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Adhesion for the use of oral cumarinal anticoagulant by atrial fibrillation patients

ABSTRACT | Objective: to evaluate the adherence of the patient with Atrial Fibrillation in Therapy with oral coumarin anticoagulant. Method: Descriptive-exploratory, cross-sectional and prospective study with a non-randomized intervention with a quantitative approach, carried out with 40 participants, the Simonetti Adherence Score and the Visual Analog Evaluation Scale were applied and after the educational intervention for analysis of Time in Therapeutic Range under CAAE: 79973017.1.0000.5462. Result: It was identified that 5% had low risk of adherence, 60% medium risk and 35% high risk. After analyzing the eight months of TTR before and after intervention, there was no significant change between the periods (p = 0.638). Conclusion: It was evidenced that the low adherence group maintained a better time in the therapeutic range related to medium and high risk. Indicative of greater impact of the educational intervention carried out by the nurse.
Keywords: Atrial Fibrillation; Anticoagulants; Medication Adherence.

RESUMEN | Objetivo: evaluar la adherencia del paciente con fibrilación auricular en terapia con anticoagulante cumarínico oral. Método: Estudio descriptivo-exploratorio, transversal y prospectivo con una intervención no aleatorizada con abordaje cuantitativo, realizado con 40 participantes, se les aplicó el Simonetti Adherence Score y la Escala de Evaluación Visual Analógica y luego de la intervención educativa para el análisis del Tiempo en el Rango Terapéutico bajo CAAE: 79973017.1.0000.5462. Resultado: Se identificó que 5% riesgo bajo de adherencia, 60% riesgo medio y 35% riesgo alto. Después de analizar los ocho meses de TTR antes y después de la intervención, no hubo cambios entre los períodos (p = 0,638). Conclusión: Se evidenció que el grupo de baja adherencia mantuvo el mejor tiempo en el rango terapéutico relacionado con riesgo medio y alto. Indicativo de mayor impacto de la intervención educativa realizada por la enfermera.
Palabras claves: Fibrilación Atrial; Anticoagulantes; Cumplimiento de la Medicación.

RESUMO | Objetivo: avaliar a adesão do paciente com Fibrilação Atrial em Terapia com anticoagulante oral cumarínico. Método: Estudo descritivo-exploratório, transversal e prospectivo com intervenção não randomizado de abordagem quantitativa, realizado com 40 participantes, aplicou-se o Escore de Adesão Simonetti e a Escala de Avaliação Analógica Visual e após a intervenção educativa para análise de Time in Therapeutic Range sob CAAE: 79973017.1.0000.5462. Resultado: Identificou-se que 5% apresentaram risco baixo de adesão, 60% risco médio e 35% risco alto. Após análise dos oito meses do TTR pré e pós-intervenção, não houve mudança significativa entre os períodos (p=0,638). Conclusão: Evidenciou-se que o grupo de baixa adesão manteve melhor tempo na faixa terapêutica relacionado ao médio e alto risco. Indicativo este de maior impacto da intervenção educativa realizada pelo enfermeiro.
Palavras-chaves: Fibrilação Atrial; Anticoagulantes; Adesão à Medicação.

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INTRODUCTION

Atrial Fibrillation (AF) is the supraventricular arrhythmia that most affects the population. It is characterized by a disorder in the atrial electrical impulse, which causes atrial depolarizations in an uncoordinated way, with a consequent loss of the contraction capacity of these cardiac chambers. [1,2] The accumulation of blood in the atria caused by this deficiency in the atrial systole, exposes the individual to the formation of thrombi. [2]

The incidence and prevalence rates of AF have increased over the years, which is related to the aging of the po-

pulation, sex, increased morbidities and worsening of lifestyle.[1,3]

The association between AF and the risk for thromboembolic factors is well known, the thromboembolic process occurs from the Virchow triad that encompasses three factors: atrial blood stasis; endothelial injury and increased blood thrombogenicity, typical of AF. The causes for this process are multifactorial, and once the thrombi are formed in the atrial chambers, they move to the systemic circulation, the brain being the most affected region, causing the stroke. [1]

Oral anticoagulation is a method of choice for the treatment of this public, with the objective of preventing thromboembolic phenomena, including ischemic strokes. The most used class of anticoagulant is that of coumarins that comprise vitamin K antagonists and may be represented by warfarin and phenprocoumon. [4]

Monitoring of treatment with Oral Anticoagulants (OAC) is performed based on the Prothrombin Time (PT) exam, which means the time for the formation of the fibrin clot, after induction in the laboratory environment. The PT is expressed through the INR (International Normalized Ratio), a method used worldwide in order to standardize the result of the PT analysis. [5-6] The ideal INR established for patients with AF is between 2,0 and 3,0. [1]

To assess the quality of treatment with OAC, the calculation of Time in Therapeutic Range (TTR) or time in the therapeutic range in the period analyzed for a given group of patients is used. [7]

To calculate the TTR one of the tests used is the Rosendaal [8] linear interpolation method, which allows the calculation of the number of days in the therapeutic interval, from a linear relationship between two consecutive values of INR with the attribution of a specific value of INR for each day. Therefore, the calculation of the percentage of days in the therapeutic interval is given by the ratio between the difference of two consecutive values of INR within the therapeutic interval, divided by the total difference between them. [7]

The ideal TTR value for OAC users is at least 70%, with this value the benefits of anticoagulation are more evident, such as the prevention of stroke. [9]

M staying in the therapeutic range is a challenge for the patient, since the use of coumarin OAC and the stability of the INR levels are related to several factors such as treatment adherence, age, comorbidities, interactions with other drugs, genetic aspects and eating foods rich in vitamin K. [5,10] Other aspects such as the level of cognition, emotional and psychological also affect the stability of the INR in the therapeutic range. [11]

The World Health Organization (WHO) defines adherence to drug therapy related as a person's behavior (taking medication, following a diet, and/or executing lifestyle changes), corresponds to the agreed recommendations of a health professional. [12]

Health education to clarify the importance of therapy, how to use medication, identification and prevention of adverse effects, drug interactions and dietary interference, is the main tool for obtaining satisfactory levels of adherence to therapeutics and consequent reduction in the mortality of these patients who make long-term use of OAC. [11]

The objective of this study was to evaluate the adherence of patients with AF in Oral Anticoagulant Therapy (OAC-T) coumarin through the research question: "what is the adherence of patients with AF using coumarin OAC?".

METHOD

This is a descriptive-exploratory, cross-sectional and prospective study with non-randomized intervention with a quantitative approach. Performed with OAC users treated at an outpatient clinic specialized in Electrophysiology at a large Public Hospital specialized in Cardiology in the State of São Paulo.

The population of this study was composed of patients with AF who were using OAC with follow-up at the institution from January 2018 to January 2019. The sample was selected randomly, recruiting patients while waiting for the results of INR. Patients were invited and advised on the objectives of the study and started after acceptance and signing of the Free and Informed Consent Term according to the eligibility criteria: age above 18 years old; literate (can read and write); patients with AF on OAC-T (Warfarin and Femprocoumon) for at least one year.

For the collection, an instrument was applied to characterize the sociodemographic aspects of the participants and the Simonetti [13] Adherence Score built to assess adherence of patients undergoing OAC treatment, in addition to the Visual Analogue Scale (VAS) (14) which allows the patient to self-assess and also the nurse's perception regarding therapeutic adherence.

The Simonetti Adherence Score was built for the public in OAC-T to assess the adherence of these users to the treatment as shown in figure 1. The score allows the assessment of OAC user adherence by the following variables: Inappropriate use, Invasive procedure, Drug interaction, Eating habits, Clinical conditions and Other factors (weight gain or gain; stress; smoking, among others). [13]

His score was calculated from the multiple regression odds ratio. Then, the intervening factors were categorized based on the score obtained as low (≤10 points), medium (11 to 30) and high (≥ 31 points) for the normal RNI event, as shown in figure 1. With C Statistic of 0,940 (CI (95%) = 0,920 - 0,960; p <0,001) showing good perfor-

mance to discriminate the occurrence of the event or not. [13]

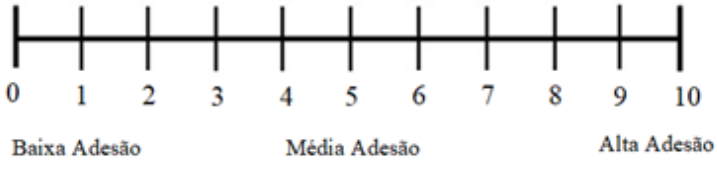
The Visual Analogue Scale aims to evaluate the user's self-perceived adherence with respect to OAC-T, assigning a score of 0-10 for their level of treatment adherence as shown in figure 2, which characterizes self-report, a method widely used for evaluate and collect information on adherence both in health practice and in research. [14] On the other hand, the nurse researcher attributed her perception regarding the research participant, also using the scale's score.

Thus, the sociodemographic instrument was applied, and right after the Simonetti Adherence Score and, consequently, the EAV. After identifying the intervening factors, adherence to OAC-T, the nurse researcher carried out the educational intervention, in order to answer questions and provide guidance according to the needs of each user and factors identified by the Simonetti Score (Inappropriate use, Invasive procedure, Drug Interaction , Eating Habits, Clinical Conditions and Other Factors) and their peculiarities, individually.

Figure 1 – Simonetti Adhesion Score Score [13]

ESCORE DE ADESÃO SIMONETTI PARA USUÁRIOS DE ANTICOAGULANTE ORAL			
FATORES INTERVENIENTES	**SIM**	**NÃO**	**ESCORE**
• Interação Medicamentosa	0	30	---
• Uso Inadequado	0	18	---
• Hábitos Alimentares	0	07	---
• Procedimentos Invasivos	0	02	---
• Condições Clínicas/Problemas de Saúde	0	02	---
• Outros Fatores	0	05	---
TOTAL	*(0 a 64)*		---
□ Baixo (≤ 10 pontos)			
□ Médio (11 a 30 pontos)			
□ Alto (≥ 31 pontos)			

Figure 2 - Visual Analog Scale [14]



After data collection, the institutional computerized system was accessed to identify and collect the INR results and the TTR value of each participant in order to analyze the behavior of the TTR in the eight months before and after the educational intervention.

The actions implemented by the nurse researcher in educational interventions were based on pedagogical strategies to simulate the adequate use of the medication, the stable dietary pattern without significant variations in the amount of vitamin K, evaluation of medications and drug interactions between the OAC and other therapies, problems health conditions that may interfere with increasing or decreasing body weight, exacerbated stress, chronic use of alcohol or tobacco and any interference with the physiology of the liver. These educational interventions were carried out individually with each patient for twenty minutes.

The level of significance adopted in this study was 0,05. To check the association between categorical variables and outcome (low, medium or high adherence), Fisher's Exact Test was used. With the Wilcoxon Signed Ranks test, the evolution of TTR before and after eight months and the intervention were analyzed. The Spearman's rho coefficient correlated the TTR with the participant's, researcher's and Simonetti's Adherence Score.

The study was approved by the Institution's Ethics and Research Committee under CAAE: 79973017.1.0000.5462.

RESULTS

Forty patients participated in this study, of which 57,5% were male, with a mean of 63 years and range between 42 and 83 years, 72,5% are married and 47,5% reported having incomplete elementary school.

Regarding professional performance, 67,5% reported not working and 65% retired, 95% have their own home, 77,5%

live in the city of São Paulo. 75% prevailed with a wage income of 1 to 3 minimum wages.

Regarding health history, 85% reported having Systemic Arterial Hypertension (SAH), 42,5% Diabetes Mellitus (DM), 35% Dyslipidemia (DLP). Among other health problems, 7,5% stood out for Acute Myocardial Infarction, Hypothyroidism and Thrombosis. The coumarin anticoagulant in use by 100% of the participants was Warfarin, with an average use time of 43 months.

It was found that there is no significant relationship between having high, medium or low adherence with the sociodemographic variables, as shown in Table 1, since they presented a $p \geq 0,05$ when the respective event occurred.

By the Adherence Score Simonetti identified in the item of drug interaction that 90% of the participants have a history of interaction when using some continuous or intermittent medication. The medications that interact with the coumarin anticoagulant most found in use among research participants were amiodarone® 20 (50%), simvastatin® 19 (47,5%), omeprazole® 7 (17,5%), anti-inflammatory five (12,5%) and levothyroxine® five (12,5%).

In inappropriate use 70% denied, and 30% reported, among those who reported, the factor that stood out was forgetfulness, that is, they did not take the daily dose, with 17,5% of the participants.

Regarding eating habits, only 12,5% showed variations or radical changes in their diet, and 7,5% after starting treatment with coumarin anticoagulant, they completely removed foods rich in vitamin K from their diet, as at some point they received this guidance.

Regarding invasive procedures, only 12,5% reported having undergone an event in the past few months. Regarding clinical conditions/health problems, 22,5% reported a cold, diarrhea and fever in 2,5% of the participants. Among other factors, 47,5% of the participants reported stress, 27,5%, 17,5% changes in body weight, 7,5% alcohol consumption and 5% said they were smokers.

After analyzing the variables of the Simonetti Adherence Score by assigning the appropriate scores, it was observed that 5% participants had a score ≤ 10 which represents low risk of adherence, 60% average risk of adherence and 35%

Table 1. List of variables and Adherence (Simonetti Adherence Score). São Paulo, Brazil 2020.

Variáveis	Categorias	Adesão Baixa ou Média		Adesão Alta		p-valor
		N°	%	N°	%	
Sexo	Feminino	12	46,2	5	35,7	0,739
	Masculino	14	53,8	9	64,3	
Estado Civil	Solteiro	4	15,4	0	0	0,252
	Casado	17	65,4	12	85,7	
	Divorciado	3	11,5	0	0	
	Viúvo	2	7,7	2	14,3	
Escolaridade	Sabe ler escrever	1	3,8	0	0	0,786
	Ensino Fundamental Incompleto	13	50	6	42,9	
	Ensino Fundamental Completo	4	15,4	1	7,1	
	Ensino Médio Incompleto	0	0	1	7,1	
	Ensino Médio Completo	6	23,1	5	35,7	
	Ensino Superior Incompleto	1	3,8	0	0	
	Ensino Superior Completo	1	3,8	1	7,1	
Trabalho	Não	18	69,2	9	64,3	0,356
	Sim	8	30,8	5	35,7	
Aposentado(a)	Não	9	34,6	5	35,7	1,000
	Sim	17	65,4	9	64,3	
Moradia	Própria	24	92,3	14	100	0,533
	Alugada	2	7,7	0	0	
Local em que reside	São Paulo	20	76,9	11	78,6	1,000
	Outras cidades de São Paulo	6	23,1	3	21,4	
Renda	Menos de 1 salário mínimo	0	0	1	7,1	0,314
	1 até 3 salários mínimos	21	80,8	9	64,3	
	Mais de 3 até 5 salários mínimos	4	15,4	3	21,4	
	Mais de 5 até 7 salários mínimos	1	3,8	0	0	
	Mais de 9 salários mínimos	0	0	1	7,1	
HAS	Não	4	15,4	2	14,3	1,000
	Sim	22	84,6	12	85,7	
DM	Não	15	57,7	8	57,1	1,000
	Sim	11	42,3	6	42,9	
DLP	Não	14	53,8	12	85,7	0,081
	Sim	12	46,2	2	14,3	

Source: Author's own elaboration, 2020.

had a score ≥ 31 which is consistent with high risk of adherence.

With the VAS, it was identified that 27,5% of the participants attributed 8 to 10 points related to treatment adherence. For the perception of the nurse researcher regarding the application of VAS, there was a greater variability of concepts, the most frequent grades were from eight to 22,5% of the participants and seven to 20% of the participants, the lowest grade attributed was four to 5 % of them.

After analyzing the TTR before and after eight months of the educational intervention, it was evident that there was no significant change in the TTR after the TTR before (p = 0,638). Among the groups (low/medium/high adherence), it was observed that there was no significant difference in the TTR (p = 0,437), showing stability between them.

However, it was observed that the group with low adherence showed a greater gain in TTR compared to the others, indicating that the educational intervention had a greater impact in this group with an average of 14,28% and standard deviation of 20,91%. However, it was not statistically significant, which may be related to the low number of participants within this group. The other two groups (medium and high adherence) had similar averages (2,28% and 2,92%) and standard deviation (36,66% and 24,55%), respectively.

The TTR was correlated with the participant's grade (r = -0,049 and p value of 0,763), the researcher's grade (r = -0,105 and p = 0,517) and with the Simonetti Adherence Score (r = -0,085 p = 0,602), which found no significant correlation between those who had high scores and high adherence score, with the increase in TTR.

With these results, we opted for another analysis removing the participants with TTR pre> 80%, as they observed that the group with TTR below this value would have more gain after educational intervention. There were 34 patients with TTR up to 80%, who found a greater proximity of significance with (p = 0,098) when compared to the analysis made with the total number of participants (p = 0,638), which corroborates that those with lower pre-TTR tend to obtain greater positive TTR results when there is an educational intervention.

DISCUSSION

It is noted that in 2010 there was a significant increase in the prevalence rates of AF with increasing age, with rates between ≥35 years of both sexes greater than twice the general prevalence, which is 596,2 for men and 373,1 among women (per 100.000 inhabitants). [3] A trend that reinforces what was found in this study, since the age range varied between 42 and 83 years with a predominance of males. This brings us to the epidemiological changes that affect the population with AF, with the aging of the population and the predisposition of males, thus leading to the need for OAC-T. [1]

> “Comorbidities such as Systemic Arterial Hypertension, Diabetes, Dyslipidemia, among others reported by the participants in this study, also did not show a significant association with treatment adherence.”

Regarding education, it was noted that there was a greater number of participants with incomplete elementary education, 47,5%, which is similar to other studies that point out a greater number of participants with 5 years of study, [15-16] which highlights a low education profile of this population. Regarding the socioeconomic profile, some studies on the subject show a salary range of up to 1 minimum wage, as in a study that out of 39 participants, 71,79% had 0 to 1 minimum wage. [15] In another, 73% of the 100 patients interviewed had an income of up to 1 minimum wage. [17] This fact differs from that found in our study in which only 2,5% of the participants had an income below 1 minimum wage.

It can be seen that the descriptive variables such as (sex, marital status, education, the fact of working and/or being retired, housing, income) had no significant relationship with having high, medium or low adherence, which can be explained by the fact that adherence to treatment has a greater interference, not only due to these factors and adherence to medication, but also from daily living habits, drug interactions, external and emotional factors of the patient. [11,18]

Comorbidities such as Systemic Arterial Hypertension, Diabetes, Dyslipidemia, among others reported by the participants in this study, also did not show a significant association with treatment adherence. What has been demonstrated in another study is the absence of a significant association with INR levels and stability. [10]

The factors analyzed by the Simonetti Adherence Score, used in this study are exactly intended to analyze adherence to treatment as a whole, considering all the variables that interfere with adherence, not only the issue of medication adhe-

rence, but also those related to habits of daily life that are linked to the behavioral aspect of each patient. [13]

The drug interaction factor in this study demonstrated use by 12,5% of participants of anti-inflammatory drugs in some cases without a medical prescription or communicated to the outpatient anticoagulation sector. Studies that analyze the factors involved in adherence, when asked about the use of drugs without a prescription, a large part of 77,8% of the participants stated that they only used drugs when indicated by the doctor. [18-19]

When it is highlighted what leads to the inappropriate use of oral anticoagulants, forgetfulness was highlighted, among the 30% that scored in this regard, 17,5% of them reported forgetfulness. In a study that addressed adherence to anticoagulants using the instrument to assess adherence - Therapist Adherence Measure (TAM), only one participant reported forgetfulness among the total of 27 members of the research. [18] In another study on the variation of (INR), which also evaluated adherence to anticoagulants based on the Morisky test, 64,0% reported regular use of the medication, respecting the dose and times. [20]

Related to food interaction, there was evidence that showed interference in the effectiveness of OAC-T, in a study 81,8% of 118 participants demonstrated knowledge of what food should be, considering the interaction between Warfarin and foods rich in vitamin K. [21]

There is a method used with OAC users from an institution specialized in cardiology from a previous study, which consists of guidelines on interactions of warfarin with food and medication, periodic assessment of INR and notification of the service by the patient when there is a change in diet or there is an adverse event such as bleeding. [20] The institution of this study, on the other hand, offers this information to the patient at the beginning of the treatment with the anticoagulant and on the returns for periodic evaluation of the INR outside the therapeutic range.

Regarding the scores attributed by the participants on self-perceived adherence and the researcher's perception, there is a predominance of high concepts among patients, and a greater variability of concepts among the researcher's notes. In a study carried out with a population also with a chronic condition that is SAH, which also evaluated the perception of adherence in the view of the patient and the professional, of the 12 patients, 6 gave the maximum score five that point them as adhered treatment, containing no adherents. In the professional's view, only three patients were scored with a score of five considered in adherence and four patients as non-adherent. [22] This shows that the patient's perception of himself tends to be overestimated, whereas that of the professional who has a more critical, analytical and thoughtful look.

“Related to food interaction, there was evidence that showed interference in the effectiveness of OAC-T, in a study 81,8% of 118 participants demonstrated knowledge of what food should be”

It is known that the value of a significant TTR to prevent thromboembolic diseases such as stroke is (TTR> 70%) and, corroborates in a cohort study conducted in 4 European countries, found that the average TTR ranged from 66% in Italy to 72.6% in the United Kingdom, while in France and Germany less than 50% of patients were classified as one (TTR> 70%). Stroke and bleeding events were found to be frequent in patients who had a TTR≤70%. [23]

The fact that the analysis of the TTR before and after the educational intervention did not show any significant change among the 40 participants, may be related to the level of absorption of the patients in relation to the instructions given at the beginning of the treatment and what is actually performed by them during the therapy. [11]

In this study, the analysis indicated, even without statistical significance, a greater gain in TTR in the low adherence group, indicating a greater benefit of this group with the educational activity. A study that evaluated among other items the adherence to the treatment of those who use oral anticoagulants, concluded that those who had already used or had been using the anticoagulant for a period of time, that is, were already familiar with the treatment, the strategy education was not efficient. [24] With that, you can see that when there is a previous contact with the treatment routine, there is a less significant gain with the educational intervention. [25]

The limitation in this study highlighted the limited data collection time that significantly impacted the sample, not affecting the results in view of the proposed objective, thus suggesting a longitudinal study with an expansive sample.

CONCLUSION

The study made it possible to know the adherence profile of the patients

involved, to identify the most common interfering factors in adherence in the studied sample, in addition to the perception of adherence by both parties, self-perceived and the nurse.

Even though there was no statistical significance, we have slight evidence that the identified group with low adherence had the greatest benefit with the educational intervention developed when the intervening factors of adherence were recognized through the applied score.

Given this, there is a need for nurses to know the profile of users of oral anticoagulants and empower themselves in decision-making to implement and innovate educational interventions.

Thus, the educational strategies carried out by nurses in clinical practice are essential in promoting adherence and preventing adverse events related to the use of coumarin oral anticoagulants, with favorable impacts on improving treatment adherence and changes in habits with a focus on maintaining International Normalized Relationship TTR recommended.

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