hospitalization	1 (0.5)	0 (0)	1 (0.5)	
Adverse drug reactions	1 (0.5)	0 (0)	1 (0.5)	
Comorbidities				0.700 ^b
Yes	180 (81.1)	15 (6.7)	195 (87.8)	
No	26 (11.7)	1 (0.5)	27 (12.2)	
Number of comorbidities besides cancer				0.248 ^b
≤ 3	145 (65.3)	9 (4)	154 (69.4)	
≥ 4	61 (27.5)	7 (3.1)	68 (30.6)	
More frequent comorbidities				
Hypertension	100 (45)	10 (4.5)	110 (49.5)	0.311 ^b
Depression	58 (26.1)	9 (4.1)	67 (30.2)	0.025 ^{b*}
Hyperlipidemias	52 (23.4)	2 (0.9)	54 (24.3)	0.140 ^b
Number of medications used				0.599 ^a
≤ 4	85 (38.3)	5 (2.2)	90 (40.5)	
≥ 5	121 (54.5)	11 (5)	132 (59.5)	
Medication Possession Ratio				0.001 ^{b*}
≤ 80%	29 (13.1)	9 (4)	38 (17.1)	
> 80%	177 (79.7)	7 (3.1)	184 (82.9)	

(a) Chi-square test. (b) Fisher's exact test. (*) 5% significance level.

0.001). A single concern-related question was significant: “these medications disturb my life” ($p = 0.002$). The final result of $BMQ < 1$ indicated a nonadherence trend for 15.3% of the patients.

Considering the ARMS adherent or nonadherent classification, significant differences were observed between the groups in relation to the BMQ domains (necessity and concerns) (Figure 1). In the group considered adherent to treatment (ARMS 12-21), it was observed that the “necessity” was 93% versus 56% for “concerns”. In the nonadherent group (ARMS > 21), “necessity” was 80%, differing from that observed in the adherent group ($p = 0.00652$). Regarding “concerns”, 67% was obtained in the nonadherent group versus 56% in the adherent group. The ratio between “necessity” and “concerns” was higher in the adherent group (1.8) than in the nonadherent group (1.108) ($p = 0.00578$). This data indicates that, regarding the BMQ in the adherent group, the understanding of the necessity of the treatment outweighed the concerns about it.

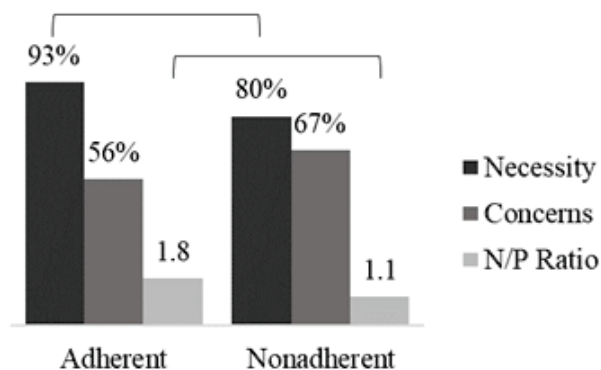


Figure 1. Comparison of BMQ domains pursuant to ARMS adherence classification. Lines above bars indicate differences between adherent and nonadherent groups according to Mann-Whitney test with a 5% significance level (n = 222)

DISCUSSION

The results found in the present study indicated a satisfactory adherence rate compared with those reported in the literature, wherein 92.8% by ARMS, 82.9% by

Table 3. Patients’ beliefs regarding oral antineoplastics necessity (N) or treatment concerns (C) according to the instrument Beliefs about Medicines Questionnaire (BMQ). n = 222

Patient’s opinion on prescription drugs	Adherence		Δ	p-value
	Yes X̄ (±SD)	No X̄ (±SD)		
N1. Currently, my health depends on these medications.	2.87 (±0.44)	2.75 (±0.58)	0.12	0.228
C1. Having to take these drugs worries me.	1.82 (±0.98)	2 (±1.03)	-0.18	0.474
N2. My life would be impossible without these medications.*	2.68 (±0.59)	2.25 (±0.77)	0.43	0.006*
C2. Sometimes, the long-term effects of these drugs worry me.	1.76 (±0.95)	2.13 (±1.02)	-0.37	0.156
N3. Without these medications, I would be very sick.*	2.83 (±0.44)	2.56 (±0.63)	0.27	0.012*
C3. These medications are a mystery to me.	1.26 (±0.61)	1.19 (±0.54)	0.07	0.613
N4. My future health will depend on these medications.*	2.76 (±0.59)	2.31 (±0.87)	0.45	0.004*
C4. These medications disturb my life.*	1.49 (±0.84)	2.19 (±0.98)	-0.70	0.002*
N5. These medications prevent me from getting worse.*	1.08 (±0.32)	1.5 (±0.73)	-0.42	< 0.001*
C5. Sometimes I worry about being too dependent on these drugs.	1.59 (±0.87)	1.88 (±1.02)	-0.29	0.264
P6. These medications give me unpleasant side effects.	2.24 (±0.95)	2.31 (±0.87)	-0.07	0.888
	N/C < 1	N/C > 1		
	34 (15.3%)	188 (84.7%)		

(*) Mann-Whitney test with a 5% significance level. (Δ) Difference between mean scores of adherent and nonadherent groups.

MPR, and 84.7% by BMQ. These percentages must be perceived as parameters for understanding the different aspects that can influence the therapy effectiveness because, despite these results, there is a concern with the real situation of these patients since the data were obtained by analyzing a single cut-off. Reports in the literature suggest that patients tend to respond to what the interviewer wants to hear instead of addressing what is preventing treatment adherence. This condition is called the “Hawthorne” effect, in which the patient demonstrates improved behaviors when being observed^{1,5}. In addition, these methods are susceptible to memory bias and the patient’s will¹⁴. New studies involving cancer patients and using BMQ, other similar instruments or even the modified BMQ have identified the need to consider patients’ beliefs regarding the use of OA, since they can have an impact in the decision to start or continue with the proposed treatment and, thus, influence the adherence process^{4,19-21} directly. According to Nguyen et al.¹⁸, the BMQ has a solid consistency in assessing patients’ beliefs about their medications, besides being a low-cost method.

The MPR value of 82.9% and the adherence rate of 92.8% obtained in this study through the application of ARMS indicate a satisfactory adherence to OA treatment among these patients, within the values described in the international literature^{1,3,7,10,13}. However, it is important to consider that these values may be overestimated since these patients were submitted to a single self-report assessment and information was complemented with medical and pharmacy records. In fact, this is one of the limitations of studies with analytical cross-sectional design, where the investigator assessed risk and outcome factors at the same time of data collection²². Regarding the adherence process, the MPR serves as a basis for identifying whether the patient has the medication in the appropriate amount, considering that the use will necessarily follow medical prescription¹⁴. Although ARMS classically has not been widely used to assess adherence in cancer patients, it has a favorable application for this population and the present results demonstrate that it can be a useful instrument for understanding the factors that affect adherence to treatment with OA.

This concern is reinforced because 75.7% of the patients had family income ≤ 3 minimum wages and it was associated with discontinuous treatment and number of interruptions. Considering that 33.4% of the interruptions were caused by problems with the provider/institution (pharmacy drug shortage, administrative problems, and hospital strike), this would impede patients to purchase drugs due to their socioeconomic conditions^{2,5,7-10,12,23}. Half of the patients indicated that treatment interruption occurred between one and three

times. The main causes of nonadherence were associated with personal and transportation problems, stressing the importance of a support network for better adherence of cancer patients^{1,6,8,10,24} to OA treatment. For the three interruptions reported, treatment-related causes such as adverse reactions or disease-related as hospitalization and exams were negligible in relation to the other factors/reasons^{4-8,10,12,23}. Only one case of medication interruption because of pregnancy was reported.

Other studies corroborate the findings and indicate the importance of using distinct and associated methods to measure adherence as well as the relevance of patient follow-up throughout the whole process of OA taking^{1,3,4,7,10,23,24}. According to Vrijens et al.²⁵, adherence needs to be assessed as a complex process, structured in three distinct components called initiation, implementation, and discontinuation. For each of these phases, patients need information and the factors that can influence them are different and can change over time, especially in long-term treatments, as with several OA.

Polypharmacy and the presence of comorbidities, despite not being significant in this study, are factors of concern and risk for nonadherence^{1-3,6-8,10,23}. The three most common health problems patients report were systemic arterial hypertension, depression, and hyperlipidemias, respectively, which are associated with the use of a large number of medications and the need for more medical appointments/care, further burdening the patient with concerns and increasing even more the need for care. Depression is frequently mentioned in the literature as a nonadherence factor, which is in accordance with the findings of this study^{1,3,4,6-8}.

From the BMQ evaluation, 84.7% of the patients presented results >1 , indicating that most patients understand the necessity and importance of using OA. Significant results for these patients’ beliefs were found in four necessity-related questions. Other studies have also used BMQ to evaluate patient’s beliefs about treatment, suggesting, for example, that the concern-related question “my medications are a mystery to me” may be determinant for adherence⁷. An integrative review has recognized BMQ as a consistent instrument for measuring patients’ beliefs about OA use, identifying that multiple factors are related and intricately, including treatment risk-benefit assessment, understanding that the necessity of treatment is more important than the concerns about it, negative beliefs, fear of adverse reactions, fear of recurrence, coping capacity, treatment information character, quality of relationship with health professionals, and previous experiences, personal or not, related to cancer treatment⁴.

Expectations around the numerous advantages of OA have not fully materialized, once the lack of access and

adherence to treatment generates serious health problems with consequences for patients, service providers, and society itself^{1-3,5,6,11}. Institutions should not neglect their responsibility to patients in relation to care. In this sense, actions related to the development of registration, monitoring and evaluation standards are fundamental for the adequate guidance of the patient regarding OA adherence, in the same way that this practice is already established for intravenous antineoplastic agents. The unique role of the oncology clinical pharmacist specialist emerges within this perspective to assist, collaborate, guide, and define practical and specific solutions to each patient, regarding access, adherence, and management of OA^{1-3,6,7,11,13,23,24}. This professional has the necessary and complete training to make/be the link between the patient and the doctor/service provider/multidisciplinary team in order to solve individual problems related to the use of these medicines^{6,7,11,13,23,24}.

In this research, reports of patients using hydroxyurea were effectively identified. In order to avoid a total interruption in case of lack of the drug in the pharmacy or to adapt to living conditions, patients deliberately reduced the number of pills taken daily or discontinued the use for 2 or 3 days per week^{1,10,11}. This fact is directly connected to the patient's poor understanding of the reasons that lead the clinician to reduce or increase the dosage of the drug after medical consultation¹. Examples like this reinforce the importance and need for health professionals to develop, in collaboration with the patient and/or caregiver, an adherence management plan²⁵.

For OA to be effective and produce clinically favorable results, it is necessary to implement collaborative models, where the management of OA therapy is centered on elements such as interdependence (sharing of information, needs, and results, plus interdisciplinary partnerships) and interrelationships (empowerment of the health team and the patient)⁶. Understanding what affects patients' beliefs regarding treatment adherence seems to be a promising way to achieve more effective results.

Collaborative work among all people involved in the use of OA is essential for better treatment adherence. Professionals should recognize and consider patients' values, beliefs, and individual needs, so that they can help them along this path, establishing a bond and empowering the patient to effectively manage its own treatment.

The present study opens many possibilities of care for patients using OA. The reality identified is not different from those mentioned in the literature, so patients require guidance or support in the use of pharmacotherapy¹⁴, especially in the area of oncology due to the risks involved, such as the risk of disease progression or significant adverse drug reaction – ADR. The goal of the investigators is

to provide a Pharmaceutical Care Outpatient Clinic specialized in the care and monitoring of cancer patients using OA drugs, centering on the patient's needs. Finally, the number of diseases and drugs for cancer treatment addressed, the impossibility of continuing the routine work until March 2019, and the absence of the clinical pharmacist specialist on the oncology team were among the study limitations.

CONCLUSION

The rate of adherence to OA was high, especially through the ARMS method, but given the severity of the disease, continuous monitoring is necessary to ensure the effectiveness of this therapy throughout the treatment, as well as to provide patients, especially nonadherents, with better self-care management skills, reducing the risks associated with this condition.

Understanding the patient's beliefs is a decisive factor in comprehending the nonadherence risks as well as in defining strategies to deal with it. Regardless of other factors, it was observed that when the patient's perception of the necessity of the treatment outweighs its concerns about it, there was higher adherence, leading the patient to follow the use of OA correctly despite the adjustments in daily life that had to be made for that.

Also, it was possible to associate nonadherence to treatment with risk factors linked directly to the patient, such as depression, family income, adverse drug reactions, personal and health problems, and the lack of transportation to the hospital. As for the risk factors linked to the institution, the results suggested the interruption of OA supply and the lack of periodic contact with the patient to identify and solve the problem of non-refilling.

Hence, this study demonstrated that there are important differences in beliefs regarding treatment (necessities and concerns) in nonadherent patients, creating new possibilities for health team interventions, as well as opening the field for new research in this area.

CONTRIBUTIONS

All the authors contributed for the study design and/or planning, collecting, analysis and interpretation of data, wording, critical review and approved the final version to be published.

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CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

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