Constant Use of Oral Anticoagulants: Implications in the Control of Their Adequate Levels

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Summary

Background: Inappropriate and subtherapeutic anticoagulants dosages may result in severe thromboembolic and bleeding complications. The use of this treatment requires special attention and strict clinical and laboratory follow-up.

Objective: To identify factors associated with appropriate control of the oral anticoagulant use, assessing the patients' knowledge and perception of the treatment.

Methods: A cross-sectional study which included 140 patients followed in the oral anticoagulation outpatient clinic from November 2005 to June 2006. A structured questionnaire was drafted and applied to obtain the clinical characteristics of the patients and their knowledge about the treatment, their compliance with the treatment (Morisky´s test) and their perception of the treatment.

Results: The main indications for the use of oral anticoagulation therapy were atrial fibrillation (61.4%) and a prosthetic heart valve (55%). The duration of anticoagulation ranged from 24 to 72 months, and phenprocoumon (58%) was the most commonly used anticoagulant. As to the perception of the treatment, 95% of the patients mentioned concern about daily use of this medication. Periodic blood tests (21.4%) and the strict intake of oral anticoagulant (12.8%) were considered limiting factors. Adequate knowledge was outstanding in patients with an international normalized ratio (INR) outside the therapeutic range (64%), compared to patients with an INR within the therapeutic range (62%), as well as compliance with treatment in patients with an INR within the therapeutic range (54%), but with no statistical significance.

Conclusion: The results of this study show a prevalence of patients using oral anticoagulant with an INR within optimal values, although a high percentage of patients do not comply with the treatment. In this population it is clearly seen that they do not fully understand the treatment. (Arq Bras Cardiol 2009; 93(5):508-512)

Key Words: Anticoagulants; drug utilization; drug control.

Introduction

Although the use of oral anticoagulants is effective, there are risks associated with it. Annual risk estimates range from 2 to 8% for bleeding, and 1 to 3% for treatment failure. Therefore, it is important to decide the appropriate moment to initiate the treatment or modify the dosage of the medication[1]. The use of these medications requires special control and strict clinical and laboratory follow-up by a multidisciplinary team due to bleeding complications. The use of oral anticoagulation therapy is considered as a safety factor for the patient, but the health care team needs to pay more attention to the issue of adherence to the medication. Poor compliance with the prescribed medication and consequently with the proposed clinical treatment has a negative impact on all aspects of health care, engenders excessive costs, and results in the sub-utilization of available treatment resources, as well as serious consequences to patients and an increase in adverse events in chronic diseases.

Sawicki[2] and Newall et al[3] described in their studies a patient education program on self-adjustment and management of oral anticoagulants, where the risk of any complication depends on the duration of medication use and the strictness of the INR control, achieved by frequent laboratory tests for dosage adjustment. Samsa et al[4] and Hirsh et al[5] stressed that, for patients with a prosthetic heart valve, the maintenance of long-term anticoagulation means adherence to a medication regimen during the patient's entire life.

Several studies[6-8] have demonstrated the existence of factors that interfere in the control of anticoagulation levels, including socio-economic factors; physiological factors; psychological factors and emotional factors.

According to the World Health Organization[9], poor adherence to medication use is currently one of the great challenges for the improvement in world health status. These conclusions demonstrate a need for further enlightenment about the medication use by the team assigned to treat this group of patients. In this context, the objective of this study

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was to identify factors associated with an adequate control of oral anticoagulant levels, assessing the patients' knowledge and perception of the therapy used.

Methods

This was a cross-sectional study which included patients followed in the oral anticoagulation outpatient clinic, at a cardiology hospital in the State of Rio Grande do Sul, from November 2005 to June 2006. In the oral anticoagulation outpatient clinic, patients are regularly tested for laboratory control of INR, and approximately 1200 patients are seen each month. Patients eligible for this study were ≥18 years old, were using oral anticoagulants, and agreed to answer the research questions.

A questionnaire was drawn, containing questions about clinical and demographic characteristics, adherence to treatment, knowledge about the therapy and the patient's perception of the oral anticoagulant use. To evaluate adherence to therapy, we used the Morisky test[7], which is a validated instrument that is applicable to different types of medication therapy. This test consists of four objective questions, used as a standardized evaluation, to assess the behavioral pattern of the patient regarding daily use of the prescribed medication. The questions address intake timing, missing doses, symptoms and side effects. The questionnaire rates the patient's adherence according to the number of correct answers. We took into account INR within the therapeutic range and INR outside the therapeutic range, with an average of five INR measurements for each patient. To analyze the patient's knowledge about oral anticoagulant use, two questions were formulated about the objective of the therapy and its main adverse effect. The ability to correctly answer both questions was considered an adequate knowledge. To identify the patients' perception of oral anticoagulant use, six questions were graduated in a score ranging from 1 to 100 points, and an ordinal number was assigned to each answer, beginning from the number 1, which corresponds to the worst perception of the therapy.

To study the difficulties with adherence to therapy, we took into account the patients' oral report and the examiner's perception. We evaluated socio-economic aspects, such as age, schooling, transportation expenses and medication used; physiological aspects, such as drug interactions, multiple medication use, diet restrictions, associated diseases and physical handicaps; and emotional aspects, such as denial of the disease, history of depression, personal problems; and cognition level, taking into account the patients' ability to understand, apply, analyze and sum up their personal health status[10].

This project was submitted to and approved by the Research Ethics Committee of the institution, and all patients signed an informed consent document. Categorical variables were described through absolute and relative frequencies, and continuous variables were described as mean and standard deviation or median and interquartile interval (25^{th} and 75^{th} percentile), depending on whether or not they followed a normal distribution. To compare the categorical variables, we used Pearson's chi-square test, with continuity correction when necessary. To compare the means between the groups, we used Student's t-test, depending on whether or not the parametric assumptions were followed. We used a significance level of $\alpha = 0.05$.

Results

Clinical and demographic characteristics

140 patients (mean age 60±11.5) using oral anticoagulants were included in the study. The main indication for the use of this medication therapy was atrial fibrilation (61.4%), followed by a prosthetic heart valve (55%). The anticoagulants used in this population were phenprocoumon (58%) and warfarin (42%), with a duration of use ranging from 24 to 72 months. The most prevalent associated comorbities were elevated high blood pressure (69.3%) and diabetes mellitus (26.4%). These results are shown in table 1.

Questions about perception of the therapy

To identify the patient's perception of oral anticoagulant use, six questions were graduated in a score ranging from 0 to 100

Table 1 – Characteristics of the population followed in the oral anticoagulation outpatient clinic (n= 140)

Characteristics	n (%)
Age*	60 ± 11.55
Female	71 (50.7)
Caucasian	129 (92.1)
Schooling	
Elementary school	117 (83.6)
Middle school	15 (10.7)
Earnings in minimum salaries*	1.31 ± 0.71
Oral anticoagulant	
Phenprocoumon	81 (58.0)
Warfarin	59 (42.0)
Duration of oral anticoagulation†	48 (24-72)
Main indications	
Atrial fibrilation	86 (61.4)
Prosthetic heart valve	76 (55.0)
Acute myocardial Infarction	32 (22.9)
Heart failure	10 (7.1)
Lung thromboembolism	9 (6.4)
Comorbities	
High blood pressure	96 (69.3)
Diabetes mellitus	37 (26.4)
Ischemic cardiopathy	33 (23.6)
Smoking habit	16 (12.1)
Stroke	13 (9.3)

** Continuous variables expressed as mean ± standard deviation or †median and 25th and 75th percentiles. Categorical variables expressed as n (%). OAC: oral anticoagulant.*

points. Our results showed that the mean score was 67.8±12.8. We observed that 95% of the patients mentioned concern about daily use of the medication, while 68% expressed insecurity regarding the possibility of bleeding. Our findings showed that bleeding occurred in 32.8% of the patients, and there were no thrombotic events. The questions showed that the patients considered the need of periodic blood tests (21.4%) and the strict intake of oral anticoagulants (12.8%) as limiting factors. These results are shown in table 2.

INR within and outside the therapeutical range

A comparison between patients with an INR within the therapeutical range and patients with an INR outside the therapeutical range showed that the knowledge about the therapy and the adherence to oral anticoagulation therapy were almost the same in both groups. There was a slight prevalence of proper knowledge among patients with an INR outside the therapeutical range (64%) and of adherence among patients with an INR within the therapeutical range (54%), but with no statistically significant difference between these results.

As to the main indications for the use of anticoagulants, there was a prevalence of patients with atrial fibrilation and an INR within the therapeutical range, as well as patients with a prosthetic heart valve and an INR outside the therapeutical range. We observed that there were more patients within the therapeutical range using phenprocoumon (62%), in comparison to those using warfarin (38%). The cognition level (38.5%), in the group within the therapeutical range, and the emotional and psychological aspects (69.2%), in the group outside the therapeutical range, were the factors that had greater impact on non-adherence. These data are shown in table 3.

Discussion

In the last few years, the use of oral anticoagulation therapy in clinical cardiology had more indications and was validated by several clinical studies[11,12]. Although oral anticoagulants are clinically indicated to prevent thromboembolic events, inappropriate and subtherapeutic dosages to maintain the INR may result in serious thromboembolic complications. Patients using this therapy have specific needs and require special attention, and consequently need strict clinical and laboratory follow-up by health care teams.

This study demonstrated, in the population followed in the oral anticoagulation outpatient clinic, an adequate knowledge about the therapy in 64% (INR outside the therapeutical range) and 54% (INR within the therapeutical range) of the patients. Similar findings were described in a study that evaluated the impact of adherence to the treatment, knowledge about the therapy and quality of life on the control of oral anticoagulation therapy. The results indicated that the knowledge about the therapy was not associated with an adequate control of oral anticoagulant levels[6], although the opposite was expected. However, our study confirmed those findings. A recent

Table 2 – - Perception of chronic oral anticoagulation therapy (n= 140)

Questions	n (%)
Concern about possibility of bleeding	96 (68.6)
Daily limitations caused by the use of OAC	18 (12.8)
Bleeding	46 (32.8)
Need of transfusion	4 (2.9)
Periodic blood tests	30 (21.4)
Concern about daily use of medication	133 (95)
Percentage score*	67.8 ± 12.8

** Continuous variables expressed as mean ± standard deviation, categorical variables expressed as n (%).*

Table 3 – INR within and outside the therapeutical range according to clinical characteristics (n=139)

Associated Factors	*International Normalized Ratio (INR)*		
	Within therapeutical range N = 50	Outside therapeutical range N = 89	P
Gender			
Female	27 (54.0)	43 (48.3)	NS
Schooling			
Elementary School	43 (86.0)	73 (62.9)	NS
Earnings in minimum salaries*	1.30 ± 0.67	1.3 ± 0.73	NS
Duration of oral anticoagulation	48 (27-75)	39 (24-78)	NS
Adequate knowledge about the therapy	31 (62.0)	57 (64.0)	NS
Adherence to oral anticoagulation therapy			
Adherent	27 (54.0)	43 (48.3)	NS
Oral anticoagulant used:			
Phenprocoumon	30 (62.0)	50 (56.2)	NS
Warfarin	20 (38.0)	39 (43.8)	
Main indication:			
Atrial fibrilation	41 (80.0)	45 (50.6)	0.001
Prosthetic heart valve	22 (44.0)	54 (60.7)	NS
Acute myocardial Infarction	8 (16.0)	24 (27.0)	NS
Adherence difficulties:			
Socio-economic aspects	11 (37.9)	18 (62.1)	NS
Cognition level	10 (38.5)	16 (61.5)	NS
Emotional aspects	8 (30.8)	18 (69.2)	NS
Physiological aspects	6 (35.3)	11 (64.7)	NS

*Categorical variables expressed as n (%) *Continuous variables expressed as mean ± standard deviation.*

prospective cohort study performed at 3 specialized clinics in Pennsylvania, to determine the effect of adherence on anticoagulation control, demonstrated that poor adherence is potentially a major source of poor anticoagulation control. The authors stressed that although patients received education about the importance of adherence to therapy, they still had difficulties maintaining adequate anticoagulation control[13].

Another retrospective study carried out by Nakkar et al[14], evaluated the management of oral anticoagulants in 82 patients, indicating that the mean duration of anticoagulation was 17 years, and 19.5% of the patients had treatment-related complications, and 73% had an INR outside therapeutic range, stressing the importance of educational programs for this population of patients, as well as the need for care guidelines to standardize this therapy among health care professionals. Long-term maintenance of this therapy is hard work, both for health care professionals and the patient. Failures tend to increase morbity and mortality, increasing the seriousness of the apprehension about therapy management, which raises costs for the public health care system[14,15].

The most used anticoagulant was phenprocoumon, with the mean duration of anticoagulation ranging from 2 to 6 years, and its main indication was atrial fibrilation. No significative thromboembolic or bleeding event occurred.

In regard to patients' perception of the therapy, the mean score was 67.8±12.8. We observed that the main concerns considered as limiting factors were prolonged daily use of the medication, adverse effects of the medication and the need of periodic blood tests, factors which may contribute to abandonment of therapy. Similar data in the literature indicate that once-a-day dosing helps improve medication adherence rates[16].

A study performed by Grinberg[17], to investigate strategies for oral anticoagulant adherence, reported that poor knowledge about the treatment is the main source of poor control of chronic diseases and adverse effects, as well as socio-economic aspects, such as earnings, schooling, transportation expenses, and the use of medication that requires continuous therapy.

Aiming at evaluating the context in which most problems occur, we divided adherence difficulties into four categories: socio-economic aspects, cognition level, emotional aspects, and physiological aspects. Our findings demonstrated that adherence difficulties were related to cognition level in 38.6% of the patients within the therapeutic range, and to emotional and psychological aspects, in 69.2% of patients outside the therapeutic range. These results suggest that there is a gap between the information provided to the patients and their understanding of the information conveyed.

It's worth remembering that there are several methods for evaluating adherence to medication treatment, all with advantages and disadvantages, and none of them is considered a golden standard. Among the most used methods, those classified by some authors[17] as direct and indirect stand out. Direct methods are based on analytical techniques that investigate if the medication was administered in the required dosage and frequency, using chemical markers which are not rapidly cleared from the body, and the measurement of the serum levels of the drug, which is more accurate but, not only highly expensive, but also an invasive method. Electronic monitoring of medication case opening is effective, but also very expensive. Indirect methods include structured interviews and tablet counting, frequently used in clinical assays in which patients are provided with medication, but they can be easily altered, and therefore are not very reliable.

Several studies the world over have demonstrated the importance of research on adherence to medication and the change in lifestyle required of patients using oral anticoagulants. The authors stressed that therapeutic quality control to maintain optimal levels of INR and therapy adherence were poor, due to a lack of and/or failure in current guidelines and the absence of health care teams who are specialized in educational programs[18,19]. The knowledge about decisive factors in therapy, such as the proper way to take the medication, the prevention and identification of main adverse effects, and drug and diet interactions, determine the success of the treatment and make adherence to therapy and the maintenance of optimal levels of anticoagulation possible, consequently reducing the morbity and mortality of long-term therapy patients[3,20].

The prognosis of patients using oral anticoagulants depends not only on the pharmacological therapy, but also on some non-pharmacological elements that are vital for the treatment. They need constant follow-up and continuing education on self-care measures, potential thromboembolic events and adaptation to the therapy. Health education is one of the charges of those who work with this population of patients, and these professionals need to develop new strategies to improve adherence to therapy.

Conclusions

The results of this study did not demonstrate the existence of an association of the analyzed variables in the subgroup with an INR within the therapeutical range compared to the subgroup with an INR outside the therapeutical range. However, despite the prevalence of patients using oral anticoagulants with an INR within the prescribed values, there are still a large number of patients who do not comply with the treatment. Further research, such as randomized studies, with systematic strategies for patient education on non-pharmacological therapies, is vital for the search of more evidence about the identified problems and also for the development of care guidelines that may identify non-adherence, in order to drastically reduce complications and fill the gap on the issue of continuous use of oral anticoagulants.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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