

## Pharmacological Adherence and Knowledge of Anticoagulated Patients

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### Abstract

**Objective:** To investigate the pharmacological adherence and the knowledge of patients undergoing oral anticoagulation therapy with outpatients.

**Method:** Cross-sectional study with quantitative approach.

**Results:** 222 patients were evaluated, of which 60.8% were classified as non-adherent and 63.1% had inadequate knowledge regarding oral anticoagulant. Non-adherence was related to the longer treatment time ( $p < 0.001$ ) and to patients with INR values outside the therapeutic range ( $p = 0.022$ ). Inadequate knowledge was associated with low educational level ( $p < 0.001$ ), sedentary lifestyle ( $p = 0.027$ ), shorter outpatient follow-up ( $p < 0.001$ ), and patients with RNI values outside the therapeutic range ( $p = 0.012$ ).

**Conclusion:** In view of the results, it is evident the need for health education strategies that address this public, considering individual understanding and pharmacological adherence as crucial in therapy.

**Keywords:** Knowledge; Medication Adherence; Anticoagulant; Nursing

### Introduction

Medicines represent one of the main therapeutic modalities in health practices and, with the significant increase in the prevalence of chronic diseases in recent decades, the use of medications to control these diseases and to prevent complications in the medium and long term has been following this profile. epidemiological [1].

In the scope of chronic diseases are present cardiovascular diseases and among these are those that need permanent therapy with Oral Anticoagulants (OACs). OACs are increasingly used drugs that have proven efficacy and safety, as well as numerous indications for the prevention and management of thromboembolic events, resulting from various heart diseases and coagulopathies [2,3].

Although recognized for their effectiveness and safety, the use of ACOs requires patients to take a lot of care. To enjoy the protective benefits of oral anticoagulation and make treatment safe, strict control of coagulation rates is indispensable [2]. Laboratory tests such as Partial Thromboplastin Time (TTP) and Prothrombin Time (PT), expressed by the International Standardized Ratio (INR), have been used to determine the quality of monitoring for anticoagulated patients [2,4].

The maintenance of desirable INR for patients who use OACs depends on factors that influence the efficacy of the drug resulting in treatment instability [2,4]. These factors are related to individual aspects, food and drug interactions. Regarding individual aspects, pa-

tient intentionality to pharmacological adherence is highlighted in the literature and has been included in the list of concerns of health professionals [5].

The concept of therapeutic compliance varies among different authors; however, it can be understood as the measure of patients' behavior corresponding to the guidance of health professionals [6]. Non-adherence to drugs, in turn, can be characterized in several ways, including ingestion of the drug at the wrong dose or time, forgetfulness and even interruption of treatment earlier than expected [7].

Therefore, adherence to any proposed treatment involves patient adaptations through active participation in lifestyle change that goes beyond the strict follow-up of drug therapy [8], being associated with education, knowledge about therapy and to several sociodemographic and clinical intervening factors [9]. Educational actions and assessment of patients' knowledge of the disease are factors that contribute to adherence to treatment with the use of OACs, promoting health and preventing complications that may pose problems for public health [9].

In this context, the specialized oral anticoagulation outpatient clinics aim to accompany patients and guide them on the necessary care with the medication, as well as on factors that may interfere with treatment [4]. The performance of professional nurses has been a differential in this scenario, despite their participation in specialized oral anticoagulation clinics still being incipient practice in Brazil [4]. In this perspective, it is important to emphasize that the patient's knowledge regarding their reinforced treatment through educational actions can contribute to medication adherence and that specialized services for the follow-up of these patients favor the development of these actions allowing a closer relationship between professional and patient.

Based on the above, the complexity of the follow-up of these patients to OAC therapy demonstrates the importance of conducting the present study since several factors may interfere with treatment-related knowledge and pharmacological adherence, leading to undesirable events such as hemorrhagic and/or thromboembolic events. In addition, the identification of the profile of patients treated at these specialized services allows a comprehensive assessment, which is a fundamental requirement to ensure better health care planning, therapeutic success and health promotion.

Considering the hypothesis that sociodemographic and clinical variables directly influence the knowledge about therapy and pharmacological adherence, the aim of this study was to investigate the factors that influence pharmacological adherence and the knowledge of anticoagulated patients in outpatient follow-up.

### Method

This is a descriptive, cross-sectional study with a quantitative approach, linked to the main project entitled "Quality of life, self-care and pharmacological adherence of patients using oral anticoagulants", developed at the outpatient clinic of a reference teaching hospital in the area of cardiology in Recife, Pernambuco, from March to June 2015.

The study sample consisted of 222 patients in outpatient follow-up and was obtained by simple randomization by lot. The study included patients aged 18 years or older, whose anticoagulant in use was warfarin, in outpatient follow-up and who demonstrated cognitive ability to respond to the interview.

Adherence assessment was obtained using the Morisky Test [10] adapted and validated for use in Brazil, in a hypertensive population [11] and applied in the context of treatments for chronic diseases, which may include therapy. oral anticoagulation therapy [2,12]. The instrument consists of four questions that allow "yes" and "no" answers and assess how patients behave in relation to the chronic use of certain medications, according to their clinical condition. The classification of pharmacological adherence is performed considering that all negative responses represent adherence to drug treatment, while if there is at least one positive response, the patient is classified as non-adherent.

The use of this instrument also allows another classification related to the questions that are answered positively. If question 1 or question 2 are answered positively, nonadherence is considered unintentional, whereas if questions 3 or 4 are answered positively, then nonadherence is considered intentional [13].

To assess knowledge, an instrument adapted and validated for use in Brazil [14] consisting of 11 questions, was used. The answer options to the questions are “know, partially know or don’t know”, and the following values are assigned for statistical purposes: zero for answer don’t know, half point for partially know and one point for answer know. Knowledge, assessed from the sum of the answers, follows the following classification: up to four points, insufficient knowledge; above four and up to eight points, regular knowledge; and above eight points, adequate knowledge [15].

Data were stored and analyzed using descriptive and inferential statistics using the IBM SPSS 20.0 software. To compare the proportions, the chi-square test was used, adopting  $p < 0.05$ .

The project was approved by the Research Ethics Committee of the institution where the study was conducted, under protocol No. 983.937 and CAAE No. 40372214.0.0000.5192.

## Results

### Sociodemographic and clinical characterization

The sample was characterized by a majority of females (64.4%), brown (57.2%), married/consensual union (54.5%), retired/pensioners (57.2 %) and with a mean age of  $54.7 \pm 13.8$  years, ranging from 18 to 87 years. Schooling was considered low, as 43.7% had incomplete elementary school and 14% were illiterate.

Regarding the main indications for OAC therapy, Atrial Fibrillation (50.4%) and Valvular Diseases (50.4%) were highlighted. The assessment of personal history showed that 91% were hypertensive, 53.6% sedentary, 15.8% had a habit of drinking alcohol and 6.8% were smokers.

Table 1 shows the data regarding outpatient follow-up of the study participants. Of the 222 respondents, 200 patients had previous INR values obtained through clinical evaluation, and 22 patients were on the first day of outpatient follow-up, thus not presenting previous values of the examination.

Looking at the results of previous INR assessments obtained on the day of the interview during the outpatient consultation, 56.5% of the patients had INR values outside the therapeutic range. Regarding current INR values, including patients who were going to the outpatient consultation for the first time, 57.2% had non-ideal values and, therefore, with anticoagulant dose inadequate for their needs.

Regarding the duration of oral anticoagulant use, it was observed that 65.8% of patients had been undergoing treatment for more than 6 months; however, 35.1% at the time of the interview had been in outpatient follow-up for at least 6 months. Outpatient follow-up was between 4.2 and 4.7 months, ranging from patients on the first day of follow-up to those followed more than 1 year.

When asked about possible complications related to the use of OACs, 21.2% reported having had hemorrhagic episodes and 11.7% thromboembolic.

### Pharmacological adherence and treatment knowledge

In the evaluation of pharmacological adherence, by applying the Morisky Test<sup>10</sup>, a non-adherence percentage of 60.8% was found. Considering also the classification of non-adherence according to patient intentionality, there was a predominance of unintentional type (115 / 51.8%) as described in table 2.

Variables	n	%
<b>RNI range - last evaluation prior to consultation</b>		
Below the indicated range	75	37,5
Normal*	87	43,5
Above the indicated range	38	19
<b>RNI band set in query**</b>		
Below the indicated range	81	36,5
Normal*- dose adjustment not required	95	42,8
Above the indicated range	46	20,7
<b>Treatment time (anticoagulation)</b>		
6 months	76	34,2
> 6 months	146	65,8
<b>Outpatient follow-up time</b>		
6 months	144	64,9
> 6 months	78	35,1
<b>Complications during treatment</b>		
Hemorrhagic	47	21,2
Thromboembolic	26	11,7
No complications	149	67,1

**Table 1:** Outpatient follow-up data of patients on oral anticoagulation therapy (N = 222). Recife-PE, Brazil, 2015.

\*: Normal INR was adopted for patients with mechanical valves 2.5 to 3.5 and for the other indications 2.0 to 3.0.

\*\*.: Including patients on the first day of outpatient follow-up.

Pharmacological adherence (Morisky Test)	n	%
Adherent	87	39,2
Unintentional adherent	7	3,2
Unintended adherent	115	51,8
Unintentional and unintentional adherent	13	5,9

**Table 2:** Evaluation of the pharmacological adherence of patients using oral anticoagulants (N = 222). Recife-PE, 2015.

The relationship of sociodemographic and clinical variables as risk and protective factors for non-adherence was also evaluated. This statistically significant analysis shows the increased risk for noncompliance among patients without adequate INR adjustment (OR: 1.279; 95% CI: 1.039 - 1.574; p = 0.02) and treatment time up to 6 months as protection factor for adherence (OR: 0.672; 95% CI: 0.515 - 0.878; p = 0.001) (Table 3).

In the assessment of patients' knowledge related to the use of OACs, only 36.9% was considered adequate, i.e. scores greater than or equal to 8 points after application of the instrument. When analyzing the association between adequate knowledge and sociodemo-

Variables	Non-adherents (n/%)	OR*	IC 95%**	p***
Age < 60 years old	90/66,7	1,149	0,912-1,448	0,224
Age ≥ 60 years	45/33,3			
Female	87/64,4	1,001	0,803-1,249	0,991
Male	48/35,6			
With companion	68/50,4	0,847	0,687-1,045	0,123
No companion	67/49,6			
Recife e RMR	101/74,8	1,126	0,874-1,450	0,341
Interior	34/25,2			
Up to 9 years of study	90/66,7	0,94	0,755-1,172	0,591
More than 9 years of study	45/33,3			
Up to 1 minimum wage	91/67,4	1,013	0,808-1,270	0,909
Greater than 1 salary	44/32,6			
In work	36/26,7	1,219	0,980-1,517	0,103
No work activity	99/73,3			
Hypertensive	126/93,3	1,386	0,844-2,277	0,129
Non-hypertensive	9/6,7			
Diabetic	22/16,3	0,886	0,655-1,199	0,406
Non-diabetics	113/83,7			
Sedentary	71/52,6	0,96	0,778-1,186	0,707
Not sedentary	64/47,4			
Smoking	8/5,9	0,869	0,535-1,413	0,539
Non-smoker	127/94,1			
Ethyism	17/12,6	0,77	0,538-1,101	0,106
Non-alcoholic	118/87,4			
Up to 6 months of treatment	35/25,9	0,672	0,515-0,878	0,001
More than 6 months of treatment	100/74,1			
Up to 6 months of follow-up	83/61,5	0,865	0,701-1,067	0,188
More than 6 months of follow-up	52/38,5			
RNI with proper fit	66/48,9	1,279	1,039-1,574	0,022
RNI without proper adjustment	69/51,1			
Spent on medication	125/92,6	1,238	0,788-1,944	0,299
No medication expenses	10/7,4			
Total	135/60,8			

**Table 3:** Evaluation of the relationship of sociodemographic and clinical variables as risk and protective factors for non-adherence to pharmacology. (N = 222) Recife-PE, Brazil, 2015.

\*: Odds ratio.

\*\*: Confidence interval (95%).

\*\*\*: Chi-square test.

graphic and clinical variables, statistical significance was observed with age below 60 years (75.6%; p = 0.004) and longer treatment time (75.6%; p = 0.018) (Table 4). When verifying the association of inadequate knowledge with the same variables, it was possible to observe significant data with shorter study time (77.9%; p < 0.001), sedentary lifestyle (59.3%; p = 0.027), shorter study time. outpatient follow-

up (75.0%;  $p < 0.001$ ) and INR without adequate dose adjustment (63.6%;  $p = 0.012$ ) (Table 4). There was no significant association between pharmacological adherence and knowledge ( $p = 0.746$ ).

Variables	Inadequate Knowledge		Knowledge Suitable		P value*
	n	%	n	%	
Age < 60 years old	79	56,4	62	75,6	0,004
Age ≥ 60 years	61	43,6	20	24,4	
Female	84	60,0	59	72,0	0,073
Male	56	40,0	23	28,0	
With companion	74	52,9	47	57,3	0,52
No companion	66	47,1	35	42,7	
RMR	99	70,7	62	75,6	0,43
Interior	41	29,3	20	24,4	
≤ 9 years of study	109	77,9	42	51,2	<0,001
> 9 years of study	31	22,1	40	48,8	
Up to 1 minimum wage	97	69,3	52	63,4	0,369
Greater than 1 salary	43	30,7	30	36,6	
In work	31	22,1	20	24,4	0,701
No work activity	109	77,9	62	75,6	
Hypertensive	127	90,7	75	91,5	0,851
Nonhypertensive	13	9,3	7	8,5	
Diabetic	22	15,7	18	22,0	0,243
Non-diabetics	118	84,3	64	78,0	
Sedentary	83	59,3	36	43,9	0,027
Non-sedentary	57	40,7	46	56,1	
Smoking	11	7,9	4	4,9	0,393
Non-smoker	129	92,1	78	95,1	
Ethyism	21	15,0	14	17,1	0,682
Non-etilist	119	85,0	68	82,9	
≤ 6 months of treatment	56	40,0	20	24,4	0,018
> 6 months of treatment	84	60,0	62	75,6	
≤ 6 months follow-up	105	75,0	39	47,6	<0,001
> 6 months follow-up	35	25,0	43	52,4	
RNI with proper fit	51	36,4	44	53,7	0,012
RNI without proper adjustment	89	63,6	38	46,3	
Total	140	100	82	100	

**Table 4:** Association between knowledge and sociodemographic and health variables (N = 222). Recife-PE, Brazil, 2015.

\* Chi-square test.

## Discussion

Non-adherence to pharmacology can be characterized as both the use of prescription drugs differently from that proposed by the health professional and the interruption of treatment [16,17] and has been evidenced worldwide as a challenge to improve health conditions as implies a decrease in mortality rates and reduces hospital costs [17].

In the present study, it was evidenced from the application of the Morisky Test [10] to evaluate the pharmacological adherence that only 39.2% of the patients adhered well to the use of anticoagulant. A very similar result was found in a study on pharmacological adherence to oral anticoagulant [2], in relation to the percentage of patients adhering to oral anticoagulation therapy (39.1%). In contrast, the high percentage of non-adherence identified, considered as an important public health problem in the context of chronic diseases [5], underscores the real need to develop appropriate coping strategies.

Another important aspect observed in the evaluation of the pharmacological adherence of the participants of the present study was the predominance of non-adherence classified as unintentional (51.8%), corroborating the findings of research conducted in patients with chronic gastrointestinal diseases regarding adherence to drug treatment [12], (78.1% of unintentional non-adherence) and demonstrating that, in most cases, non-adherence is due to forgetfulness and carelessness regarding the time to take the medication. This finding may also indicate patients' lack of concern about using the medication correctly [12].

It is noteworthy that failure to use OAC properly, either through forgetfulness or even interruption of treatment, can have important repercussions on the patient's life, leading to misalignment of anticoagulation intensity, measured by INR, to inadequate optimal doses according to each clinical condition and, consequently, a higher risk of treatment-related complications.

In the present study, 21.2% of patients reported having at some point in their treatment hemorrhagic episodes, corroborating the results of previous studies [2,18] and 11.7% reported the occurrence of thromboembolic events. It was also possible to observe that when analyzing the interviewees' most recent INR records, most were outside the recommended therapeutic range, similar to other studies that evaluated INR in outpatients from public and private institutions [19,20].

When assessing pharmacological adherence according to sociodemographic and clinical variables, it was possible to observe a higher percentage of non-adherence among patients without adequate adjustment of INR and with treatment time longer than 6 months. We also evaluated which factors constituted risk and protection for non-adherence and adherence, respectively, to the use of oral anticoagulants, in which, statistically significant, the increased risk for non-adherence was identified among patients without adequate INR adjustment ( $p = 0.02$ ) and treatment time of up to 6 months as a protective factor for adherence ( $p = 0.001$ ).

The higher risk for pharmacological noncompliance among patients without adequate INR adjustment, that is, who did not have drug dose stability, corroborates a study [21] whose results showed that non-adherent individuals require more time to achieve this stability. In a study on pharmacological adherence to oral anticoagulant [2], in turn, no significant associations were observed between dose stability and INR values with medication adherence.

Regarding the finding that treatment time of up to six months is a protective factor for adherence, although no similar evidence has been identified in the various studies analyzed, this fact may be justified by the greater commitment and determination of patients to follow the guidelines and recommendations provided by professionals in the multidisciplinary teams at the beginning of oral anticoagulation therapy.

In a study on patient knowledge and adherence to oral anticoagulation [19], the authors state that well-structured educational actions should be used to improve adherence to oral anticoagulation therapy, as well as the patient's level of knowledge about the proposed treatment. Nurses play a key role in implementing these strategies. Educational interventions are also relatively simple and inexpensive measures [22], ensuring a substantial reduction in the risk of treatment-related complications and hospitalizations and, consequently, in the cost to the health system.

Based on the above, it is clear that, in addition to pharmacological adherence, the success of OAC therapy also depends on the patient's understanding of drug use [19]. In this context, in relation to the interviewees of the present study, the majority presented inadequate

knowledge in relation to the OACs, as it corroborates with national and international researches, where important knowledge gaps are found [19,23].

A statistically significant relationship was found between adequate knowledge and age below 60 years, as well as with longer treatment time, corroborating the literature, where evidence shows that patients under 60 have better knowledge regarding medication [23]. Prolonged treatment is also estimated to narrow the patient's relationship with the prescribed drug, providing longer experience and promoting greater understanding of all aspects related to therapy in order to promote better knowledge.

There was a statistically significant association between inadequate knowledge and low education, physical inactivity, shorter outpatient follow-up and inadequate adjustment of INR values according to the clinical indication of the use of OACs. A study conducted in a private anticoagulation outpatient clinic, in which results indicate patients with a high level of education, showed a significant number of participants outside the therapeutic range, indicating that education does not exempt them from difficulties in understanding and knowing their treatment, from adhering to the medication and/or possible complications resulting from the use of OACs [20].

Regarding physical inactivity, a recent study aimed at assessing the prevalence of the 'Sedentary Lifestyle' nursing diagnosis in individuals with hypertension and its association with clinical indicators and related factors, found that one of the most frequently found factors it was poor knowledge about the benefits of physical activity [24]. It is possible that patients do not attribute physical value to its true value in maintaining adequate INR values, where its practice minimizes risks of complications related to medication use. Therefore, it can be inferred that inadequate knowledge represents one of the factors that hinder the necessary understanding for sensitization and the fulfillment of physical activity [24].

The results of the present study also demonstrated the relationship between inadequate knowledge and shorter outpatient follow-up and inadequate adjustment of INR values, drawing attention to the importance of valuing the initiation of OAC therapy and outpatient follow-up, aiming at stimulate the effective participation of patients in their treatment, seeking to ensure adequate knowledge about therapy, control of INR values and better adherence to medication [25].

In this perspective, the development of educational strategies that favor the understanding of aspects such as the reason why treatment is necessary, the importance of laboratory control, the ideal INR values according to each clinical condition, the possible complications (risk of bleeding and thromboembolic phenomena), dietary restrictions, drug interactions, as well as necessary lifestyle changes.

The nurse, as a member of multidisciplinary teams that provide assistance to patients using OACs, should act by developing educational actions that allow the optimization of the orientation process of these individuals. The performance of this professional should also seek comprehensive care [26] in which individual needs will be investigated and where the patient should be encouraged to expose their difficulties regarding the use of medicines, in order to allow the development of ideal strategies. of coping.

Finally, although there is evidence that treatment with OCs requires adequate knowledge and adherence to recommendations by patients [23], in the present study no statistically significant association was found between pharmacological adherence and knowledge, suggesting that knowledge about The treatment with OCs, by itself, does not necessarily imply good adherence to pharmacological therapy, corroborating the fact that adherence is a multidimensional [27] and fluctuating [21] phenomenon, influenced by several other factors.

## Conclusion

The study raises the problem and complexity that involves the chronic use of OACs, seeking to know the population followed by the oral anticoagulation clinic, as well as factors associated with pharmacological adherence and patients' knowledge about their therapy. In this context, it was possible to highlight the influences of certain sociodemographic and clinical variables on both knowledge and pharmacological adherence, proving the previously established hypothesis. In addition, it was also possible to raise increases in clinical practice,

especially regarding the assistance of professional nurses, the development of health education strategies and the improvement of the quality of outpatient care.

Considering the complexity of OAC treatment and the factors associated with this treatment, care planning is essential. The challenge is to take the necessary measures to improve patient compliance and information to ensure risk-minimizing care, with attention to individual needs and directed, especially by nurses, in pursuit of the best educational strategy.

### Study Limitations

As this is a primary study in the northeast region, it was not possible to make comparisons with the reality of this population.

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